How SIMILAR or DIFFERENT are we from each other?

A MOLECULAR GENETICS UNIT

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DISCLAIMER: These materials are still being piloted. Please check back for more fully developed materials or contact Joe Kracjik (krajcik@umich.edu).

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Table of Contents

How Similar or Different are We From Each Other?
Unit Map

Lesson	**1**			
Title	**How similar or different are we from each other?**			
Time	2 days			
Learning Goals	LG1 - Nature and function of proteins			
Object	Introduce driving question of the unit			
	Consider that differences in cells can contribute to differences in our selves (use skin color as example) and introduce idea that protein do this work.			
Section	**Activity**	**Pgs in teacher guide**	**Pgs in student reader**	**Assessment opportunity**
I	Using the student reader - Scientific Explanations	3	1, 3-4	
	Group activity - Explore similarities and differences (S/D) between humans	3	6-9	
	Generating discussion - Reflect on S/Ds on multiple levels	4-5		
	Using the reader - Making biological comparisons	5-7	10	
	Reviewing discussion - Similarities and differences observations	7-9		
	Reviewing discussion - Intro to the driving question	9-10		
II	Using the reader - How cells work in our bodies	11	11	
	Problem Solving Discussion - Focusing on cells	11-12		
	Using the reader - Components of the skin	12	12	
	Reviewing discussion - skin on the cellular level	12-15		
	Generate a prediction about skin color	15		
	Class activity - experiencing different skin color	16-17		
	Generating Discussion - Forming Scientific Explanations	17-18		
	Wrap-up	18	13-14	

How Similar or Different are We From Each Other?
Unit Map

Lesson	**2**			
Title	**Exploring proteins**			
Time	5-6 days			
Learning Goals	LG1 - Nature and function of proteins			
	LG2 - Biochemical basis for traits			
Object	Explore how proteins carry out the work of the cell and difference in cell function			
	Learn about protein structure and function: amino acids sequence determines protein shape and function.			
	Learn that protein function depends on protein shape			
Section	**Activity**	**Pgs in teacher guide**	**Pgs in student reader**	**Assessment opportunity**
I	Reviewing discussion - What makes melanin	21-22		
	Using the Reader - Tyrosinase - How does this protein affect skin color?	22-24	16-18	Q 2
	Using the Reader - Don't Pass the Milk, Please	24	19-22	Q 3
	Reviewing Discussion - Don't Pass the Milk, Please	25-28		checkpoint
	Group activity - How is lactose intolerance treated?	28-29	23-24	
	Thinking about ethical problems	29-30	25-28	
II	Using the Reader - Proteins	30	29-30	
	Class activity - Where are proteins in chickens?	31	31-32	
iii	Using the Reader - Proteins Shape is Dependent on Amino Acids	32	33-34	Q 3
	Reviewing Discussion - Proteins have a Specific Shape	32-35		
	Teacher explanation - What are Proteins Made of?	35-36		
	Using the Reader - Thinking about scale	36	35	whole activity
IV	Teacher explanation - Preparing to work with Toobers	36-38	36	
	Group activity - Modeling with Toobers	38-39	36-39	Q 7
	Summarizing discussion - What affects protein shape?			
	Reviewing Discussion - Proteins have a specific shape - 2	39-41		
V	Group activity - Building a model of a real protein	41-42		
	Reviewing Discussion - Proteins have a Specific Shape - 3	42-44		checkpoint
VI	Teacher explanation - Protein example	44-45	40-41	
	Group work - How do proteins do their work?	45-46	40-46	comic strips
	Circle chart	46	2	
	Wrap- up	46	46-49	Q 2, 3

How Similar or Different are We From Each Other?
Unit Map

Lesson	**3**
Title	**Exploring genes**
Time	4-5 days
Learning Goals	LG2 - Biochemical basis for traits
	LG3 - Nature and functionof DNA
	LG4 - Genes as information for building proteins
	LG5 - Molecular nature of genes and mutations
Object	Learn that genes are instructions for assembling proteins
	Learn that genes are found in DNA and the DNA is a long chain of repeating chemical units that make up the “language” of the genetic code.
	Learn how mutations in genes can effect proteins structure and function using the LDL Receptor as an example.

Section	**Activity**	**Pgs in teacher guide**	**Pgs in student reader**	**Assessment opportunity**
I	Using the Reader - Familial Hypercholesterolemia	50	51-53	
	Summarizing discussion - Familial hypercholesterolemia	51-53		
	Reviewing discussion - Genes are a a set of instructions	54-56		
	Using the Reader - Genes and Gregor Mendel		54	
II	Group Activity - Building DNA model	56-57	55	
	Teacher Explanation - What is DNA? Where is DNA?	57-59		
	Using the Reader - Optional readings about DNA		56-60	pg 60
Iii	Teacher Explanation - How to Decode DNA	59-62	61-62	
	Group Actiivity - Making a model of transcription and translation	62-64	64	checkpoint
IV	Using the Reader - Mutations	64	65-67	
	Group Activity - Determing the effect of mutations	65-66	68-71	Q 2
	Reviewing Discussion - How do mutations affect proteins?	66-67		
VI	Video - From Cells to DNA	68		

How Similar or Different are We From Each Other?
Unit Map

Lesson	**4**			
Title	**Are genes always working?**			
Time	3-4 days			
Learning Goals	LG2 - Biochemical basis for traits			
	LG7 - Different cells use different genes			
	LG 8 - Environment and genes			
Object	Different cells are different because they use different genes.			
	Another level of similarities and differences is the presence or absence of specifc proteins.			
	Discussing the ethical aspects of altering whether or not genes or on or off.			
	Modeling skin color biology.			
Section	**Activity**	**Pgs in teacher guide**	**Pgs in student reader**	**Assessment opportunity**
I	Generating discussion - How are different cells different?	73-75		
	Using the Reader - Genes can be turned on and off	75	76	
II	Generating discussion - Why is Jason lactose intolerance	75		
	Using the Reader - A Closer Look into Gels	77	76-77	
	Reviewing discussion - Understanding gel electrophoresis	78-80		
	Group work - exploring about lactose intolerance	80-84	78-82	pg. 82
	Reviewing discussion - Drawing conclusions from the data	84-86		
III	Using the Reader - The Environment Can Turn Genes On and Off	87	83-85	
	Using the Reader - Adding to the Circle Chart	87	2	
	Reviewing Discussion - Genes and environment	87-89		
	Using the Reader - Erythropoietin	89	86	
	Ethical problem - Altering genes for athletic performance	89	86-88	pgs. 87-88
	Using the Reader - Wrap up		89-91	Q 3

How Similar or Different are We From Each Other?
Unit Map

Lesson	5
Title	Exploring Genomes
Time	2-3 days
Learning Goals	LG9 - Constituents of a genome
Object	Become familiar with what the human genome is – what does it include and how
	Explore how similar or different genomes are between different humans or humans and different animals.
	Realize the benefit of exploring the genome for identifying diseases easily and quickly.

Section	Activity	Pgs in teacher guide	Pgs in student reader	Assessment opportunity
I	Using the Reader - Priya Should Find Out if She Inherited a Fatal Disease (Or should she?)	93	93-94	
	Problem Solving Discussion - What is a Genome - Making a Map	93-97		
	Using the Reader - Human Genome	97	94-95	Q 1 & 2
	Teacher Explnanation - How much DNA is there in Every Cell?	97-99		
	Group Activity - Scavenger Hunt - Filling up the Map	99-100	96-97	Q 3
	Extra credit: Exploring the genomes of othe organisms.	100-101		
II	Review of Driving Question	101-102		
	Group activity- comparing humans and chimps	102-103	97-98	
	Reviewing Discussion - How much variation is there?	103-106		checkpoint
	Using the reader - Wrap up		99	

How Similar or Different are We From Each Other?
Unit Map

Lesson	**6**
Title	**Why do some people have diseases and others do not?**
Time	3-4 days
Learning Goals	LG2 - Biochemical basis for traits
	LG3 - Nature and functionof DNA
	LG4 - Genes as information for building proteins
	LG5 - Molecular nature of genes and mutations
	LG6 - Heritable material
Object	Revisit idea of genes coding proteins- this time in the context of sickle cell anemia
	Revisit idea of mutations and model affect of a gene mutation on the hemoglobin protein.
	Learn how not all mutations are necessarily bad by exploring case of malaria resistance and the sickle cell mutation.
	Learn that DNA is the heritable material and can pass on gene mutations.
	Student discuss ethical aspects of genetic testing

Section	Activity	Pgs in teacher guide	Pgs in student reader	Assessment opportunity
I	Using the Reader - One-Eyed Cat No Hoax	110	101-102	Q 2
	Class activity - Blood cells under the microscope	110	103	
	Generating discussion - Sickle cell disease	110-112		
	Using the Reader - Sickle Cell	112-113	104-105	
	Video - Sickle cell disease	113		
	Introducing New Information - Hemoglobin iand its Role in sickle cell disease?	113	115	
	Group work - analyzing hemoglobin	115-116	105	pg. 105
	Reviewing discussion - How does the mutation in the hemoglobin gene affect red blood cells?	116-119		
II	Problem Solving Discussion - What is a genetic disease?	119-120		
	Using the Reader - How can sickle cell disease be passed to me? And How Do Children Receive Their Parents' Genes?	121	107-109	Q 3 & 4
III	Ethical Problem - Determined by community input	separate	separate	
	Using the Reader - Are all Mutations Bad?		110-111	Q 2
	Generating discussion - Are all mutations bad?	121-123		
IV	Teacher Explanation - Instructions for Sharing Work	123		
	Class actvitiy - Sharing Research Projects	123		
V	Using the Reader - Circle Chart	124	2	whole chart

Materials List

1 Set teacher materials per teacher (Teacher guide, Teacher Version of Student Reader, Slides)

1 Student reader per student

copies of chromosomes, and human and chimp DNA comparisons

microscopes (~4 per teacher)

From 3D Molecular Designs (http://www.3dmoleculardesigns.com/news2.php#toobers)

- Toobers for modeling (~8 per teacher)

From Flinn

- Flinn DNA Molecular Model Set, 11-tier (AP6317) (~8 per teacher)
- Pipet, Beral type graduated (AP1516) (~1 per teacher)
- Biuret Test Solution (B0051) (~1 per teacher)
- Polypropylene cups (AP5442) (~1 per teacher)
- Glucose test strips (T0004) (~1 per teacher)

From Carolina Biologicals

- Human Sickle Cell Anemia, smear (ER-31-7374) (~2 per teacher)
- Human Blood Film, smear (ER-31-3158) (~2 per teacher)

Available locally

- Assorted color pushpins, 100 ct (~3 per teacher)
- lactase pills (~1 box per teacher) - Note: generic pills often have sugars in them which will affect the results, check ingredients or buy name brand.
- milk
- chicken (white, dark, skin, liver)
- plastic bags for holding chicken
- hand sanitizer or gloves
- materials for making comic strips, posters, brochures

Introduction

Overview of Unit

Targeted audience, content and sequencing

This unit is intended for an introductory high school biology course for 9th-10th grade students and covers molecular genetics and genomics. The unit is expected to take 4-5 weeks.

Molecular genetics is key to all modern understandings of biology. In contrast to classical genetics (which focuses on abstract concepts like dominant and recessive alleles and Punnett squares to explain the appearance of physical features and disease), molecular genetics focuses on the molecular nature of genes and how they influence cells and whole organisms. Thus, the ideas that genes found in DNA and are instructions for building proteins are central to understanding molecular genetics. For the last three decades researchers have actively engaged in understanding questions in molecular genetics and have actively used techniques to manipulate genes and proteins to understand the biology of organisms better. This insight has had major influences on medicine and society. For example, it is very common in the news to hear about a newly discovered gene linked to a specific disease or behavior, and it is more common now for doctors to use techniques based on gene sequences to make prognoses.

Genomics is the newest frontier in biology. Genomics is the study of the entire genetic makeup of an organism (i.e. a genome). In contrast to traditional ways of talking about genetics, which typically involve one or a few genes, genomics considers the entire genome or large portions of a genome, and therefore focuses on many genes or DNA sequences. Advances in genomics will change (and has already changed), the way both biological research and human medicine are conducted. Thus, genomics fundamentally is large-scale molecular genetics. An influx of data has and will result from genomics research and it will exponentially increase the number of genes linked to disease and that are screened in doctor's offices. Not too far off in the future, individuals will be able to obtain the entire DNA sequence of their own genome, which will have tremendous medical and social implications. Thus, it is absolutely essential for the next generation of adults to develop deeper understandings about molecular genetics and genomics if they are to understand advances in biology and medicine.

The main objective of this unit is to connect molecular mechanisms to cellular function and appearance so that students will develop a better understanding of how genes can influence our physical features and health. Given this objective, the overall learning objective is for students to understand that genes are instructions for encoding proteins, and that these proteins carry out functions in cells which directly determine structure and function of cells, tissues, organs, and consequently whole organisms. Often the teaching of genetics leaves out this essential connection between genes and proteins; as a result a "black box" between gene and phenotype (the physical manifestation of a gene or genes, such as eye color, height or skin color) is left for many students.

The bridge that connects genes to phenotype is proteins, since this is what a gene encodes and this is what does the work of the cell. Hence, a fair amount of attention is devoted to proteins in this unit. In fact the unit begins with content on proteins before going onto content about DNA in order to emphasize the centrality of proteins to cell function and organism appearance and physiology.

The unit is divided into 6 lessons:

1. Similarities and differences – The students begin to explore the driving question of the unit: How similar or different are we? Students experience skin color difference at a cellular level.
2. Understanding proteins – After examining the cellular differences in the first lesson, students in Lesson 2 begin to explore proteins as the workers in cells and begin to understand the molecular differences between different proteins using flexible protein models.
3. Genes and their relation to proteins – Armed with an understanding of proteins from the second lesson, students learn what genes are and how cells "decode" them to generate proteins.
4. The molecular basis of genetic diseases – The lesson reinforces the idea that how genes are the directions for making proteins and extends students' understanding of how different forms of protein can lead to disease by exploring the molecular basis of sickle cell disease. Additionally, students focus on explore ethical issues relating to direct to market genetic testing.
5. Cells use specific genes at specific times and places – Students connect ideas and phenomena they encountered in the first 4 lessons with the concept that specific genes are being used at specific times and places. Lesson 5 also explores an ethical issue: altering gene transcription to improve athletic performance.
6. Genomes – After learning some specifics about genes in previous lessons students explore how genes are related to chromosomes and genomes.

Topics not covered in this unit include meiosis, mitosis and classical genetics (i.e. content such as alleles and Punnett squares). Cells must be covered before this unit and it is suggested that meiosis and mitosis be covered before this lesson. Classical genetics - while typically covered before molecular genetics - might actually make more sense after this unit so we suggest covering classical genetics after this unit.

DESIGN OF THE UNIT

Standards-based

In developing this unit, first science benchmarks and standards from the Benchmarks for Science Literacy (1993) and the National Science Education Standards (1996) documents were identified that concern molecular genetics and scientific inquiry practices. We refer to these as benchmarks and standards as learning goals. Having identified learning goals, we combine content standards with inquiry standards to develop what we refer to as "learning performances", because others in science education, such as National Research Council, stress the importance of learning science content in the context of scientific inquiry. The learning performances are the means by which students will show their understanding of the standards (learning goals). As an example, take the inquiry standard

from the NRC that states students will "...analyze and interpret data..." and the standard from NRC that "genes are segments of DNA molecules.." to come up with the learning performance that "students will analyze a pool of DNA sequences and make conclusions about the degree of similarity or difference in the sequences." The rest of the unit, including context, activities and assessments are designed around these learning goals and learning performances.

1. **Nature and function of proteins**: The work of the cell is carried out by the many different proteins. Proteins molecules are long, usually folded chains made from 20 different kinds of amino-acid molecules. The function of each protein molecules depends on the specific sequence of amino acids and the shape the chain takes is a consequence of attractions between the chain's parts. (AAAS, pg. 114, 5C:9-12#3)

2. **Biochemical basis for trait:**. An organism's traits reflect the actions (and inactions) of its proteins. AAAS considering this but not published yet)

3. **Nature and function of DNA**: In all organisms, the instructions for specifying the characteristics of the organism are carried in DNA, a large polymer formed from subunits of four kinds (A, G, C, and T). The chemical and structural properties of DNA explain how the genetic information that underlies heredity is both encoded in genes (as a string of molecular "letters) and replicated (by a templating mechanism). Each DNA molecule in a cell forms a single chromosome. (NRC, pg. 185, 9-12:C2#1)

4. **Genes as information for building proteins**: The genetic information in DNA molecules provide the instructions on assembling protein molecules. The code is virtually the same for all life forms. (AAAS, pg. 114, 5C:9-12#4)

5. **Molecular nature of genes and mutations**: Genes are segments of DNA molecules. Inserting, deleting, or substituting DNA segments can alter genes. An altered gene may be passed on to every cell that develops from it. The resulting features my help, harm, or have little or no effect on the offspring's success in its environment. (AAAS, pg. 109, 5B:9-12#4)
6. **Heritable material:** The information passed from parents to offspring is coded in DNA molecules (AAAS, pg 108, 5B:9-12#3)

7. **Different cells use different genes**: The many body cells in an individual can be very different from one another even though they are all descended from a single cell and thus have essentially identical genetic instructions. Different parts of the instructions are used in different types of cells, influenced by the cell's environment and past history (AAAS, pg. 109, 5B:9-12#6).

8. **Environment and genes**: Most physical and behavioral characteristics that an individual possess are the combination of both genes and environment. (AAAS considering this but not published yet).

9. **Constituents of a genome**: A genome consists of all of the DNA found inside a single cell or virus. The genome contains all the genes required to build, maintain and propagate the cell,

or a multicellular organism. For humans the genome includes all the DNA within both 23 pairs of chromosomes within the nucleus and the DNA in the mitochondria. The human genome consists of about 3 billion base pairs and is estimated to have 25,000 genes. The smallest free living organism, a bacteria has about 500,000 base pairs and 5,000 genes. Most of the human genome is noncoding DNA, while only a small fraction is protein coding. The non-coding DNA includes some small parts that are highly variable DNA, which can be used to identify people. The genomes of any two humans are highly similar (99.9% identical to be exact). (Written by Aaron Rogat with the input of genomic experts).

Inquiry-based

This unit will be hands-on and inquiry-based so that students must actively engage with the content in order to make sense of it, and hopefully develop a deeper understanding of molecular biology and modern genetics. “Inquiry” in our unit means that students will be asked to engage in scientific practices such as asking questions, making predictions, analyzing data, developing conclusions, providing explanations and critiquing other people’s conclusions.

Multiple representation and phenomena

Students will be exposed to multiple representations and phenomena through out the unit such pictures and videos of cells, proteins and organisms, and 3-D physical models of molecules. In addition, where possible, real-life organisms or cells will be provided for students to explore and observe. These representations and phenomena serve as additional ways to explore and engage in the content. We will also make an effort to talk about real examples that illustrate the content objectives such as the LDL protein and its role in familiar hypercholesterolemia. These phenomena and real life examples are also intended to capture the interest of the students.

Ethical and Societal issues

The unit will also incorporate social, and ethical issues with which to frame the learning of the science content. These issues are meant to also engage the students in the science content by adding relevance and interest to the content. In addition, it is clear that advances in molecular genetics and genomics will influence many social and ethical issues; therefore, it is critical that students also begin to think about how the science will impact their own lives. Students will learn about how advances in genetics can shed light on important social issues like race and health and help to shape our notions and views of others and ourselves. Thus, in this unit students will learn both science content and how science can influence society.

For more information about including ethical dilemma activities in the classroom:

http://www.nwabr.org/education/index.html

Classroom Discourse

Adapted from IQWST Front Matter

Traditional "Discussion"

A traditional view of teaching and learning is that teachers "deliver" instruction, and students learn by watching and listening. In that model, classroom discourse typically involves a teacher posing questions, one or more students responding, the teacher evaluating responses as right or wrong, and the teacher moving on to the next question or task when he or she is ready to do so.

This type of sequence may involve questions such as:

- What did we learn from this activity?
- What are the 4 things we've decided are important . . . ?
- What are the behaviors of X that we have talked about so far?
- What did we observe/see/learn/do …?

These types of questions are useful. For example, they provide a quick, whole-class recap of learning before moving on to new ideas. But, too often this type of question-and-answer activity is the primary form of classroom discourse. It puts the teacher at center stage, and students' questions and their learning in the background. This kind of teacher-led initiation-response-evaluation (I-R-E) sequence is what often passes as "discussion" in a classroom, disguising the fact that real discussion is a give-and-take of ideas.

Classroom discourse—including discussion

A give-and-take of ideas is the preferred form of classroom discourse. IRE should be used sparingly. Instead, classroom talk should center on engagement and thoughtfulness. Teachers pose questions that push students' to think more deeply about what they have observed, experienced, or read. Students ask questions that arise out of their own interests or confusion—and they ask questions of each other as well as of the teacher. Thoughtful dialogue is critically important if students are to make sense of activities and concepts. Discussions provide them with opportunities to express their understanding and to learn from each other. Discussions also provide the teacher with information about the sense students are making—what they are "getting" as well as "not getting." But, discussions and Q&A are not the same kind of activity. Aim to help students develop skills as thinkers and problem solvers, in part, through participating in thoughtful discussions.

Developing a discourse-centered classroom culture

To develop good discussion skills, students must learn what it means to participate actively in science class. Often, this means new ways of interacting. How do teachers encourage students to question one another, the teacher, and themselves—in productive ways? How do teachers establish a

classroom culture in which discussion occurs among students rather than between the teacher and those students who raise their hands?

First, teachers may need to think about classroom discourse in new ways:

- All students need opportunities to participate and encouragement to participate.
- A primary goal is to get students to listen to and respond to each other.
- Discussion is about thinking together, not about generating right answers. Even wrong answers provide opportunities to learn if the culture of the classroom is such that "figuring things out" is of primary importance.
- Writing ideas before discussing them is a good way for students to think before they are asked to share ideas aloud.
- Readings and other homework are intended to be followed-up with in-class discussion, thus the materials provide follow-up suggestions and alternatives.

Second, students need to learn their role in discussion:

- Students need to listen to one another. To develop a culture in which listening is important, ask questions like:
- How does your idea, Anna, compare with Will's idea [the previous speaker]?
- What can you add to what Will just said?
- How could you say [group A's] conclusion so that your younger sister could understand it?
- What could you add to make [the previous speaker's] idea clearer?

Third, after sufficient practice and a clear message that this is really what is expected of them, students begin to respond to one another without the teacher prompting them to do so. How long before that will happen? That depends, in part, on how often students have opportunities to practice and become comfortable with this way of communicating.

Three Types of Discussion

Identified below are three primary types of discussion that could be employed in a science classroom. Each type requires some time—time invested in students' sense-making and deep learning. Although a discussion is likely to be composed of more than one of these types, teachers may be better able to support student learning by recognizing the structure of each type of conversation. Part of the job of facilitating discussion is to be aware of what type of discourse is "in play," and being aware of the "rules" for each.

Generating

- Involves sharing ideas without evaluating their validity.
- Ideas are written on the board or overhead as they are generated.
- Includes prompts such as:
    - What have you observed or experienced?

- What else is on your group's list?
- What do you/other people think about when they hear the word ___?
- Who has a different idea/response/way of thinking about this?
- What do you know about [topic X]?

Reviewing

- Involves putting ideas together, or assembling multiple activities into a coherent whole. May also include generalizing from specific activities to a more general conclusion.
- Reviewing discussions may include making connections to personal experiences; to the driving question; to the previous or the following lesson; or to knowledge gained in other units, lessons, or subject areas.
- Includes prompts such as:
    - How does _____ help us think about other times when _____?
    - How can we put these 4 ideas together into one process that we might call "the water cycle"? What happens 1st, 2nd . . . ?
    - What do we know about _____ so far?
    - How does this help us think about the driving question?
    - Yesterday we talked about ___; how does today's activity help us think about ___?
    - How does this connect to ____?

Problem Solving

- Involves figuring things out or making sense of readings or activities.
- Pressing for understanding means going deeper, beyond the surface answers.
- May involve challenge, debate, or argument in which Ss justify their ideas.
- May involve revision of previous ideas as students learn new information that calls into question the limitations of what they "knew" previously.
- Includes prompts such as:
    - How does X compare with Y?
    - How can . . .? How might . . . ?
    - How do you know? What evidence supports that idea?
    - What does it mean to say …?
    - Why doesn't our old model work to explain this new phenomenon?
    - Why can't …?
    - How could we figure this out?
    - What new questions do you have?

Additional Strategies

- Reflective toss: Throw back the students response/question to the students, rather than evaluating.
- Student roles: to encourage cognitive and physical engagement.

A final thought about Discourse:

It's hard work to facilitate a good discussion! In reality, one problem for teachers is they may not

have seen good models of this in their own experience as students. Teachers should make it a goal to begin to establish discourse norms on the first day of class, and should give themselves and their students time to get used to a give-and-take culture of sharing, listening, and learning together.

Context (a driving question):

This unit is framed by what we refer to as the Driving Question. The Driving Question is an open-ended question that the students may not be able to answer at the beginning but by the end of the unit should be able to answer more completely. It should relate to their own lives and also serve as another means to put the content of the unit (the standards) into context in order to make sense of it all—many in science education feel that science taught as disconnected fact is not effective instruction. The Driving Question is meant to be revisited throughout the unit so that students are challenged to make sense of what they are learning currently in the unit with what they have previously learned in the unit.

Addressing students prior knowledge:

Students often approach new content with prior ideas including misconceptions. These misconceptions can impede the learning of new content. Therefore, we try to identify potential misconceptions and address these misconceptions directly or through teacher guidance. The units therefore identify student misconceptions were possible; we structure activities around these ideas or encourages teachers to address these misconceptions directly during the lesson.

Educative curriculum:

The teacher guide, includes overviews and outlines of the day-to-day lessons. In each lesson efforts are made to include instructional suggestions and tips, appropriate student answers, and potential pitfalls and conceptual challenges for students. These features are called “educative” and serve to inform the teacher so that they can better enact the material.

Grey boxes like the one below serve a few different purposes. In the case below, the box serves to explain the purpose and the objective of the preceding discussion. In other cases, the boxes help to define a term that might have an ambiguous or unclear meaning in these materials, indicate where background information about a specific topics can be found, point out when we have been intentful about language use, or to indicate places where students previous conceptions might give them difficulties.

Discussion objective: Students should not be expected to have the right answer at this point. The objective is to consider reasonable explanations for different skin colors.

Checkpoint boxes serve as formative assessments throughout the unit. Although it might not be necessary to ask your students the question explicitly, you should feel comfortable that most of your students would respond correctly. If you do not feel that your students have learned the material adequately, further discussion and review of the material will be necessary.

Checkpoint:

Can your students answer the following questions:

1) What carries out most of the work of cells?

Answer: proteins

2) What is one way that two people can differ biologically:

Answer: they can have proteins that function differently

The Driving Question for the unit

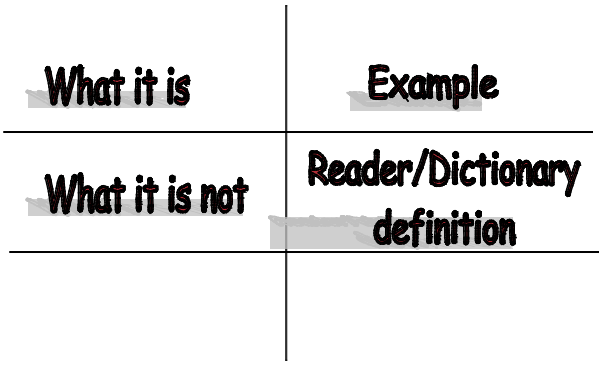
This unit is framed around one question: “How similar or different are we from each other?” By the end of the unit, students will learn how genetically similar humans are to other humans . Students will also understand what determines and influences similarities and difference between and within species (i.e. how differences in genes can influence phenotypes). It is the intent of the unit to highlight how recent findings from genomics research demonstrates how people from different races and ethnicities are actually very similar at the genetic level and that this can have a positive affect on social constructs like race. The unit will also attempt to demystify what it means to have a “gene” for a particular disease and to have a “mutant” gene” by talking about mutation as simple “variations” in genes.

Reading Strategies

Learning from text in science is often a difficult task for students. Science text is often bombarded with organization that is devastating for students who are unaware of text structure or are lacking specific domain knowledge in science. Using reading materials in science classrooms is the most prominent method of learning in science, and although they are meant to the be the primary source of learning and have an impact on student learning, reading materials in science are often hard for students to grasp. These materials have provided some strategies that may be helpful for students when reading the texts in their readers. Each reading has suggested reading strategies. The strategies are NOT meant to be used as individual activities. The TEXT that the student is reading is the activity, and the reading strategies are to support the students reading comprehension. Below are a description of them (Additionally, there are blank templates in the Appendix):

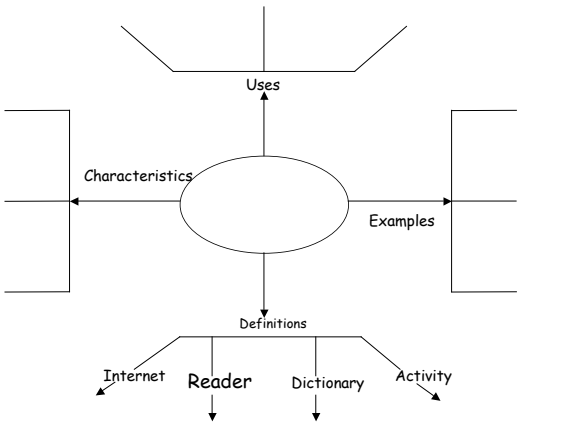
Vocabulary Concept Cards: Students use these cards to help them become acquainted with science vocabulary and concepts. In the “What it is” quadrant, students write what the word IS or means. In the “Example” quadrant, students write an example of the word or concept. In the “What it is not” quadrant, students write what the concept or word is not. This helps them differentiate the word/concept with other words/concepts. In the “Reader/Dictionary definition” quadrant, the students research the definition of the word/concept and write it there.

Vocabulary concept cards



Concept Definition Maps: This strategy helps students think about different aspects of a concept they are learning, like “Gene”. In the center circle, students write the concept. In the “Uses” areas, students write what the concept is used for. For example, one use for of Gene is Instructions for proteins. In the “Example” area, students write an example of the concept. In the “Characteristics” area, students write attributes of the concept. For example, one characteristic of Gene is that it is made up of DNA. Finally, in the “Definitions” area, students research the word in the specified resources and write the definitions.

Concept of Definition Map (Schwartz, 1988)



Semantic Features Chart: In this strategy, students explore the features of different concepts and words. On the horizontal axis, the teacher or students decide on concepts to explore. On the vertical axis, the teacher or students decide on features to explore about each concept. In the cells of the chart, the students write YES or NO depending on whether the concept has a particular feature. For example, in the first column, the feature would be “Hold all DNA in organism”. For Chromosome, students would write YES, for DNA molecule, students would write NO and for Gene, students would write NO.

Semantic Feature Analysis

FEATURES OF THE OBJECT/PHENOMENON

TARGET CONCEPTS	H... in organism					
Chromosome	Yes					
DNA molecule	No					
Gene	No					

-

Preview Guide: This strategy helps asses students’ prior knowledge, elicit and/or expand their prior knowledge, set a purpose for reading, and help organize the text. Provide questions about the text in the left column for the students to answer. Then, students answer the questions before they read the text, then after they read the text.

Preview Guides

Question	Before Rdg	After Rdg
1. Why would doctors need to know about chromosomes, genes, and DNA?		
2. How are chromosomes related to genes?		
3. How are genes related to DNA?		
4. What do proteins do for the body?		
5. How are proteins related to disease?		
6. What do you think the disease “familial hypercholesterolemia ” is?		

Anticipation-Reaction Guides: This strategy can be used for the ethical dilemmas. This help the student think about what they think/know before they read the dilemma and afterwards.

Anticipation-Reaction Guides

	Before Reading	After Reading	
Ethical Dilemmas	What do you think?	What does the author think?	What do you think now?
Should genetic test kits be marketed to the public?			

Background Content

This section is intended to provide you with background information about several of the topics covered in this unit. Also included are web resources with even more information about these topics.

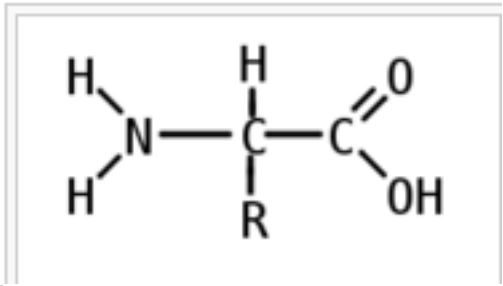
Proteins

While most people think of food when they hear the word protein, most molecular biologists think of the small structural and functional components that help make up the human body as well as all other living organisms. While both groups are right in how they think about protein, here we will think of proteins the way molecular biologists do.

To keep our bodies running every day, proteins perform a wide variety of functions. Acting as enzymes to speed up reactions, transporting substances throughout the body (as with hemoglobin which will be explained later), making our muscles move with proteins such as actin and myosin, giving structure to our cells so that they can grow and divide, and regulating tissues with proteins such as human growth hormone and insulin.

Proteins are made up of building blocks called amino acids, so named because they contain both an amine functional group and a carboxyl functional group (see picture below). Proteins are made up of 20 different types of amino acids, eight of which are considered “essential” because they can only be obtained through diet, and twelve of which are “non-essential” because they can be made by the

body from precursors that are already in the body. Similar to a string of beads, proteins are a string of amino acids joined by peptide bonds. These peptide bonds are formed when the hydroxyl group on the carboxyl (OH on the COOH group) and one hydrogen from the amine group (H from the NH2) are removed to form a water molecule. What results are two amino acids bonded together with a peptide bond.



The general structure of an amino acid. The amine group (NH2) is to the left and the carboxyl group (COOH) is to the right. The R group is a group that varies among amino acids. It is what makes each of the 20 different from one another.

Proteins can be all sizes. Some proteins can be as small as 12 amino acids long while others can be several thousand amino acids long.

The structures of proteins generally depend on the properties the amino acids of which they are made and the order of the amino acids in the chain. There are three broad classifications of amino acids: non-polar hydrophobic (water fearing), polar hydrophilic (water loving) and charged. How these different side groups of amino acids are ordered determines in part how they are presented in space. Hydrophobic amino acids like to avoid water and they generally fold so they are internal to the protein. Hydrophilic amino acids like to interact with water molecules so they tend to be external to the protein. The opposite is true if the protein is in a lipid environment like a cell membrane; proteins in cell membranes generally have hydrophobic amino acids on the external part of the protein. As one might expect, oppositely charged amino acids attract each other and play an important role in determining structure. Additionally, the charged amino acids also play a role in any enzymatic activity that the protein might carry out.

There are four general classifications of the structure of proteins. Primary (1°) structure refers to the sequence of amino acids in a chain. Secondary (2°) structure describes the degree of coiling or pleated sheet formation within the chain. Tertiary (3°) structure refers to the way the chain is

folded three dimensionally. Quaternary (4°) describes the interaction of two or more peptide chains. Hemoglobin (which will be discussed with sickle cell disease) is an example of a protein with quaternary structure.

To study particular proteins, scientists often use gel electrophoresis. For electrophoresing proteins a polymer called polyacrylamide, which has a consistency comparable to tough Jell-O, is used. The polymer (under magnification) looks like a thick mesh of fibers. A solution of many different proteins in a mild detergent is injected into the polymer.

The gel is connected to two electrodes, one end negative and one end positive. The detergent molecules surround each protein molecule and since the detergent molecules are negatively charged, the proteins surrounded by detergents are attracted toward the positive end. As the molecules move a separation takes place. Bigger molecules cannot move through the polymer as well and therefore do not travel as far. Smaller molecules move more easily through the polymer and make it closer to the positive electrode. Bigger proteins end up closer to the starting line and smaller proteins end up closer to the finish line. Scientist can then see the proteins by staining the gel with a dye that sticks to proteins and if they wish, harvest the proteins and study them individually.

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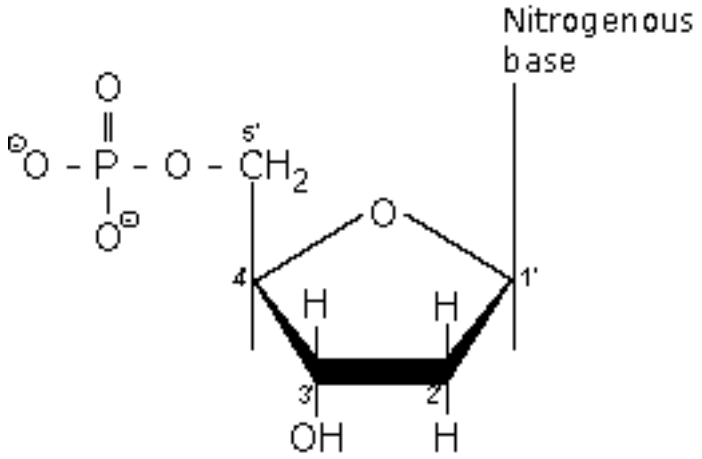
DNA and RNA

Nucleic acids are made of chains of units called nucleotides. Each nucleotide is made of three components: a 5-carbon sugar, (deoxyribose in DNA and ribose in RNA) a base and a phosphate group.



A DNA nucleotide.

What makes each nucleotide different is the base, which is attached to the 5-carbon sugar and the phosphate group. There are five types of bases, (four in DNA and four in RNA): A (adenine), G (guanine), C (cytosine), T (thymine) and U (uracil). A, C, and G are found in RNA and DNA; T is found in DNA and U is found in RNA. The bases are also classified as either purines (A and G) or pyrimidines. (C, U, and T). When any two nucleotide chains are bound together (DNA-DNA, DNA-RNA, RNA-RNA), a purine on one chain must bond with a pyrimidine on the corresponding chain. More specifically, A must bond to T or U and C must bond to G. C and G form three hydrogen bonds, while A and T or U form only 2 hydrogen bonds. (See picture below)

Each of our cells has a nearly uncountable number (about $3x10^9$) of these A-T and C-G bonds (called base pairs). All of that DNA is organized into chromosomes. Each chromosome is a single long piece of DNA. Some of the DNA on a chromosome contains instructions for making proteins , or genes, but about 98% of all DNA is something else. The “something else” includes genes that no longer work, viral DNA from viruses that infected our ancestors long ago, repeated sequences of the same DNA, and many more elements that seem to be important but scientists are still figuring out. Often, the extras DNA is referred to as “junk” DNA. This may be a misnomer, but until more research is done, we can not be sure.

No one knows yet exactly how many genes are in our DNA but current estimates are around 25,000. Each individual gene is made up of many sets of three bases called codons. The gene consists of the codons in between the start and stop codons. Since three nucleotides make up one codon and there are 4 possible bases then there are 64 possible codons (4x4x4). One codon is considered the “start codon” (AUG) since it begins the gene, several codons are called “stop codons” (UAG, UGA, and UAA) since they signal the end of a gene, and the others code for various amino acids.

Most human genes have breaks in their DNA sequence that are not part of the instructions for building proteins, although the entire sequence of the DNA is transcribed into mRNA. The breaks are called introns. After the gene is transcribed, special mechanisms in the cell “splice” or cut out the introns. The parts that are used are called exons. Some scientists believe that much of human complexity comes from using a single gene “spliced” in many different ways to create instructions for several proteins.

The chromosomes are not the only areas that keep DNA. Some genes (exactly 37 genes which code for 13 proteins) are found in mitochondrial DNA. This type of DNA is slightly different physically and probably evolved differently than chromosomal DNA. Physically, it is found in a double helix like chromosomal DNA, but instead of a linear string, it loops back on itself and forms a circle of DNA, not surprisingly called “circular DNA”.

From DNA to RNA to Proteins

If the information kept in DNA could not somehow be translated into something useful, then no life could take place. We have discussed proteins and DNA thus far. How these two are related is that DNA (more specifically the genes within the DNA) code for specific proteins. The processes that carry protein synthesis out are called transcription and translation, and another nucleic acid called RNA (ribonucleic acid) is the molecule that makes it possible.

Genes are a set of instructions for making proteins. The processes of creating a protein from genes are called transcription and translation. Since all DNA is contained in the nucleus and protein synthesis takes place in the cytoplasm of the cell, the information contained in the DNA must somehow be transported outside of the nucleus. This is the process of transcription.

The first step in transcription involves a protein called RNA polymerase (RNAP). RNAP binds to DNA and the DNA double helix begins to unwind. The RNAP moves along one side of the unwound DNA molecule (which can now be thought of as a template) and RNA nucleotides are added to it, forming a chain. When the RNAP hits a certain sequence of nucleotides on the DNA template called the termination sequence, the RNAP stops transcribing. The newly formed chain (now called mRNA) removes itself from the DNA template, and the DNA template rewinds itself.

Once the RNA is transcribed, the splicing process described above can take place.

Now that there is a working copy of the DNA in the form of RNA proteins can be formed. This occurs in a process called translation. This process takes place in the cytoplasm and requires four components: a ribosome, the mRNA strand, transfer RNAs (tRNA), and amino acids.

First, the mRNA travels out of the nucleus where it was made, and it encounters a ribosome in the cytoplasm. The ribosome binds the mRNA strand at the ribosome-binding site that contains an AUG codon (the “start” codon). When the AUG codon is in place in the ribosome, the rest of translation can begin.

This is where a different type of RNA called tRNA comes into play. Each tRNA molecule has a three-lettered code called the anti-codon on one end and a specific amino acid (based on the anti-codon) on the other. Remember that the mRNA is bound to a ribosome. Let’s imagine that the codon on the mRNA that is bound to the ribosome is AUG. A tRNA with the anti-codon UAC would bind to the AUG codon on the mRNA. The amino acid that corresponds to the anti-codon UAC is methionine. Therefore, a methionine comes off and will be the first amino acid in the newly forming polypeptide chain. All proteins start with a methionine since it is the start codon. However, many proteins are later processed and often the first several amino acids are cut off from the rest of the protein.

Now, the ribosome moves along the mRNA chain to the next three-lettered codon. Lets pretend that it is GUC. A tRNA molecule with the anti-codon CAG (with the amino acid valine attached) will bind to the GUC codon. The valine comes off after it forms a peptide bond between the carboxyl group of the tyrosine and its own amino group. Now there are two amino acids in the polypeptide chain. The ribosome continues to move along the mRNA, the tRNA molecules continue to bind and release their amino acids, and peptide bonds continue to form among new amino acids. This goes on until the ribosome binds a special codon (UAG, UGA, or UAA) called the stop codon. A release factor binds to the mRNA and the polypeptide chain breaks away.

The newly formed polypeptide chain takes on a characteristic structure determined by the sequence of the amino acids. A new protein molecule has just been formed.

Gene Expression

If every gene were being transcribed and translated into proteins in every cell our cells would be a mess. Genes need a way to be turned on and off based on where their cells are located in the body. Genes coding for instructions for a protein needed in muscles do not need to be expressed in the iris of the eye. Genes for generating eye color need to be expressed in the iris. The question is how does a cell turn a gene on and off? How does the cell know whether or not to transcribe a gene?

Part of this task is left up to a sequence in DNA known as the promoter. Promoters are generally found near the beginning of a gene, but not in the gene itself. Depending on what type of cell it is, several different types of proteins might bind the promoter of a single gene. RNA polymerase recognizes the promoter and the proteins bound to the DNA and knows that it needs to transcribe the nearby gene.

Some genes are physically turned “off” by the cell. A strategy for turning a gene off is known as DNA methylation. This process is defined as adding a methyl group (-CH3) to a cytosine (the other three base pairs do not accept a methyl group). Genes in which the cytosines are heavily methylated seem to not be transcribed.

Gene expression is important for several reasons:

Cell differentiation - When each zygote is still just a mass of cells, all of the cells are exactly the same. The process of cells acquiring a specific function is called cell differentiation. For instance, cells that are destined to be brain cells will begin to take on characteristics of a neuron. Certain genes important for neuron function will be turned on, while genes unrelated to neuron function will be turned off. Cells that have not been differentiated are known as stem cells in animals. Researchers are currently investigating how to take the undifferentiated stem cells and turn them into cells of their choice.

Environmental response - In order for our bodies to be able to adapt to our environment, they need to respond to our environment. One of the ways they do that is by changing what genes are on and off. Examples used in this unit include the tanning of skin and the amount of red blood cells in response to oxygen levels. Other examples include our body's response to long term stress, hormones, or diet.

Genomes

So far, we have used the word genome, and not defined it. But what is the genome really? The simplest definition for a genome is the sequence of all of the DNA in a cell. This includes not only all of the genes coded for in the DNA, but all the other parts. We have essentially the same genome in each of our many cells.

Humans have 3×10^9 (3 billion) base pairs in one set of chromosomes. Since humans have two sets of chromosomes, that comes to 6 billion base pairs in each of our cells. This fact begs a question. How similar is each person compared to every other person in the world? Humans are genetically 99.9% similar to each other. While at first glance this statistic makes it seem like we are almost identical to each other, but one has to remember the number of base pairs that we possess. Being 99.9% similar means that there is one difference in every one thousand base pairs. Since we have 6 billion base pairs in every cell, being 99.9% similar means having 6 million differences in base pairs.

Examples

There are many examples of how slight changes can affect phenotype in different people. The following highlight some of the biology of the four traits covered in this unit.

Skin color

A common and very visible example of how the .01% difference in genome can be seen in skin color. Melanin, which is the pigment responsible for human skin color is produced by melanocytes located in the epidermis of the skin. All people, regardless of skin coloration have approximately the same number of melanocytes. Additionally, we all make the same types of melanin. Differences in the amounts of three types of melanin make up all the variation you find in human skin color. The differences in skin color among people can be attributed to the extent of which the genes for proteins that make melanin are expressed. These differences in phenotype are directly related to the small differences in the genomes of each individual. Some individuals lack the gene for producing melanin all together. This condition is called albinism.

One of the proteins responsible for making melanin is tyrosinase. Tyrosinase works early in the process and catalyzes the reaction of the amino acid tyrosine with oxygen to form DOPA, a precursor of melanin. Another protein converts DOPA to another molecule and so on down the assembly line until melanin is made. A problem at the step of tyrosinase will disturb the activity further down the

assembly line and melanin will not be made.

http://en.wikipedia.org/wiki/Skin

http://en.wikipedia.org/wiki/Skin_color

http://en.wikipedia.org/wiki/Suntanning

Familial Hypercholesterolemia

Another example of genomic differences in people, is a disease known as familial hypercholesterolemia (FH). This genetic disease causes a condition in which carriers of this gene have abnormally high LDL (low-density lipoprotein) levels. The high LDL levels cause many problems including heart disease at a young age. Additionally, fatty deposits develop in the body, especially at joints such as the knees. FH is caused by a mutation in the gene that codes for the LDL receptor protein. The LDL receptor removes LDL particles from blood plasma. LDL cholesterol usually circulates the body for 2 1⁄2 days before it is cleared by the liver. Since the LDL receptor does not clear LDL particles properly in patients with FH, this genetic condition doubles the amount of time that the cholesterol takes to be cleared, thus elevating cholesterol levels.

http://en.wikipedia.org/wiki/Familial_hypercholesterolemia

http://en.wikipedia.org/wiki/LDL_receptor

Lactose Intolerance

Another example of a genetic difference is the cause of lactose intolerance. Lactose, a disaccharide, is present in dairy products. The reason that people and animals can digest milk is the enzyme lactase. Most people can break down lactose when they are very young because the cells in their intestines are still making lactase. However, for most of the world's population, lactase production slows down or stops entirely. Without lactase, naturally occurring bacteria that live in our intestines break down the lactose, but generate gas in a fermentation process. The gas produces uncomfortable and unwelcome symptoms: gas, stomach cramps, bloating, and diarrhea.

http://en.wikipedia.org/wiki/Lactose_intolerance

Sickle-cell disease

Some genetic differences can result in extremely chronic illnesses. Sickle-cell disease is one such condition. Sickle-cell disease results from a change in a gene that codes for hemoglobin a main component of red blood cells. When cells with "sickle" hemoglobin de-oxygenate, the hemoglobin sticks together forming long chains that change shape of the red blood cell into a crescent moon or sickle shape. When these red blood cells change shape, they can cause clots in the arteries, blocking oxygen from getting to down stream tissues, thus causing serious consequences such as heart attacks and strokes.

Sickle-cell disease in a recessive disease that is thought to be common in populations with a high incidence of malaria because carrying a single copy of gene that makes “sickle” hemoglobin protects that person from malaria.

http://en.wikipedia.org/wiki/Hemoglobin

http://en.wikipedia.org/wiki/Sickle_cell

http://en.wikipedia.org/wiki/Sickle_cell_trait

Lesson 1: How similar or different are we from each other?

Overview

Objective

The main objective of this lesson is to introduce the driving question "How similar or different are we from each other?" and help students begin to realize that any two humans have more biological similarities than differences. This driving question was developed to 1) help engage and interest students , and 2) help students contextualize all the knowledge they will learn over the next few weeks .

It is also important to help students realize that in order to understand this question we must explore the cellular components of our bodies and the molecules that allow those cells to function (i.e. proteins). Students are introduced to one example— skin color— to help them understand that we have to look at cells and the functions of those cells if we are to understand how similarities and differences in people can result.

Connection

This lesson sets up the Driving Question that students can revisit through out the unit. Students should learn content in each of the following lessons that will allow them to more completely answer this question at a more scientifically accurate level. This lesson also sets students up for lesson 2, which considers cells and proteins and their influence on physical appearance.

Description

- *Students compare and identify the biological similarities and differences between different people and different organisms.*
- *Students are introduced to the driving question of the unit "How similar or different are we?"*
- *A specific example of skin color is given that allows students to consider skin differences at the cellular level — a prelude to considering the role of proteins in influencing the biology of an organism.*

Learning Goals

National Standards

LG1 Nature and function of proteins - The work of the cell is carried out by the many different proteins. Proteins molecules are long, usually folded, chains made from 20 different kinds of amino-acid molecules. The function of each protein molecules depends on the specific sequence of amino acids and the shape the chain takes is a consequence of attractions between the chain's parts. (AAAS, pg. 114, 5C:9-12#3)

Michigan Standards

B2.4d Analyze the relationships among organisms based on their shared physical, biochemical, genetic, and cellular characteristics and functional processes.

[The learning goal addressed in this lesson is darkened.]

Learning Performance(s)
1. Identify similarities and differences between and within different species based on physical evidence.
2. Generate an initial hypothesis about the degree of similarity between and within different species based on physical morphological evidence.
3. Construct an initial explanation for why skin color could vary in different people and provide a reasoning statement that includes skin cells functioning differently.

Using the Reader

The reader has also included these learning performances for the students. At this point, direct the students to the learning performances. The reader uses the term Learning Goals. Try to monitor the students progress regarding these learning performances (Learning Goals) by occasionally returning to them and reminding the students that they should be acquainted with these skills.

Prior Knowledge

- Basic familiarity with internal organs such as the brain, the lungs, and the heart. Students should realize that all animals have these organs.
- Tissue in the human body is made of cells.

Student Misconceptions

- Students may be unaware of the central role proteins play in biological processes.
- Students may have difficulty determining which differences are biologically based.

Time

2 days

Materials

PowerPoint slides

Student readers

Instructional Sequence

Section I: Introducing the unit: How similar or different are we?

Purpose: Get students to start thinking about physical differences and similarities between themselves and their classmates. The discussions held during this lesson will provide a context and a foundation for the rest of the unit as well as providing you with an idea of students prior knowledge about similarities and differences.

Using the Reader

Introduce the students to the student reader. Depending on your classrooms's culture students can take it with them or leave it in the classroom, but they will need it in class for most parts of this unit**.** Have students read the text about writing scientific explanations on page 3 and 4 of the reader. This will give them some practice on scientific writing.

Group Activity -- Explore similarities and differences

The reader provides the students with a chart that documents the similarities and differences between people in the classroom. Students should talk to the person sitting next to them, then fill in the charts with characteristics that they think make them similar and different. Also, the students are asked to make predictions about where they think their similarities and differences come from.

Ask students to consider:

- Obvious characteristics (e.g. skin color, height, number of hands etc.)
- Subtle characteristics (e.g. nose shape, length of fingers etc.)
- Health (e.g. lactose tolerance, allergies, asthma, vision, acne etc.)

Before talking about their charts as a whole class, ask students to talk about their charts with each other in small groups and answer the questions. Direct them to the prediction columns- ask them to think and talk about what they think is responsible for the similarities and differences they recorded. It is not important that students have the right answer at this point.

Teacher Note - Defining a term

"Biological" in this context means any features relating to the natural characteristics of an organism. This includes the cells or organs that make up an organism or the biological molecules that are found in an organism. What is not included in this term are any features that do not relate to the natural characteristics of an organism such as different clothing, or different hair styles.

Generating Discussion - Reflecting on similarities and differences on multiple levels

Reconvene students into whole class and share what groups found. If necessary, identify features that are not biological.

Rationale: This discussion is an important discussion because it allows the students to bring forth their ideas to the whole class. Students are encouraged to articulate their ideas to everyone, and use the evidence that they gathered (through observation) to make causal predictions. This also allows them to hear other people's ideas and modify their own. It also allows the teacher to know what their thoughts are from the activity they just did.

Discussion Strategies: In this type of discussion, you are trying to help students put together what they learned through the activity and how that might relate to themselves, which can be difficult for students.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their differences and similarities?
- Predictions: Would this change if they were to compare themselves to another person? What about a member of their family?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.
  For example: Student: "Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too."
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

  For example: Student: "Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as "WHY" and "HOW DO YOU KNOW THAT" when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- What have you observed or experienced?
- What else is on your group's list?
- What do you/other people think about when they hear the word ___?
- Who has a different idea/response/way of thinking about this?
- What do you know about [topic X]?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

- Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

  For example: Suzie, “How come DNA is passed to the offspring?”

  Teacher, “Why do YOU think DNA is passed to the offspring?”

Discussion Focus Questions

- What similarities and differences did your group find?
- Did you find more similarities or differences?
- If you spent more time do you think you could have found more similarities or more differences?
- (If health related differences were not mentioned) How would this list look if you someone in your group had a disease like asthma? (pick a disease you think your students would already be familiar with, e.g. cancer)
- Where do you think the similarities and differences come from? Are they part of you or are they because of things around you?

Have students complete the questions on pages 8 and 9.

<u>Using the Reader</u>

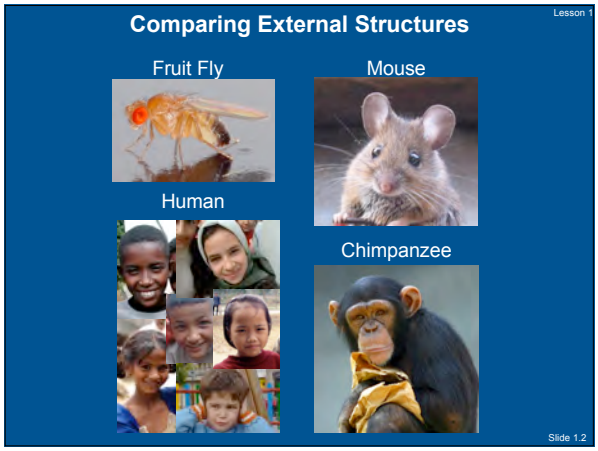
Ask the students to answer the questions on Page 10 after reading the description of Biological in the reader.

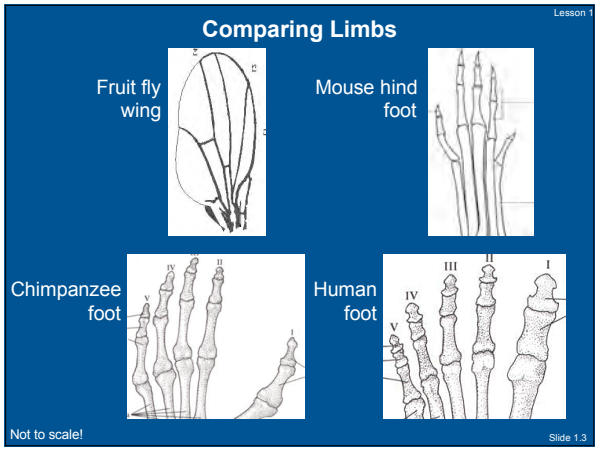
Encourage students to think about similarities and difference between people from different parts of the world:

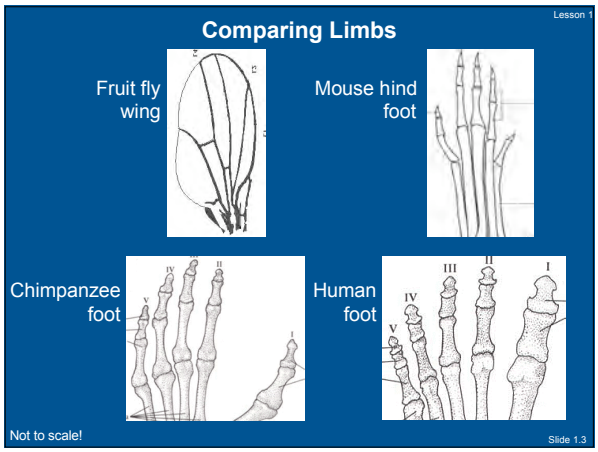
Slide 1.1 - Ask

- If you were to do the same task with students from another place in the world, how would your list be different?
- Where do you think the similarities on your list come from? The differences? (This might be a good opportunity to find out what ideas student have about genetics since some students may bring up the idea of genes—if these ideas are brought up in class discussion, teachers can ask students to clarify what they are suggesting about genes and appearance. Many students may link genes to appearance, but few, if any, will know how this occurs. The "how" is the focus of this unit.)

After the class explores these questions and gets ideas out, explain that in this unit students will learn how these physical similarities and differences can develop.







Slide 1.2, 1.3 and 1.4 - Encourage students to think about similarities and difference between different species. Help students think about how humans compare to other animals, by showing the series of PowerPoint images of a fly, a mouse, a chimp, and a human. The first slide focuses on external features, the second on limb structure and the last on brain structures

- For each slide, ask the whole class to identify what is similar or different between these different organisms.
- Ask the students to use their 1 through 100 scale to rank how similar they are to these other organisms.
- Ask if considering the similarities and differences between all humans and other organisms makes them think about changing how they ranked the similarities between them and their group. If it has changed, how and why?

The point of thinking about internal structures is to get students to think about bodily functions and the organs that carry out those functions. Later we want students to think about explanations for diseases that affect organs such as the brain. In addition, this comparison of internal structure helps extend the structures of comparison beyond just the surface structures and pushes students to think more broadly about difference and similarities in organisms.

Reviewing Discussion: Similarities and Differences Observations

Rationale: This discussion serves the purpose of helping students realize that there is a continuum of similarities between these different organisms- some animals have much more in common with humans and some have very little (although even very distant ones have some similarities). Ultimately we will want students to realize that those animals that share more similarities with humans also have more similar genomes than those animals that are more different.

Students are encouraged to connect the activity that they just did in class with this discussion. Making these connections are helpful for transferring their knowledge to other parts of the units as they arise.

Discussion Strategies: In this type of discussion, you are trying to help students put together what they learned through the activity and how that might relate to themselves, which can be difficult for students.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their differences and similarities?
- Predictions: Would this change if they were to compare themselves to another person? What about a member of their family?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.
  For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

  For example: Student: “Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these 4 ideas together into one process that we might call “the water cycle”? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

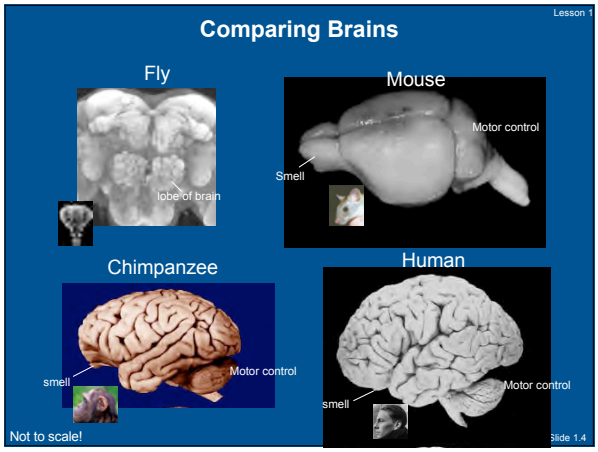
Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”



Introduce driving question of the unit: Use Slide 1.5 or write on the board the driving question: “How similar or different are we from each other?”

Have the students predict how similar or different they are from another person on a scale of 1 to 100, 100 being completely alike, in their student reader on page 7 if they have not done so already.

Ask the students to share their response to the driving question. Push them to expand their answers beyond a number.

Reviewing discussion - Introducing the driving question

Rationale: This discussion serves the purpose of helping students realize that what they are going to learn relates to them directly by emphasizing the Driving Question. The Driving Question helps students ground what they are learning to something relatable and relevant to them. Through this discussion, students can practice making predictions, giving explanations, and using evidence.

Students are encouraged to connect the activity that they just did in class with this discussion. Making these connections are helpful for transferring their knowledge to other parts of the units as they arise.

Discussion Strategies: This type of discussion involves putting ideas together, or assembling multiple activities into a coherent whole. It may also include generalizing from specific activities to a more general conclusion. Reviewing discussions may include making connections to personal experiences; to the driving question; to the previous or the following lesson; or to knowledge gained in other units, lessons, or subject areas.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their differences and similarities?
- Predictions: Would this change if they were to compare themselves to another person? What about a member of their family?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up

questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.
  For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: “Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these 4 ideas together into one process that we might call “the water cycle”? What happens 1st, 2nd . . . ?
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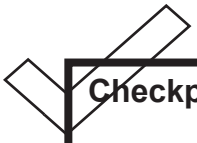


Checkpoint:

Do students understand the driving question? What ideas students already have about similarities and differences between different people and different organisms?

There is no right or wrong answer to the driving question.

Section II : Exploring biological differences: Skin color as an example

Purpose: Students begin to explore differences at a biological level using the example of skin color. Begin to establish a model of skin color in humans. Student will also make their first attempt at connecting what they know about cells to a trait they can observe, skin color, using a modeling activity.

Using the Reader- How Cells Work in Our Bodies Pg. 11

Ask students to read the section about cells and complete one of the reading strategies suggested in the introduction of the reading. This can be assigned as homework or done in class. The reading strategy is intended to help the student organize the reading in a way that makes sense to them. After they complete the reading strategy, go over the different ways that your students used the strategies. This can give students different ideas of how to read scientific text.

Problem Solving Discussion - Focusing on Cells

Rationale: Students should come to the conclusion that cells within our body are different and that cells in different people are different. This discussion is important because it can help students make connections between what they already know about cells and what they read in their readers in “How Cells Work in Our Bodies.” Here is a good time to find out students prior knowledge on the subject and how they think it relates to the reading.

Discussion Strategies: In this type of discussion, you are trying to help students think about what they know and make revisions of previous ideas as students learn new information that calls into question the limitations of what they “knew” previously. When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their differences and similarities?
- Predictions: Would this change if they were to compare themselves to another person? What about a member of their family?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”

- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and

similarities and differences.

For example: Student: “Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does X compare with Y?
- How can . . .? How might . . . ?
- How do you know? What evidence supports that idea?
- What does it mean to say …?
- Why doesn’t our old model work to explain this new phenomenon?
- Why can’t …?
- How could we figure this out?
- What new questions do you have?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Using the Student reader - Components of the Skin, p. 12

This reading gives the students some background about skin (what it is made up of, the layers and how skin color comes about). At the end of the reading, there are questions that requires the students to write scientific explanations. Be sure to emphasize this framework, they will use it often throughout the unit. This could also be assigned for homework.

Reviewing discussion - Skin on the cellular level

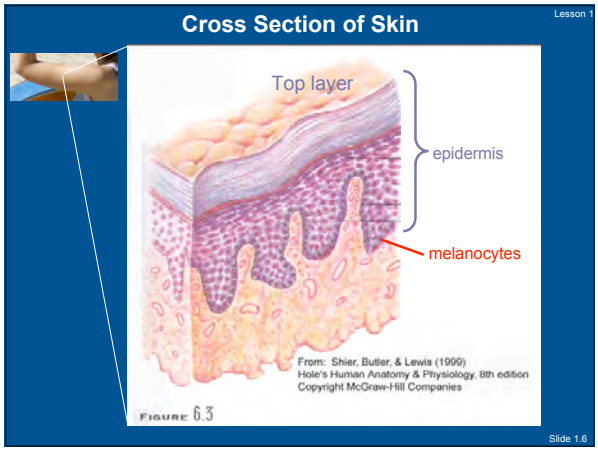
Ask the students to summarize what they have read. Show them the PowerPoint slides and ask them to explain the images.

Rationale: This discussion will help students bring together major points that they have learned so far.

Discussion Strategies: In this discussion, you are trying to help students connect the reading to what they already know.

Here are some points to guide you:

Slide 1.6 - Focus on only a few points relevant to skin color.



- Skin is composed of cells that form layers
- The top layer is called the epidermis which can be envisioned as two parts- the epidermis and dermis.
- The epidermis is where skin color is made so we will focus on it
    - A top layer called the epidermis that is comprised of tightly packed dead and living cells – this layer provides strength to our skin
    - It has a flat, dead layer of cells at the very surface (these are the cells we see at the surface of our body) and a deeper layer of round, living cells

Discussion Strategies: In this type of discussion, you are trying to help students put together what they learned through the activity and how that might relate to themselves, which can be difficult for students.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their differences and similarities?
- Predictions: Would this change if they were to compare themselves to another person? What about a member of their family?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

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- Ask students to consider a previous response while formulating their own. (See above example in quotes).

- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: “Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these 4 ideas together into one process that we might call “the water cycle”? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

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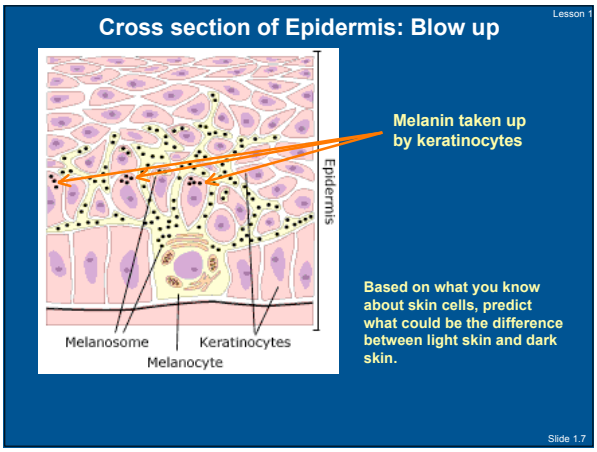
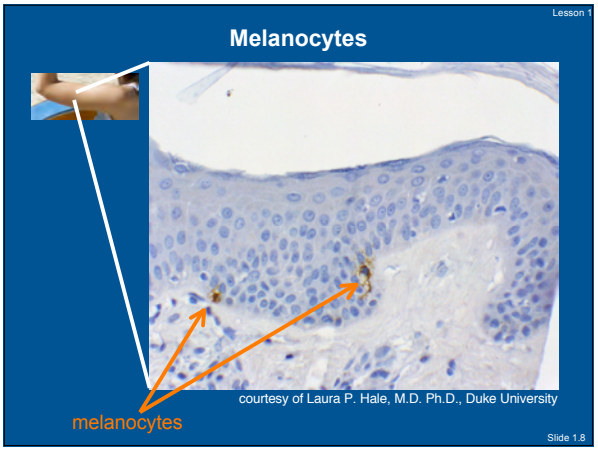
For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”





Slide 1.7 to 1.8 - Spread across the bottom of the epidermis are pigment producing cells called melanocytes. Melanocytes produce a dark pigment molecule called melanin. Melanocytes can be thought of as melanin producing factories in our skin. The melanin pigment is released by melanocytes and is taken up by the keritinocytes. The octopus-like shape of the melanocytes allows its “arms” to deliver melanin to all the other cells.

Focus on melanocytes and point that these cells must do work—they have to produce the melanin pigment so that other cells can take up the pigment. One could also say that these cells have to carry out the work of producing melanin.

The picture in Slide 1.8 shows real cells. A special stain was used to highlight the melanocyte.

Review Skin Components with Class: Students do not need to memorize the different parts of the skin, but they should be able to recognize what a melanocyte is and what it does: a type of skin cell that makes melanin for other skin cells.

Teacher Note - Background Information

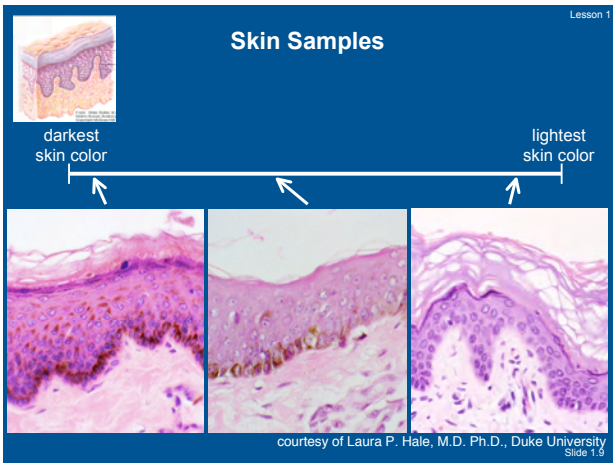
Background information about skin cell biology and skin color can be found in the Introduction or at the following websites:

http://en.wikipedia.org/wiki/Skin
http://en.wikipedia.org/wiki/Human_skin_color
http://www.safetyline.wa.gov.au/institute/level2/course16/lecture129/l129_02.asp
http://www.besthealth.com/besthealth/bodyguide/reftext/html/skin_sys_fin.html
http://encarta.msn.com/encyclopedia_761569048/Skin.html

Generating a prediction about skin color differences

Ask the students if they remember the driving question: How similar or different are we from each other? Prompting might be necessary.
Prompt the student the following questions:

- Think about your drawing of how your skin is the color it is. How would it be different if your skin was darker or lighter?
- How would your drawing be the same if your skin was light or darker?



Class activity - Experiencing different skin color

Slide 1.9 - Reveal the final slide with pictures of different skin colors taken through a microscope. Give the students a minute to examine the slide and think about what they are seeing.

Ask the students:
- What differences do you see?
- What similarities do you see?

Students might notice a lot of differences: the amount of pink purple and blue, the structure of the cells, the size of the cells. These differences are all due to the way the skin was prepared for the microscope and stained. Make sure they focus on the difference in the brownish spots, these are the melanosomes.

Point out that there are lots of different colors of skin and that these are just three examples along a spectrum.

Explain that in general, all humans have the same number of melanocytes. (a similarity)

Explain that all the skin colors on the spectrum are made from varying amounts of the same three types of melanin. (a similarity)

It appears that the prediction about the amount of melanin is correct. Since this appears to be correct, our next step is to try to understand more about this difference .
- What else have we learned about skin and skin color that might help us make a predictions?

Ask students to write their prediction about how dark and light skin might be similar and different in their student readers.

Ask several students to share their responses with the class.
- Is their any evidence that the student used to make that prediction?
- Do other students have different ideas?

Students could respond
darker skin has more melanocytes
darker skin makes a darker melanin
darker skin makes more melanin (this is the correct answer)

they both have melanocytes
they both have keritinocytes

Generating Discussion- Forming Scientific explanations

Discussion Rationale: Students should not be expected to have the right answer at this point. The objective is to consider reasonable explanations for different skin colors. Encourage students to communicate by forming scientific explanations. This involves sharing ideas without evaluating their validity. Ideas can be written on the board or overhead as they are generated.

Discussion Strategies: You can have the students fist try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their differences and similarities?
- Predictions: Would this change if they were to compare themselves to another person? What about a member of their family?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

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- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: “Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- What have you observed or experienced?
- What else is on your group’s list?
- What do you/other people think about when they hear the word ___?
- Who has a different idea/response/way of thinking about this?
- What do you know about [topic X]?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Teacher note - Language Use

The use of light and dark to describe skin color in this unit is intentional. While your students might use terms such as black and white when describing skin, describing skin as dark and light is not only culturally sensitive, it is a more accurate description of the actual color of human skin. No one has truly white or truly black skin.

For the same reasons, we placed the samples of skin color on a spectrum to represent how skin color happens in nature.

Using the Student Reader- Wrap-Up (pgs 13-14)

This last part of the lesson is meant to help the student synthesize all of the information they have learned in Lesson 1. Have the students complete this section. Help the students recall concepts and vocabulary that they have learned thus far. They will revisit these concepts and vocabulary words at later parts of the unit.

Checkpoint:

If we want to explore how two different organisms are different at a biological level, what must we look at?

Answer: We must look at cells and the function of cells to begin thinking about what makes two things biologically similar or different.

Lesson 2: Exploring Proteins

Overview

Objective

The objective of this lesson is for students to learn what proteins do in cells, how proteins carry out their functions, and what influences their function. Students should understand by the end of this lesson that (1) proteins carry out most of the work of the cell, (2) that each protein has a specific shape that allows it to carry out its work (much like a tool has a specific shape for its function), and (3) that the order of amino acids in a protein determines its shape.

Connection

This is a key lesson to learning what proteins are and do. It takes off where lesson one left off with cell function and goes to the molecular level. It also is a prelude to lesson 3 where students learn that genes are instructions for building proteins.

Description

- *Students begin with skin color differences and the protein tyrosinase.*
- *Students then consider the example of lactase protein; students learn about its function and its influence on health.*
- *Students perform an activity to demonstrate that adding lactase to milk generates glucose.*
- *Students consider an ethical dilemma: availability and cost of lactose free dairy products.*
- *Students determine that protein is found throughout the body by performing an assay for protein on chicken parts.*
- *Students consider the jobs that cells need to perform and how proteins do the work involved in those jobs.*
- *Students then learn about amino acids and their role in determining protein shape by building models of proteins.*
- *Students then build models of part of the lactase protein and learn how amino acid sequence determines the shape and function of proteins.*

Learning Goals

National Standards

LG1 Nature and function of proteins - The work of the cell is carried out by the many different proteins. Proteins molecules are long, usually folded chains made from 20 different kinds of amino-acid molecules. The function of each protein molecule depends on the specific sequence of amino acids and the shape the chain takes is a consequence of attractions between the chain's parts. (AAAS, pg. 114, 5C:9-12#3)

LG2 Biochemical basis for traits - An organism's traits reflect the actions (and inactions) of its proteins. (AAAS considering this but has not published yet)

Michigan Standards

B2.2 Organic Molecules - There are four major categories of organic molecules that make up living systems: carbohydrates, fats, proteins, and nucleic acids.

B2.2C Describe the composition of the four major categories of organic molecules (carbohydrates, fats, proteins, and nucleic acids).

B2.2D Explain the general structure and primary functions of the major complex organic molecules that compose living organisms.

B2.2x Proteins - Protein molecules are long, usually folded chains composed mostly of amino acids and are made of C, H, O, and N. Protein molecules assemble fats and carbohydrates; they function as enzymes, structural components, and hormones. The function of each protein molecule depends on its specific sequence of amino acids and the shape of the molecule.

B2.2f Explain the role of enzymes and other proteins in biochemical functions (e.g., the protein hemoglobin carries oxygen in some organisms, digestive enzymes, and hormones).

[The learning goal addressed in this lesson is darkened.]

Learning Performance(s)
Students assemble models of protein using Toobers.
Students explain how the order of amino acids in a protein determines its shape and consequently its function.
Students explain how properties of amino-acid such as charge, hydrophobicity, and size can affect protein shape.
Students explain how a change in amino acid order can affect protein function
Students explain how changes in proteins might affect a cell's ability to it's job

Prior Knowledge

- Cells: Students should realize all living organisms are comprised of cells and that for humans (as well other animals and plant) have tissues and organs that are comprised of many cells. Students should know be familiar with what a few specific cell types – e.g. red blood cells.
- Functions important to all living organisms: e.g. taking in food, breaking down food, building molecules, releasing waste, etc.

Student Misconceptions

- Students may be unaware of the central role proteins play in biological processes.
- Student confuse the difference between amino acids and protein- sometime calling protein amino acids, and amino acids proteins.
- Student have difficulty with the scale of molecules, proteins, cells. They have difficulty knowing which is bigger. Some may mistake proteins for cells or visa versa.

Time

7 days

Materials

PowerPoint slides and projector

Student readers

Overhead with key for colored thumbtacks

Toobers- 5-7 (enough for groups with 4-5 students)

Thumbtacks

Materials for protein activity and lactase activity (See Section I and II)

Section I: What carries out the work of the cell?

Purpose: This section aims to help students understand how two specific proteins work so that they can start to form ideas about how important shape is to protein function.

Reviewing Discussion -What makes melanin?

Discussion Rationale: This discussion is meant to help the students summarize what they learned in their reading.

Discussion Strategies: You can have the students fist try it on their neighbor, then reconvene as a class and share their explanations.

Here are some points/questions to guide you:

- What are proteins?
- What do proteins do?
- How is the protein we eat related to the proteins in our body?

Review from Lesson 1:

What needed to be examined to understand why some people might have darker skin?
How do you think the melanin in cells gets made?

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?
- Predictions: Would this change if they were to compare themselves to another person? What about a member of their family?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

  For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”
- Ask students to consider a previous response while formulating their own. (See above example

in quotes).

- Encourage students to ask other students questions about their predictions and similarities and differences.

  For example: Student: “Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together into one process that explains how proteins are made? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

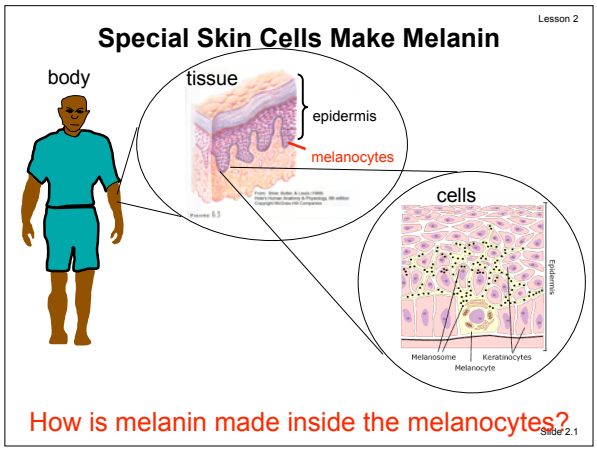
For example: Suzie, “How come DNA is passed to the offspring?”

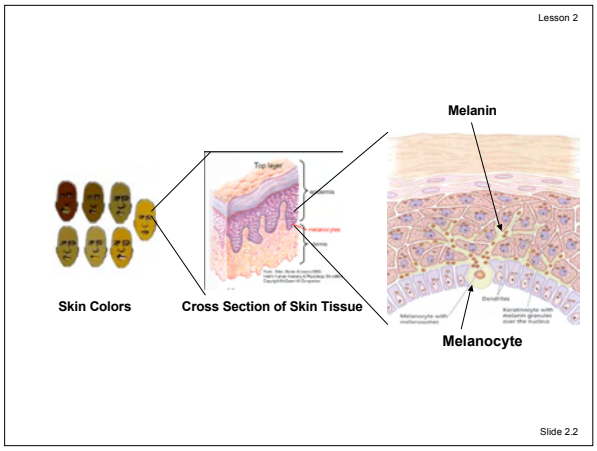
Teacher, “Why do YOU think DNA is passed to the offspring?”

<u>Using the Student Reader- Tyrosinase: How does this protein affect skin color?</u>

Assign students to read this text about Tyrosinase on page 16-18 and to answer the questions as the end. This text introduces students to the biology of skin color. The main points that students should come away with are that skin has cells called melanocytes. Within the melanocytes, a protein called tyrosinase is involved in the production of melanin. Although everyone has the same number of melanocytes, the tyrosinase acts differently in people, giving them different levels of melanin and therefore different shades of skin colors. The reader suggests reading strategies to help with comprehension. Assist students in using them, or encourage them to work in pairs. You can use the completed strategies to go through the next slides, when talking about the reading, or when talking about tyrosinase.

Go over how one protein, tyrosinase, does its work:

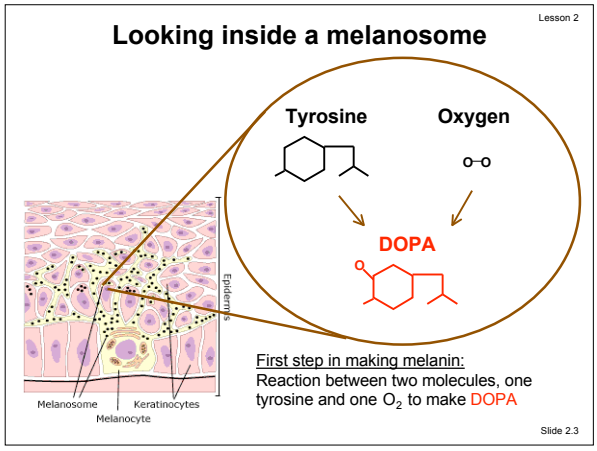




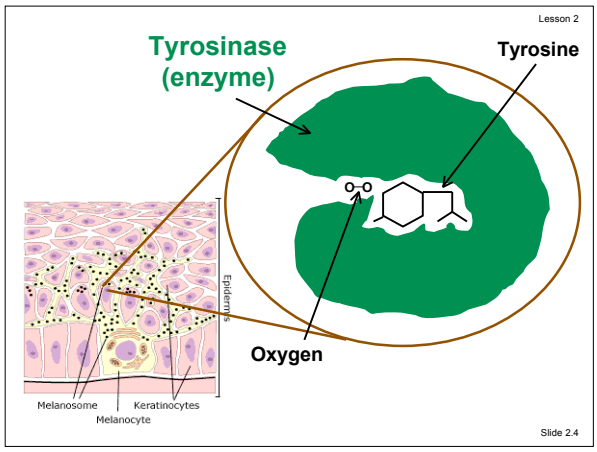
Slide 2.1 & 2.2 - Remind students about what they have already learned about skin color. Make the connection from visual whole body traits, to tissues, and to cells. This connection is one of the common places students struggle when learning this material. Introduce the question.

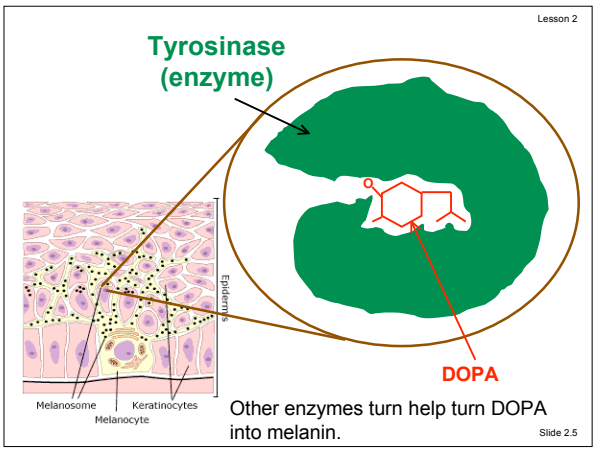
How is melanin made inside the melanocytes?

Hopefully, students reading will help them to think of proteins.



Slide 2.3 - Introduce the first step in making melanin: the conversion of tyrosine to DOPA. Although we won't cover the other steps, there are many more steps after this to make melanin. The emphasis on the molecules is that they have a specific **shape**, not to memorize the molecule. Explain that tyrosinase mixed with oxygen don't automatically form DOPA, they need help. That is where proteins come in.





Slide 2.4 and 2.5- Show cartoon image of tyrosinase turning tyrosine to DOPA with oxygen. Point out that students do not need to know the molecules or processes. Focus on the way the **shape** of the protein matched the shape of the tyrosine, and the tyrosinase inside of cells helps the process of making melanin by helping to form new molecules.

Prompt students to think about how people could differ because of their proteins: Ask students the following:

> Given that proteins make melanin and we know that in people with darker skin, more melanin is produced, and in people with light skin, less melanin is produced, what might be the difference between light skinned and dark skinned people?
>
> Answer: their proteins might work differently

Objective: Students should learn that shape is an important aspect of proteins. Tyrosine fits in tyrosinase. The specifics of the molecules involved are not important for the students to remember.

Teacher Note - Background Information

Background information about tyrosinase and melanin can be found in the Introduction.

Using the Student Reader - Don't Pass the Milk, Please (pg 19)

Have students read "Don't Pass the Milk, Please" and answer the questions. This reading is a story about a young boy who is lactose intolerant. Help students understand that lactase is a protein that helps people break down lactose in milk. Jason did not have lactase, and is therefore lactose intolerant. The reader suggests the use of reading strategies. Assist the students in their use or encourage students to work in pairs.

Reviewing Discussion -Don't Pass the Milk, Please

Discussion Rationale: This discussion is meant to help the students summarize what they learned in their reading and prepare for the next section.

Discussion Strategies: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

Here are some points/questions to guide you:

- What was wrong with Jason?
- What do the students know about lactose intolerance?

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Think/Pair/Share:

Students can try it on their neighbor first, then share with the whole class.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?
- Predictions: Would ___ change if they were to ___ ?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

  For example: Student: "Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too."
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

  For example: Student: "Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as "WHY" and "HOW DO YOU KNOW THAT" when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these 4 ideas together into one process that we might call "the water cycle"? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today's activity help us think about ___?
- How does this connect to ____?

Supporting Communication

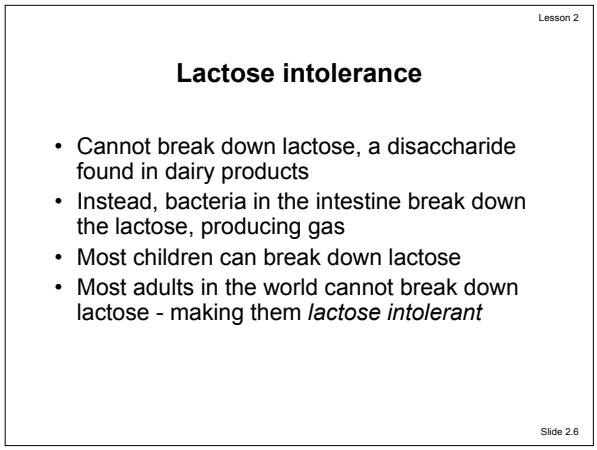
Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

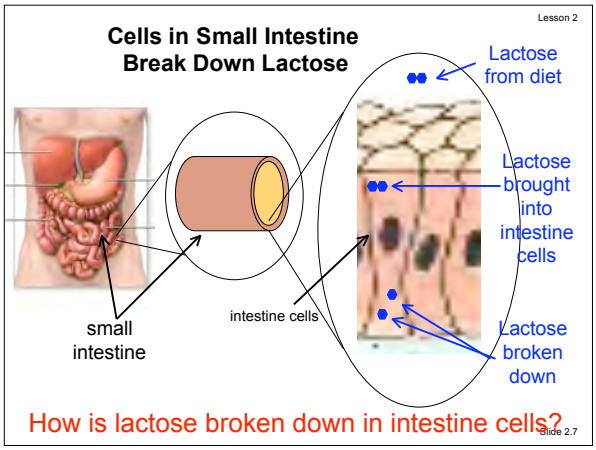
Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Review lactose intolerance with the following slides:



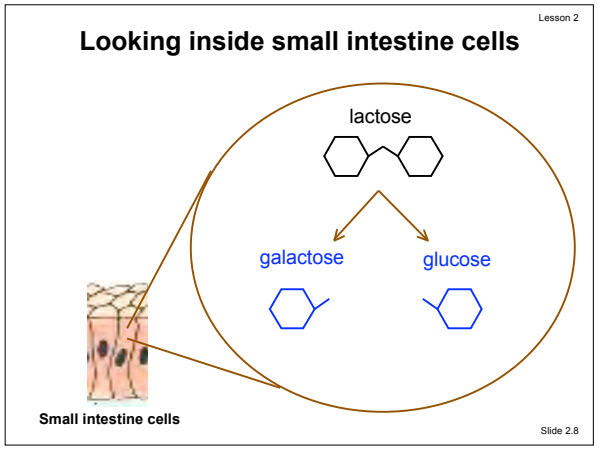


Slide 2.6 - Briefly discuss the biology of lactose intolerance. This discussion might proceed differently depending on whether students have read Section 2.1 of the Student reader.

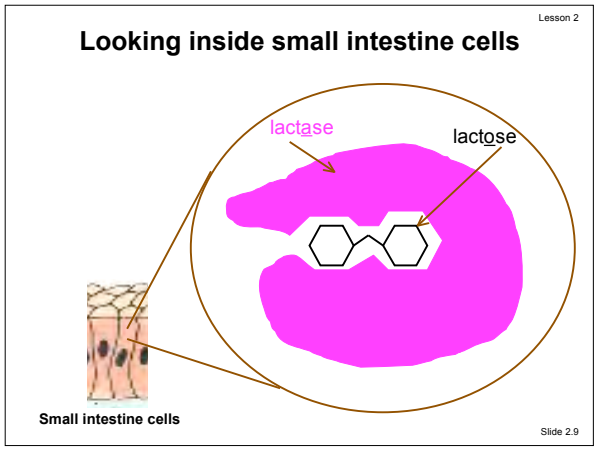
Slide 2.7 - Again make the connection from visual whole body traits, to tissues, and to cells. This connection is one of the common places students struggle when learning this material. Introduce the question.

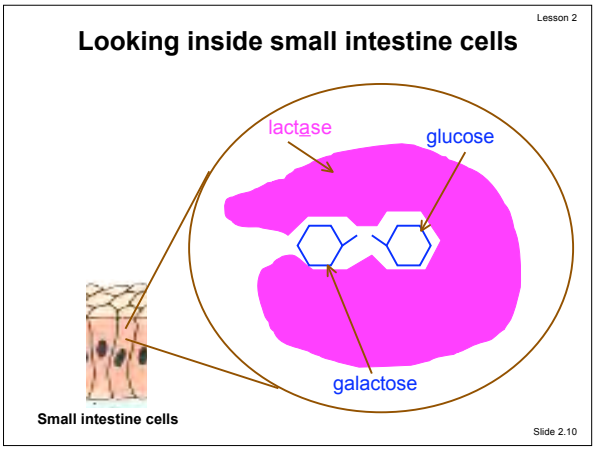
How is how is lactose broken down inside intestine cells?

Hopefully, students work on the previous activity will help them to think of proteins.



Slide 2.8 - Introduce how lactose is broken down into galactose and glucose. Again the emphasis on the molecules is that they have a specific **shape**, not to memorize the name of the molecule. Ask the students if they think lactose can break down all by itself or if it needs help.





Slide 2.9 and 2.10- Show the cartoon image of lactase turning lactose into galactose and glucose. Point out that students do not need to know the molecules or processes. Focus on the way the **shape** of the protein matches the shape of the lactase, and the lactase inside of cells helps break down lactose. The words lactase and lactose are very similar. This is a perfect opportunity to point out that many proteins end in -ase and saccharides end in -ose.

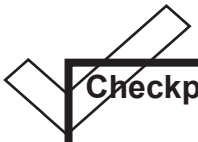
Prompt students to think about how people could differ because of their proteins: Ask students the following:

> What might be the difference between a person who can break down lactose and one who is lactose intolerant?
>
> Answer: their proteins might work differently

Objective: Again students should learn that shape is an important aspect of proteins. Lactose fits in lactase. The specifics of the molecules involved are not important for the students to remember.

Teacher note - Language use

We have intentionally used the term saccharide in these materials because students often get confused or draw on misconceptions when we call them sugars.



Checkpoint:

Can your students answer the following questions:

1) What carries out most of the work of cells?

Answer: proteins

2) What is one way that two people can differ biologically:

Answer: they can have proteins that function differently

Group activity - Lactase breaks down lactose - Reader pgs. 23-24

In this activity students will determine whether the medication taken for lactose intolerance is lactase. The will gather the evidence that when the medication is added to milk, glucose is generated.

Teacher Prep

Materials

- Lactase enzyme supplement pills (check ingredient list to make sure that the pills do not contain dextrose or sucrose)
- Pill crushing tool (mortar and pestle, kitchen mallet, hammer)
- Milk
- Glucose test strips
- Small cups for reaction

Preparation

1) Crush 1⁄2 pill for each group
2) Pour 5-10 mLs of milk for each group in a small cup
3) Provide each group with the following
   a. Crushed 1⁄2 lactase pill

b. 5-10 mLs milk
c. 2 glucose test strips

4) Make sure that glucose test strip bottle is at central location so that students can compare colors

Notes:

The glucose test strips will continue to change color as time passes. It is important that the students compare their strip to the bottle at the 30-second time point and record the results. They should not compare their strips at the end of the experiment.

The lactase pills will probably not dissolve completely, but this did not generate problems in our trials.

Before students start the activity, ask students if they have heard of medicine people can take for lactose intolerance. What do they think is in the medicine? Is it the same thing that they have learned about? How will they know?

They will know because when it is added to milk glucose will be produced.

The students will also make this prediction in their reader.

Explain that they are going to explore how lactose intolerance medicine works.

Break students into groups to follow the protocol in the student reader to complete the activity.

When students have completed the activity, ask them as a class:

- Was there glucose in the milk before they added the medication? After?
  no, yes, after
- What do they think happened?
  the medication broke down the lactose into glucose and galactose
- Would the medication do the same things if you swallowed them instead of mixing them into milk ahead of time?
  students might have a harder time, but the medication does work the same in the human body
- What evidence do they have that the medication is lactase?
  they know that glucose was produced, if they look at the box, they will see that the pills are made of lactase

Thinking about Ethical Problems - Reader pgs. 25-28

In this activity, students will consider the ethics of a proposal about the regulation of lactose in dairy products sold in the United States. Before the activity begins, place four sheets of paper around the room, one that says “completely agree”, one “agree”, one “disagree”, and the last “completely disagree”. Large pieces of butcher paper would work well. Alternatively, each group could be provided with an overhead.

Before addressing this topic, it will be important for your students to spend some time considering what ethics is, why it might be important, and how ethics will be discussed in the classroom. Ask students to read about ethics and answer the questions included. Ask a few students to share their

answers. As a class brainstorm about additional rules the class should include when dealing with an ethics problem.

Instructional note - Reading strategy

Consider using a concept card to help students think about the term “ethics”. What is ethics? What is not ethics? What is an example of an ethics problem?

Have students read about the proposed change to the sale of dairy products in their student reader and answer the first three questions. Ask individuals or groups to share some of their answers to the questions. Determining what the ethical problem is will likely be difficult for some students. Learning to recognize ethical problems is difficult and not the focus of this activity. If necessary, help students to see that the ethical problem is how to fairly treat people who are lactose intolerant.

As a class, brainstorm about potential stakeholders (some examples include: people who are lactose intolerant, people who are not lactose intolerant, dairy farmers, supermarket owners, companies that make lactase, government, etc.). Keep track of the stakeholders on the board, the overhead, or on sticky notes. Assign groups or individuals a stakeholder to consider and have each group consider the next questions in the student reader.

Ask each group to determine whether or not their stakeholder agrees with the position of adding lactase to all dairy products. Once they have determined their level of agreement, one member of the group can add their stakeholder to that piece of paper or overhead (completely agree, agree, disagree, completely disagree).

As a class, review which stakeholders agree or disagree. Ask groups to explain what concerns their stakeholder had and why their stakeholder agrees or does not agree.

For the stakeholders who do not agree with the solution, what other solutions would they agree with? How do other stakeholders feel about the alternative solutions?

Wrap up this activity by asking students to consider what solution they think is the best one and why? Some students might find it intimidating to share their personal opinions with the whole class, but encourage each student to write what they think. **Remind students that their is not a right or a wrong answer here, but it is important to have a reason for what they think.**

Section II - Where are proteins?

Purpose: The purpose of this section is to give students the opportunity to prove that proteins are all parts of our body and to think about what specific work they might be doing in our body.

Using the Student Reader - Proteins - Reader pgs. 29-30

Ask students to read “Proteins- What Exactly are They For” and answer the questions. This reading is meant to give students an overall idea of where they get proteins and how the body uses it. The reader suggests that the students use a reading strategy to help with reading comprehension. Help students with this strategy or have students work on them in pairs.

Group Activity - Where are proteins in chickens? - Reader pgs. 31-32

In this activity students will test different chicken parts (leg, liver, heart) to determine if they have proteins in them.

Materials
- Biuret solution
- Water
- Dish soap
- Table salt
- Chicken pieces – white meat, dark meat, liver, skin,
- Plastic bags
- Beral-Type pipets, or other device for measuring liquid
- Small cups or test tubes for Biuret reaction

Preparation
1) Cut chicken into pieces about the size of a large pea, enough so that each group has each type of chicken part
2) Put each piece of chicken into a separate plastic bag and label bag with chicken part type or have students label bags
3) Make the mixing solution by adding 1 drop of dish soap and 1 tsp of salt to every 15 mLs of water – make enough so that each group has about 15 mLs
4) Distribute to each group
    a. Set of four bags with each type of chicken piece
    b. 15 mLs Biuret solution
    c. 15 mLs mixing solution
    d. 5 small cups or test tubes for reaction
    e. 6 pipets (1 for mixing solution, 1 for Biuret solution, 1 for each type of chicken)

Ask students to answer the questions at the beginning of the activity in their student reader, and then share them with the class: where do they think they will find protein in a chicken?

Explain to the students that in this activity they will find the answer to that question. Break the students into groups and have them follow the protocol in their student readers.

When students have completed the activity, ask the whole class the following questions:
- What were the results of your experiment?
- Where they what you predicted?
- Are there any parts of the chicken that don't have protein?
- Do you think the same is true for humans?
- What is your scientific explanation?
- Where do you think proteins are in your body?

Section III: What are proteins made of?

Purpose: This section is intended to introduce students to the idea that amino acids make up proteins and that the order of amino acids can determine the structure of the protein and consequently the function of the protein.

Using the Student Reader - Protein Shape is Dependent on Amino Acids

Ask students to read “Protein Shape is Dependent on Amino Acids” and answer questions (pgs. 33-34_. This reading is about the molecular structure of proteins. It stresses the functions of amino acids and the shape of proteins. These are very important points for students to come away with.

The reader suggests that students use reading strategies to help with comprehension. Assist students in their use or have them work in pairs.

Reviewing Discussion - Proteins have a specific shape

Discussion Rationale: This discussion is meant to help the students summarize what they learned in their reading and prepare for the next section. Students can use this time to share their reading strategies with one another. This process will help students hear what others have learn and have opportunities to ask each other questions about their understanding.

Discussion Strategies: You can have the students fist try it on their neighbor, then reconvene as a class and share their explanations.

Here are some points/questions to guide you:

What do they think were the important points of this reading?

What are some characteristics of proteins that make people unique?

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Think/Pair/Share: Have students try it on their neighbor first, then share with the class.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain differences and similarities?
- Predictions: Would their ideas change if they ____?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”

- Ask students to consider a previous response while formulating their own. (See above example in quotes).

- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: “Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together to explain ____? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

Supporting Communication

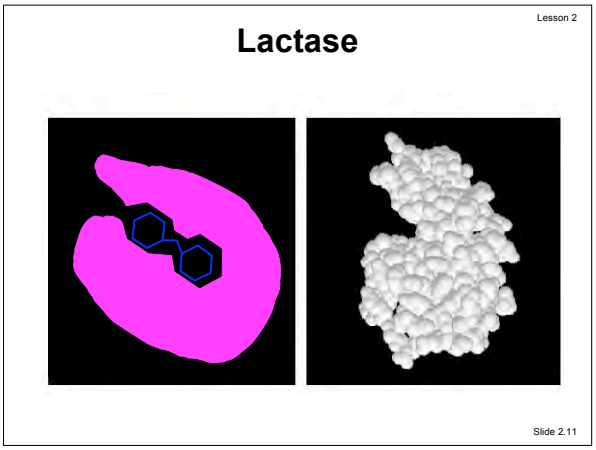
Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Review what the students have read using the following PowerPoint slides:



Slide 2.11 - Introduce the idea that proteins have a three-dimensional shape: Explain to students that all proteins have a three-dimensional shape and that proteins can be envisioned as tiny machines or

tools in which their shape is critical to their function. You can try discussing proteins as tiny machines or tools inside and outside of cells that carry out work (i.e. electric drill, electric screw driver, wrench, hammer, screw, bolt). Analogous to machines, proteins have a three dimensional structure that is important for their function.

Discuss the idea of models so that students realize that we can represent the same thing with different models and show different ways to represent lactase.

- Explain what a model is or ask if students have ideas of what models are from previous experience in science, such as a model of globe or map.
- Models:
  - representations of objects or processes in nature (like the water cycle) that we normally cannot see because they are too big or too small to see with our own eyes
  - allow us to make predictions, and test predictions, so we can understand the objects or processes in nature that we cannot see easily. In this case, proteins are too small to see; we can't even see them with a light microscope
  - can be pictures like the one shown here or 3-D physical objects like a globe, and that we can draw or build different types of models to represent the same thing
- The type of model we choose depends on our purpose

Continuing with Slide 2.11 explain to students that proteins are actually three-dimensional molecules, but that we often show proteins in 2-D images so students have to use their imagination and think of the proteins as 3-D. Show cartoon image of lactase and another image of lactase (called a space-filling model). Stress that both of these images represent the same protein. The space-filling model is more realistic, since it tries to show the actual atoms that make up the lactase protein (however, both images are meant to represent the lactase protein). Explain that proteins are in fact large molecules composed of lots of atoms.

Instructional note - Student conceptions

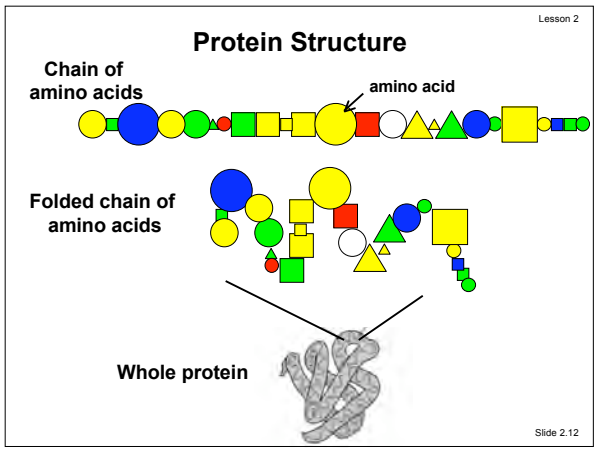
It may be difficult for students to understand that models do not have to look exactly like the original object because the models students are most familiar with are model cars and model airplanes that are exact scale replicas. Thus it may take some examples to illustrate this—for example the world can be represented in different ways- a globe, a flat wall map, a topographical map of the world. They all represent the world and some more or less accurately however they all show or reveal different things. Similarly, we use representations of molecules that serve our purposes (e.g. show all the atoms, make it easy to understand, show all three-dimension etc.).

If you show a representation that is new to students do not assume students will know it is a protein or that they know how interpret the image. You may have to point out what they are looking at is a protein and help them make sense of the new representation. It may also be useful here to point out what each kind or representation affords the viewer to help students realize why different representations are used (e.g. better 3-D understanding, easier to visual the chain, easier to recognize all the atoms and types of atoms, etc.)

Focus on the shape of the “pocket” in lactase and tyrosinase and how the pocket fits with the substrate: Proteins have a specific shape appropriate for their function. If necessary, return to image of tyrosinase and lactase and focus on the how the molecule (tyrosine in the case of tyrosinase, or lactose in the case of lactase “fit” nicely in the enzyme. Ask students what would happen if the “pocket” region of these proteins did not fit the molecules they work on. Would they still work? What kind of changes would they expect?

Objective: Students should have a stronger grasp on how the shape of proteins is important for interacting with various substrates or other parts of the cell. Students should understand that proteins can be represented in different ways and be able to recognize the representations included in this unit.

Teacher explanation - What are proteins made of?



Slide 2.12 - Explain that proteins are comprised of chains of amino acids. One should think of proteins as long chains of smaller units folded on top of themselves. Point out the “beads-on-a-string like nature of the image. Point out the “beads” (amino acids fold on themselves and which makes up part of a bigger fold.

Instructional note - Student conceptions

Some students confuse the difference between amino acids and protein-- sometimes students will call proteins amino acids, or they will call amino acids proteins. Thus, be very explicit and point out or indicate very clearly what the differences here are and alert students to the point other students often confuse the two. Emphasize that proteins are made of amino acids (not the other way around!) and thus the smaller units in these diagrams are the amino acids and the entire chain is a protein.

Explain that there are 20 different kinds of amino acids used to make proteins. Each type has different physical properties:

- size
- charged or uncharged (represented by color in the slide)
- shape

The students will explore some of these properties in later activities.

Checkpoint:

Could your students answer the following question?

If you were to describe what a protein looks like to a friend how would you describe it?

Answer: looked like a chain of smaller pieces folded on itself—proteins are made of amino acids, has a "mouth"

Student reader - Thinking about size - Reader pgs. 35

In this activity the students will rank the following words in order from largest to smallest. Some of the items are about the same size and can be grouped together.

protein, amino acid, melanocyte, nucleus, cell, tyrosinase, lactase, melanosome, mitochondria, melanin, lactose, human intestine, human, fruit fly

Assessment opportunity - Hopefully their answers will be mostly correct or give you the opportunity to address any misconceptions that students have developed.

If students are not convinced about the correct scale, it might be necessary to return to previous representations to address their problem areas.

Section IV. What determines protein shape.

Purpose: Students explore model of proteins to understand how amino acids influence protein structure.

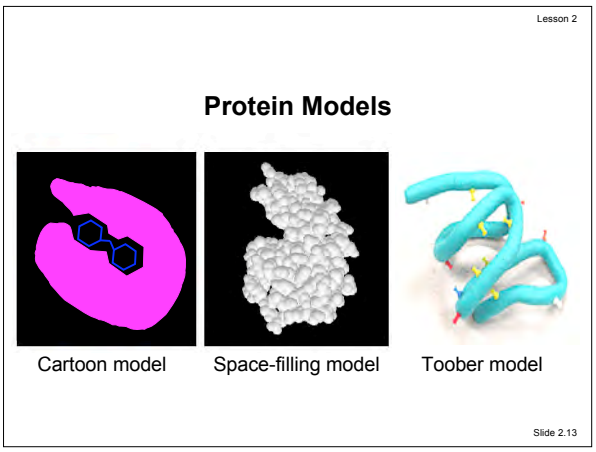
Teacher Explanation - Preparing to work with Toobers

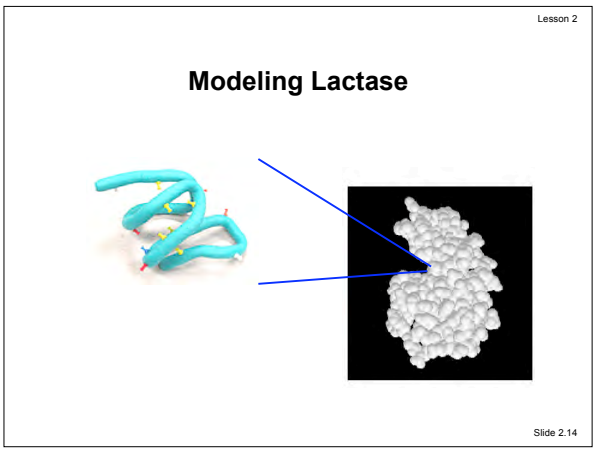
Remind students about:

- the connection between protein shape and protein function
- proteins are essentially long chains folded on top of themselves

Inform students that since shape is so important for proteins they will now engage in an activity that will let them explore how amino acid influences protein structure.

Introduce Toobers as models of proteins by pulling out a Toober (flexible tube that can be bent and folded) and explain this will be a **model of** a protein chain.





Slide 2.13 - Show side by side images of Toobers and a backbone model of a protein to emphasize the point that these Toobers are used here to model the amino acid chain of a protein.

- Remind students about the previous discussion about models. In this case, proteins are too small to see; we can't even see them with a light microscope.
- Also note that models will not look exactly like the real thing but will be useful for exploring how amino acids affect protein shape.

Slide 2.14 - Explain to students that the model they will build is not a whole protein, but a small 15 amino acid section of a much larger protein.

Discuss some of the properties of amino acids

Properties to discuss:

charge (positive or negative), and

hydrophobicity (hydrophobic = water hating; hydrophilic = water loving), and

cysteine-cysteine link (when two cysteine happen to lie next to each other in a folded protein, they can form a strong bond).

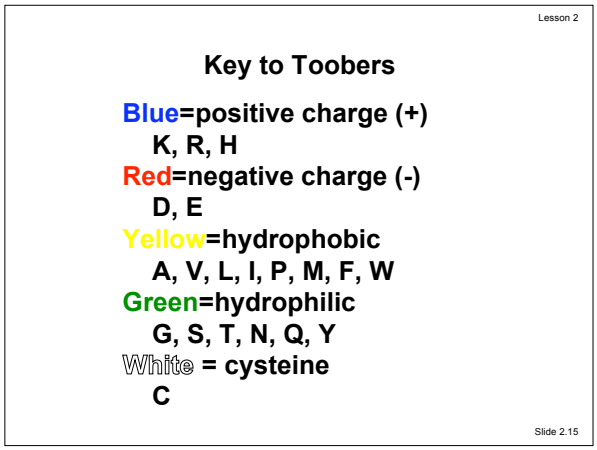
Students do not have to memorize which properties go with each amino acid, but they have to realize that there are different properties like charge, hydrophobic and sulfur containing. There are in fact other properties, but these are enough for these students.

Explain the following “rules” that amino acids follow. Have the students follow in their student reader pg 36.

a. Charge
   - Positive and negative charged amino acids attract each other
   - Amino acids with the same kind of charge repel each other

b. Hydrophobicity
   - Hydrophilic amino acids attract water
   - Hydrophobic amino acids repel water and hydrophilic amino acids
   - Hydrophobic amino acids attract other hydrophobic amino acids.

c. Cysteines
   - Cysteines are a type of amino acid. When two Cysteines are next to each other, they attract and form a strong bond. These strong bonds contribute to protein shape formation.



Slide 2.15 - Explain color code for Toober modeling activity: different colored thumbtacks are models for amino acids and each color is assigned different physical properties. Each color has letters after it. These represent one of the 20 amino acids. For now we will just focus on color. The tacks will then be pushed into the Toober to make a model of a chain of amino acids or a small part of a protein.

This slide can be left up for the remainder of the activity, or the following can be written on the board:.

Blue=positive charge (+)
Red=negative charge (-)
Yellow=hydrophobic
Green=hydrophilic
Orange=Cysteine

Group activity - Modeling with Toobers

Break students into groups. Each group will take 15 thumbtacks at random (pick out of a box without looking). The protein that the students make will not be real but will give them the opportunity to work with the Toobers and familiarize themselves with the rules.

Ask each group to place the thumbtacks into the Toober in any order they want to.

Ask students to bend the Toober with tacks according to “the rules” for amino acids. Have them draw as best they can what the folded protein they created looks like in the student reader.

Ask students what they think would happen if they replaced a tack with a different color tack.

Ask some groups to replace two of the red tacks with blue tacks and ask them to draw the resulting folded protein. Ask other groups to swap two of the yellow tacks with green tacks and ask them to draw the resulting protein.

Ask students to describe in words what is different.

Reviewing Discussion -Proteins have a specific shape 2

Discussion Rationale: Students discuss results as a whole class and identify important points of activity through a series of questions about amino acids and protein shape.: Reconvene the class and have them answer the following question after comparing protein from each group.

Discussion Strategies: You can have the students fist try it on their neighbor, then reconvene as a class and share their explanations.

Here are some points/questions to guide you:

a. How many different shapes were created?
   Answer: should as many as there are groups. This means there are huge number of shapes that can be created from just a certain number of amino acids.

b. Why do you think the shape changed when you swapped different acids? Make sure both types of groups get a chance to answer and explain what happened to their toober.

d. Would it be possible to swap just one amino acid for another and get a change? Explain.
   Answer: Yes you could swap one amino acid for another and get a change if they might have different properties (such as swapping a hydrophobic amino acid for a hydrophilic amino acid) and this would change the interactions between amino acid in the protein

e. Would it be possible to swap an amino acid for another and not get a Change? Explain.
   Yes you could swap an amino acid for another one and not get a change because two amino acids might have similar properties (like swapping a hydrophobic amino acid for another hydrophobic amino acid and therefore would not change the amino acid interactions).

f. What does this activity say about the role of amino acid sequence in protein shape?
   Answer: amino acid sequence determines the shape of proteins

g. If you were to delete an amino acid (i.e. thumb tack) or add a new one, do you think it would

change the shape of the protein? Why?
Answer: Yes, because it would change the order or amino acids in a protein and change the shape.

h. The human body is estimated to have at least tens of thousands of proteins even though there are only 20 amino acid that make up proteins. Explain how you can get so many different proteins using just 20 parts.
Answer: There is a huge number of different ways these proteins could be put together leading to a huge number of different shaped proteins.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Think/Pair/Share: Have students try it on their neighbor first, the share with the whole class.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their differences and similarities?
- Predictions: Would this change if they were to change the amino acid sequence?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

  For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

  For example: Student: “Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together to explain ____? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Checkpoint:

The main point to get from this activity is that amino acid sequence determines the shape of the protein because it is the properties of the individual amino acids that determine protein shape. Ask students in the class the following questions to check for understanding:

1) What determines protein shape?

Answer: The amino acids sequence

2) How does amino acid sequence influence proteins shape?

Answer: Different amino acids have different properties like being hydrophobic or hydrophilic or negatively charged or positively charged. These properties determine how the amino acids in the protein will interact with each other in the protein.

Section V. How does protein structure affect protein function?

Purpose: build a model of a real protein (lactase) and explore how change its amino acid sequence can affect its function.

Group activity - Building a model of a real protein

Explain to students they will now make a model of a real protein, lactase. Ask students if they remember what lactase does. Show previously used slides if necessary.

Remind students about what they have learned about how proteins work as enzymes:

- facilitate the formation or breakage of bonds helping to form new molecules
- "fit" with substrate (lactose in this case)

You can use Slide 2.8 and 2.9 to refer back to these ideas. The lactose fits in the "pocket" of the lactase and is broken into galactose and glucose.

Break students into groups and write the 15 amino acid sequence below on the board. Explain that this part of the protein is part of the "pocket" of lactase. It is only a small part of the protein; the whole protein is almost 2000 amino acids long! Have each group collect the appropriately colored thumbtacks for each amino acid following the rule stated in the last section. Explain that each letter represents a different amino acid.

DIPIY ITENGVGLTN (AA 1266-1280)

Note this is only part of the active site (i.e. the mouth) of lactase. The complete sequence is in the Appendix.

Let student know that the folds they generate may not be completely accurate, but will form a representation of the molecule that they can manipulate. Sometimes models are not completely accurate, but they can give us information and ways to think about problems that are hard to visualize.

After students have built their model try to identify a pocket in the model (i.e. a spot that looks like a pocket where a lactose molecule can fit). This step might take a creative eye.

Ask the students to draw their results in the student reader.

After identifying a mouth in the protein, ask the students to swap a tack in mouth. Ask the students to identify how the shape has changed and draw the results.

Reviewing Discussion -Proteins have a specific shape 3

Discussion Rationale: This discussion is meant to help the students summarize what they learned while building the proteins using the toobers.

Discussion Strategies: You can have the students fist try it on their neighbor, then reconvene as a class and share their explanations.

Here are some points/questions to guide you:

a. What happened to the shape of the pocket after each amino acid change (i.e. tack change)?
b. Do you still think the lactose will fit in the pocket?
c. How do you think these changes would affect the ability of lactose to break down lactose?
d. What might happen to the person who has this abnormal protein? Would they be able to break down lactose?

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Think/Pair/Share: Have students try it on their neighbor then share with the class.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?
- Predictions: Would this change if they were to ____?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

  For example: Student: "Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too."
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.
  For example: Student: "Why do you think that changing amino acids makes a difference?

Follow-up Questions: Use follow-up questions, such as "WHY" and "HOW DO YOU KNOW THAT" when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together to explain ____? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today's activity help us think about ___?
- How does this connect to ____?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, "How come DNA is passed to the offspring?"

Teacher, "Why do YOU think DNA is passed to the offspring?"

Checkpoint:

Based on what you learned from these activities with protein models, what general statements can you make about amino acid sequence in proteins and its relationship to function?

Answer:

1. The amino acid organization (i.e. the arrangement of amino acids) in the protein determines the protein's shape or structure.
2. If the protein structure is disrupted the function of the protein could be affected

Note - Students may not immediately come up with these ideas. If this is the case, ask prompting questions like: since you just related changes in the order of amino acids to protein shape or structure, what can you say about this relationship?

Section VI. Examples of proteins

Purpose: Explore specific examples of proteins and how they do their work. The point is for students to

1) review some basic types of proteins and the different types of work that proteins do
2) develop better images in their minds of how protein shape is important to function.
3) allow students to review the protein examples they have seen and the examples they will encounter later (tyrosinase, lactase, LDL receptor, hemoglobin)

Teacher Explanation - Protein example

Remind students of the importance of protein shape to function.

Remind them of the analogy of proteins to machines (such as drills, screwdrivers, and screw).

Demonstrate how to make a comic strip to show what type of work tyrosinase does. (Example in the Appendix)

Ask the students to answer the following questions about your demonstration:

a) What work is the protein is doing? (putting 2 things together, tyrosine and oxygen)
b) How is the shape of the protein here important for its function? (Molecules have to fit)

c) What would happen to this cell if the protein could not work? (it would not make DOPA, and then melanin would not be made either)

Group work - How do proteins do their work - Reader pgs. 40-48

Divide students into groups and assign each group a protein to work with. Have the students read the relevant part of the student reader and generate their own comic strips. Encourage students to be creative and use their own analogies. Depending on time, provide the materials for students to make larger posters or generate a class comic book.

Groups working on lactose should show a protein breaking a molecule.

Groups working on hemoglobin should show a protein moving oxygen.

Groups working on LDL receptor should show a protein bringing LDL into cells.

All groups should demonstrate that their protein has a specific shape and that the shape matches the substrate.

Instructional note - Background information

If you would like more information on other types of proteins, you can check out the following website which lists other type of proteins.

http://www.imb-jena.de/~rake/Bioinformatics_WEB/proteins_classification.html

Once the groups have finished their comic book, ask each group to share their project.

Assessment opportunity - Comic strips provide students an excellent chance to explain their understanding of proteins using their own analogies, words and pictures. Push the students to explain their work both to you and their classmates. Check to make sure that your students are using terms appropriately and understand the structure function relationship and the role that their protein plays in a trait.

Help students synthesize general themes after sharing their representation. Ask students the following questions in a whole class discussion. Students can record answers in student guide.

a) What kind of things did the proteins do?
Answer: Stick things together, break things apart, move things from one place to another

b) How was shape important for each type of protein
Answer: The lactose fit into a mouth in lactase as did the tyrosine into a pocket in tyrosinase. The LDL particle fit into a mouth in the LDL Receptor and oxygen in hemoglobin.

c) A cell from your small intestine and a cell from your skin do very different things. One releases digestive enzymes to break down food while the other protects you from the outside world.

However, these cells both have to take in oxygen and sugar. Based on the activity above, explain how it is that these cell types can do very different things, while also doing some of the same things?

Answer. Some proteins are found in all cell types and allow them to carry out the same function in all the cell types, but some proteins are unique to only one type of cell and allow the cell to carry out a unique function.

Student Reader - Circle chart

The Circle Chart is the chart on page 2 of the student reader. The intention of this chart is to allow students an opportunity to make connections between the levels of trait, biology and environment, a concept many students struggle with. Throughout the unit, the students will revisit the chart and fill in information as they learn it.

Consider making a large chart and keeping it in a public place for use throughout the unit.

Ask students to turn to the correct part of the students reader. Prompt students to think about what they have already learned.

- What traits have they learned about? (skin color, lactose intolerance)
- What could they observe on an organism level? Can they see the color of skin? How can they figure out if someone is lactose intolerant?
- What type of cells would they look at to determine skin color? What type of cells if they were trying to determine if someone was lactose intolerant? Are there differences in those cells that one could see with either of these traits?
- If they could see the proteins in skin cells what type of protein would they see? What protein would they look at to determine lactose intolerance?

Have students fill in the chart with the information discussed. The students might have some ideas about environment that they can include, but the environment will get covered more later in the unit (Lesson 4). A sample of this chart with answers is in the Appendix.

Using the Student Reader- Wrap Up (pgs 47-49)

This last part of the lesson is meant to help the student synthesize all of the information they have learned in Lesson 1. Have the students complete this section. Help the students recall concepts and vocabulary that they have learned thus far. They will revisit these concepts and vocabulary words at later parts of the unit.

Lesson 3: How can two people have different versions of the same protein?

Overview

Objective

The objective of this lesson is for students to learn that genes are instructions for assembling proteins by building protein models from a given DNA sequence; the LDL Receptor gene is used as an example to illustrate this point. Students also learn that DNA is comprised of four chemical subunits and that the order of these subunits determine the amino acid sequence of proteins—students should learn that this is how genes provide instructions for building proteins. Transcription and translation processes are discussed only to help students see the connection between genes and proteins, thus, only overviews videos are shown to students so that students understand the basic idea of what is going on. By the end of the lesson, students should be able to explain that genes are instructions for assembling proteins that changing a gene sequence (i.e. a mutation) can lead to changes in the protein—which can also have negative effects on cell function and the health of the organism.

Connection

This lesson is central to understanding what genes and DNA are. This lesson builds off of insight about proteins (function and structure) learned in lesson 2 and provides a rationale for why genes are needed—to provide instructions for making proteins. This lesson also sets the stage for understanding how individual differences can come about (i.e. through gene mutations that affect proteins), understanding that is central to answering the Driving Question of the unit. This lesson also is central to understanding ideas in the next two lessons.

Description

- *Students are introduced to a genetic disease called Familial Hypercholesterolemia (FH) that can be caused by a faulty protein, specifically the LDL Receptor protein. This leads to a discussion of how proteins could be built improperly because the instructions for the proteins (i.e. genes) are altered.*
- *Students then consider what might be different or similar among individuals with, and without, FH by looking at hypothetical protein data (either amino acids sequence data and/or gel electrophoresis data).*
- *Students then engage in a class discussion to consider how different people can have different sequences for the same protein; this then leads to discussion of the need for instructions for making proteins and genes.*
- *Students explore models of DNA. Next students build models (Toobers) or part of the LDL Receptor protein using a DNA sequence.*
- *Students then predict and model the effect of mutations on the LDL Receptor protein.*

Learning Goals

National Standards

LG2 Biochemical basis for traits - An organism's traits reflect the actions (and inactions) of its proteins. (AAAS considering this but has not published yet)

LG3 Nature and function of DNA - In all organisms, the instructions for specifying the characteristics of the organism are carried in DNA, a large polymer formed from subunits of four kids (A, G, C, and T). The chemical and structural properties of DNA explain how the genetic information that underlies heredity is both encoded in genes (as a string of molecular "letters) and replicated (by a templating mechanism). Each DNA molecule in a cell forms a single chromosome. (NRC, pg 185, 9-12:C2#1)

LG4 Genes as information for proteins - The genetic information in DNA molecules provide the instructions on assembling protein molecules. The code is virtually the same for all life forms. (AAAS, pg. 114, 5C:9-12#4)

LG5 Molecular nature of genes and mutations - Genes are segments of DNA molecules. Inserting, deleting, or substituting DNA segments can alter genes. An altered gene may be passed on to every cell that develops from it. The resulting features my help, harm, or have little or no effect on the offspring's success in its environment. (AAAS, pg. 109, 5B:9-12#4)

LG6 Heritable material - The information passed from parents to offspring is coded in DNA molecules. (AAAS, pg 108, 5B:9-12#3)

Michigan Standards

B2.2 Organic Molecules - There are four major categories of organic molecules that make up living systems: carbohydrates, fats, proteins, and nucleic acids.

B2.2C Describe the composition of the four major categories of organic molecules (carbohydrates, lipids, proteins, and nucleic acids).

B2.2D Explain the general structure and primary functions of the major complex organic molecules that compose living organisms.

L4.p2 Heredity and Environment (prerequisite) - The characteristics of organisms are influenced by heredity and environment. For some characteristics, inheritance is more important. For other characteristics, interactions with the environment are more important. (prerequisite)

B4.1 Genetics and Inherited Traits - Hereditary information is contained in genes, located in the chromosomes of each cell. Cells contain many thousands of different genes. One or many genes can determine an inherited trait of an individual, and a single gene can influence more than one trait. Before a cell divides, this genetic information must be copied and apportioned evenly into the daughter cells.

B4.2 DNA - The genetic information encoded in DNA molecules provides instructions for assembling protein molecules. Genes are segments of DNA molecules. Inserting, deleting, or substituting DNA segments can alter genes. An altered gene may be passed on to every cell that develops from it. The resulting features may help, harm, or have little or no effect on the offspring's success in its environment.

B4.2C Describe the structure and function of DNA.

B4.2D Predict the consequences that changes in the DNA composition of particular genes may have on an organism (e.g., sickle cell anemia, other).

B4.2x DNA, RNA, and Protein Synthesis - Protein synthesis begins with the information in a sequence of DNA bases being copied onto messenger RNA. This molecule moves from the nucleus to the ribosome in the cytoplasm where it is "read." Transfer RNA brings amino acids to the ribosome, where they are connected in the correct sequence to form a specific protein.

B4.2f Demonstrate how the genetic information in DNA molecules provides instructions for assembling protein molecules and that this is virtually the same mechanism for all life forms.

B4.2g Describe the processes of replication, transcription, and translation and how they relate to each other in molecular biology.

B4.4a Describe how inserting, deleting, or substituting DNA segments can alter a gene. Recognize that an altered gene may be passed on to every cell that develops from it and that the resulting features may help, harm, or have little or no effect on the offspring's success in its environment.

B4.4c Explain how mutations in the DNA sequence of a gene may be silent or result in phenotypic change in an organism and in its offspring.

[The learning goal addressed in this lesson is darkened.]

Learning Performance(s)
Students determine what the amino acid sequence of a protein given a DNA sequence.
Students assemble models of protein molecules based on a prescribed DNA sequence.
Students predict the affect of changing the DNA sequence on protein structure and function.
Students use models of proteins to show the effect of deletions, insertions, or substitutions on protein structure and function.

Prior Knowledge

- Cells: Students should realize all living organisms are comprised of cells and that for humans (as well other animals and plant) have tissues and organs that are comprised of many cells. Students should also know that cells have a nucleus which is an organelle in the cell. They will learn in this lesson that the nucleus contains DNA.
- LG1 (Nature and function of proteins): Students need to be familiar content covering proteins from Lesson 2, especially the idea that proteins are long chains for amino acids and that the order of amino acids determine the protein shape, which in turn is determines the protein function. Students should have been introduced to the LDL Receptor protein from 2 (if students did not get this content from the previous lesson, more time will have to spent talking about how this protein works and functions).

Student Misconceptions

1. Students are unaware of central role proteins play in biological processes.
2. Some students are unclear about where genes are found -- some students think genes are found in places other than the nucleus of every cell (i.e. such as in “the blood” or “the brain”)
3. Some students don’t always realize genes exclusively code for proteins or that a gene produces a product. Students sometimes think genes can also code for cells and cell functions (something beyond proteins).
4. Some students have difficulty making connections between genes and proteins.
5. Some students have difficulty understanding the function of RNA.
6. Some students are unaware that nucleotides are actually a unit on the DNA strand, and that the letters “A,T,G, C” each represent one of these units on the DNA strand.
7. Some students are unclear about the relationship between chromosomes, genes and DNA and often mislabel these parts. Related to this challenge, students are unclear where all chromosomes, genes, and DNA are located.
8. Some students may be able to connect genes to protein by listing all the pieces, but still be unable to transfer knowledge about this connection to explain the underlying cause to a disease or physical appearance they have not studied before.

Time

4-5 days

Materials

PowerPoint slides and projector

Student readers

Toobers and thumbtacks

DNA modeling kits

Materials for modeling transcription and translation (sequence handout, string is optional)

Section I: FH and the LDL Receptor Protein

Purpose: Set students up to explore the differences in people that result from differences in genes by talking about differences in people with FH. Students analyze hypothetical gel electrophoresis data and amino acid sequence data of the LDL Receptor protein

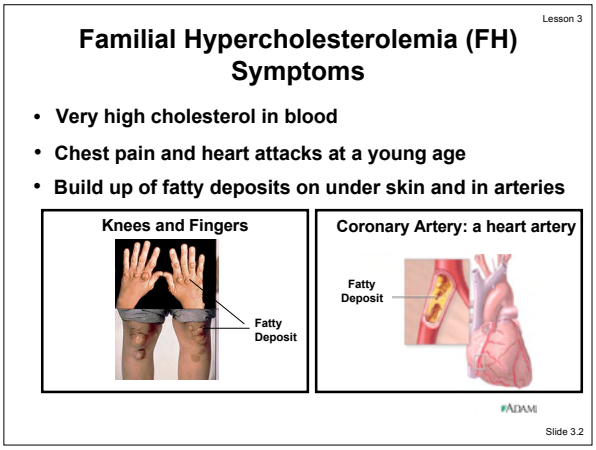
Student reader - Familial Hypercholesterolemia - pgs. 51-53

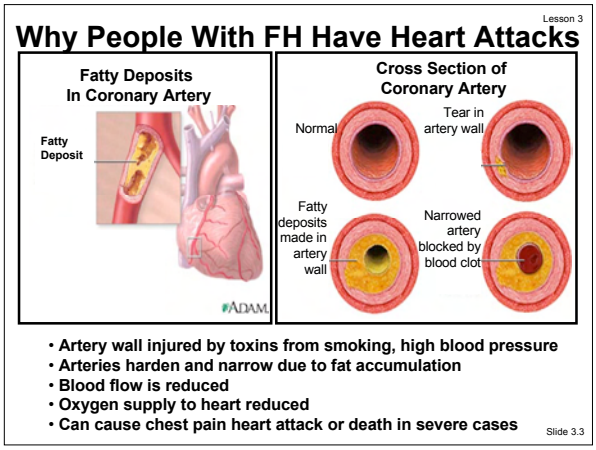
Ask the students to read about familial hypercholesterolemia and answer the questions that follow.

Summarizing discussion - Familial hypercholesterolemia

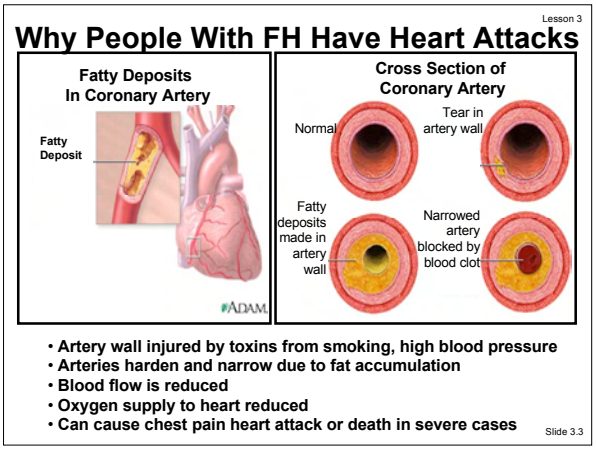
Discussion Rationale: Students should understand that in FH, the LDL receptor does not function properly. They should be prepared to think about what might be the instructions for making proteins.

Slide 3.1 - Ask students what they think might cause this disease. The pictures show fatty deposits on the knees and fingers. If the students have done the reading, they might guess familial hypercholesterolemia.





Slide 3.2 and 3.3 - Review with students Familial Hypercholesterolemia (FH for short) a disease that results when the LDL Receptor Protein does not function properly. Go over symptoms. Explain how there are people with a disease called FH in which cholesterol builds up in the blood stream and forms fatty deposits (or plaques) in arteries which eventually block blood flow through arteries and which can lead to chest pain and even hard attacks.



Slide 3.4 - Ask students to recall the function of the LDL Receptor protein and go over its role in taking in LDL and cholesterol. Ask students to recall its function (may want to provide hints if they do not remember its function). Go over its function in taking in LDL and associated cholesterol from the blood stream. Show the image of this protein in a cell and ask students if they remember this image and what the LDL Receptor is doing in it. All students need to know is that cholesterol is a fat molecule found in the cell membrane that is modified to form other molecules with similar structures like the hormones testosterone and estrogen – students do not need to know the details of any structures.

Discussion Strategies: You can have the students fist try it on their neighbor, then reconvene as a class and share their explanations.

Here are some points/questions to guide you:

- What do you think might cause the disease?
- Let's review the function of LDL and how it is associated with cholesterol.
- Ask students what they might find if they looked at the LDL receptor in a healthy person as compared to a person with familial hypercholesterolemia.
- Students should consider the fact that the LDL Receptor protein might not function properly in the person with FH. There might be a different amino acid sequence.
- Ask how a person with FH could end up with a different LDL Receptor protein. Set up students to think about genes and proteins (the central topic of this lesson).
- Ask how can two people have different amino acid sequences for the same protein?

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?
- Predictions: What do you think would happen if a person's LDL functioned appropriately?
- Do you think this is something that can be passed to offspring?
- What are some things from the environment that can make this disease worse? Better?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

  For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.
  For example: Student: “Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together into one process that explains how proteins are made? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Instructional note - Student conceptions

As a reminder from lesson 2, some students confuse the difference between amino acids and protein— sometimes students will call proteins amino acids, or they will call amino acids proteins.

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Reviewing discussion - Genes are sets of instructions

Discussion Rationale: Through class discussion, help students understand that some sort of instructions must be used to put amino acids into the right order. Identify "genes" as the instructions that provides information for assembling specific proteins.

Discussion Strategies: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

Here are some points/questions to guide you:

Remind the students about modeling part of the lactase protein using Toobers. Ask them how they knew what amino acids to use and what order to put them in?

Ask them where they think their cells get the "instructions" for how to make lactase? What about the directions to make tyrosinase or LDL receptor.

Ask the students if they have ever used instructions to make things before? They all followed instructions to model proteins with Toobers, but they might have made, cookies, or built a model car, or helped put together furniture.

Ask the students what were important aspects of the instructions they followed? Did the instructions tell them which parts to use? Did the instructions tell them what order to put the parts together?

Ask the students what information they think instructions for making proteins should have? What instructions did they need to build their Toobers?

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Think/Pair/Share: Students can try it on their neighbor first, then share with the class.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

  For example: Student: "Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too."
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.
  For example: Student: "Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together into one process that explains how proteins are made? What happens 1st, 2nd . . . ?
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Supporting Communication

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Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Explain that the instructions for making proteins is in genes.

If your class has already discussed genes as they relate to heredity, tell the students that these are the same genes, but that now we are going to look at what genes actually look like and how genes work in cells.

Explain that students need to consider genes as “instructions for making proteins” and that all proteins have a corresponding gene. So every protein they have learned about from the previous lessons has a gene that provides instructions for building it.

Students are likely to hold onto the idea of genes relating to heredity. Build on these ideas. Ask them where they got their genes? If genes are the directions for how to make a specific protein, do they think that their parents make the same proteins as they do?

Ask students what they think would happen if the instructions for making their Toobers were changed?

Would they have made the same shape protein?

What does this mean if genes are changed, for example, if the gene for the LDL Receptor protein was changed how would this affect the LDL Receptor protein?

Checkpoint:

What do you think a gene is based on your discussion of genes in this section.

Students should understand a gene is instructions for a protein. It tells you what amino acids go into a protein and in what order.

Students should also still connect genes to herdity.

Section II. What are genes and what is DNA?: Lessons from the LDL Receptor.

Purpose: Introduce students to the nature of DNA and allow them to identify the important structural characteristics relevant to DNA (see below for characteristics students should identify).

It is advised that teachers try to assemble the DNA models on their own prior to doing it in class so that they are familiar with what has to happen.

Group activity - Building models of DNA - Reader pgs. 55

Ask students if they know what genes are made of

If no one knows, tell them they are made of DNA.

Ask if anyone knows what DNA looks like?

Some students might have some ideas, but this question is mostly to lead into the building of DNA models.

Tell the students that today they are going to build a model of DNA.

Divide the students into groups and give each group a kit with the components to build the DNA models. (Note: these kits have been slightly modified from the packaged version: the DNA bases are labeled with A, C, T, or G; the deoxy-ribose and phosphate chains are intact to reduce the amount of time spent on a part of the activity with less instructional value.) Direct the students to the instruction for building their models in their student readers.

The point here is not to tell students what the structure is, but to allow students to explore and find out some of features on their own.

It might take students a while to assemble the whole model.

Help students figure out what the order of the bases is in their model. It will differ between the groups depending on how they put the bases on the model. This is the first step in reading the instructions for

making a protein?

Reconvene the groups and discuss the following questions

a. How many different types of pieces are found in the center? Are there any patterns to how these pieces fit? What are they?
b. How many different pieces are found on the outside of the model? Is there a pattern to these pieces? What are they?
c. What else did they notice about their models? Does it look like what they expected?

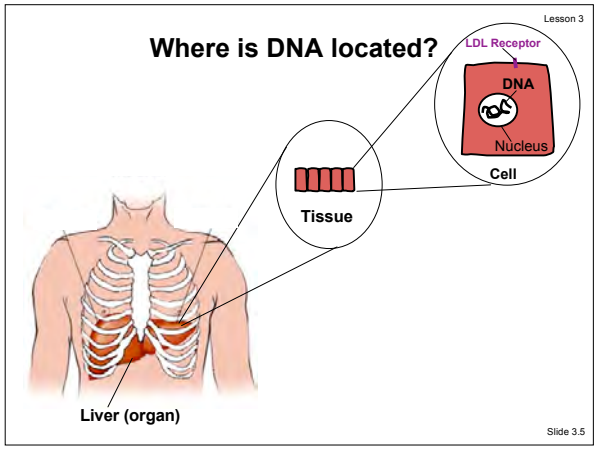
Teacher Explanation - What is DNA? Where is DNA? How is DNA organized?

Instructional note - Student conception

Some students incorrectly separate DNA and genes (in other words they often think they are separate entities) and do not realize that genes are segments of DNA. Some students may think that DNA or genes, or both, are located in the cytoplasm of the cell and not in the nucleus. Some students may think genes act all over the cell and have a very unclear understanding of where DNA and genes are located. Some may not appropriately relate DNA to genes. Some students confuse genes and chromosomes and don't' always know the proper relationship between these.

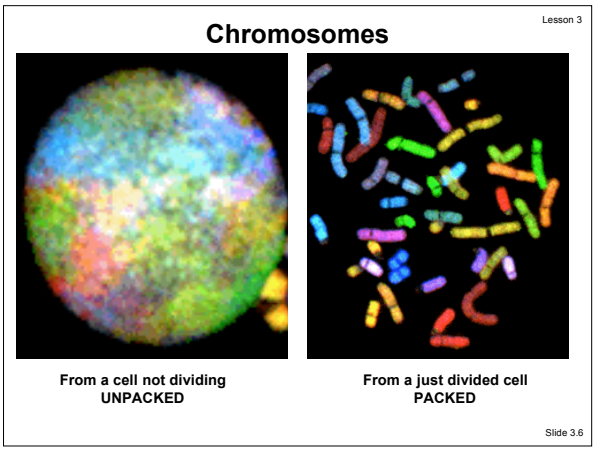
We give several opportunities in this unit to talk about the relationship between these entities during this unit— during such opportunities ask students questions that push them to identify these relationships and after students identify relationships, clarify them as explicitly and clearly as possible.

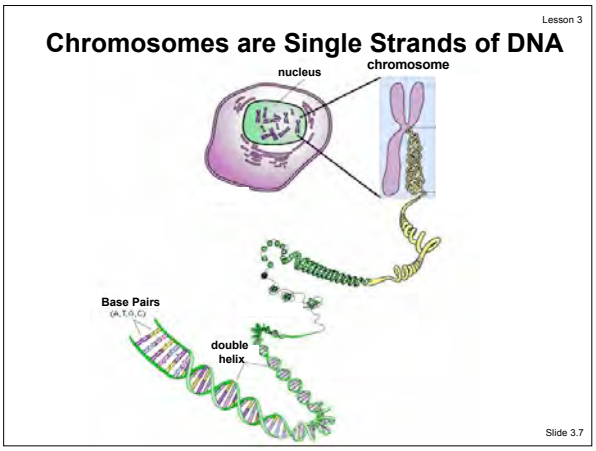
Show the "What is DNA?" movie.



Slide 3.5 - Ask students where they think DNA is located— because in order to know how genes are read to make protein, we need to know where DNA is located. Do they think DNA is in every cell? The cartoon image emphasizes the relationship between DNA, cells, and tissues/organs.

Point out that DNA is found in nucleus, which is in a cell, which is in a tissue, which makes up an organ, which make up our bodies (students often have difficulty with levels of scales, so take opportunities to move through the scales with the students). Also point out that this image only shows a liver cell, but in fact, DNA is in every cell of our body. It is in the nucleus of our bone cells, skin cells, brain cells, muscle cells, etc. We just show a blow up of a liver cell because the LDL Receptor protein, which was discussed earlier, is found in liver cells.





Slide 3.6 - These are two different pictures of chromosomes in nuclei of cells. Explain to student that chromosomes are very long pieces of DNA with thousands of genes on them. In this case each chromosome is stained with a different color.

Chromosomes can be packed or unpacked.

Slide 3.7 - Show another representation to show how chromosomes are actually one long strand of DNA tightly folded and wrapped up and point out that a gene is just one small segment of this. Multiple representations are shown to help students realize that chromosomes are actually one strand of DNA tightly folded and wrapped up. Point out that a gene would be just a tiny segment along this DNA strand.

Instruction note - Consider using a Semantic Feature Analysis Chart or Concept Card

At this point in the lesson the students have been introduced to some new or poorly understood vocabulary. Consider using a strategy to help your students sort these words out and start to figure out how they are related. Think about comparing genes, chromosomes, DNA, and bases. How are they the same? How are they different? How are they related to each other? (See the front matter and appendix for templates/examples of these strategies)

Instruction note - Student conception

Teachers and researchers note that students often do not realize that the “A, T, G, & C” represent molecular subunits of DNA. Therefore, it is important to explicitly point out that these letters represent part of the DNA strand. We suggest circling, pointing directly on image, or indicating the bases in a strand of DNA when introducing Adenine, Thymine, Guanine and Cytosine.

Checkpoint:

Ask students: What is the relationship between DNA, a gene, and a chromosome and where genes are located?

Student should realize that chromosomes are made of DNA and that just one segment of this DNA strand is a gene. Genes are found in the nucleus because they are located on chromosomes, which are in the nucleus.

Consider assessing students by using the analogy of instructions. What is one set of instructions? Lots of sets of instructions? The language of the instructions?

Section III. How does the cell “read” a gene to make a protein?: Lessons from the LDL Receptor

Purpose: Students assemble part of the LDL Receptor protein (in the form of a Toober) from a DNA sequence to understand how genes can provide instructions for making proteins. This serves to reinforce the idea that genes are instructions for assembling proteins.

Teacher explanation - How to decode DNA - Reader pgs. 61-62

Briefly remind student what the function of LDL Receptor is and its effect on cholesterol from the beginning of the lesson. Show the image of this protein in a cell and ask students if they remember what its function is.

As discussed earlier, if there is a protein there must be a gene.

Tell students they will now learn how to read a cell’s instructions for assembling protein. Explain that in order to learn this, they will build a model of part of the LDL Receptor protein from part of a gene.

Instructional note - Student conception

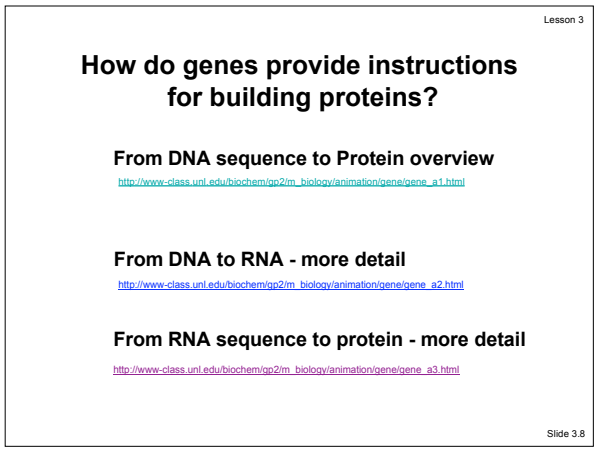
Students don't always realize that the letter symbols A, G, C and T represents actual chemical units as part of a longer molecular chain. Be explicit and point out this point out or indicate on representation what the letter in DNA represent.

Ask students the following:

> If genes are made of DNA, and we need genes to tell us how to make proteins, and proteins do all the work of the cell, how important is it to keep out DNA safe?
>
> Hopefully they will understand that it is very important to keep DNA safe.

Explain to students that to keep DNA safe, it is always stored in the nucleus.

Show the animations movies of transcription and translation at the websites below . It is important for students to see the molecules in motion to help them understand the process of transcription and translation.



Overview video: from DNA to protein

http://www-class.unl.edu/biochem/gp2/m_biology/animation/gene/gene_a1.html

For the animations, it may be useful to tell student to ignore printed text in the animations and simply listen to you narrate what is going on in each, so that they can focus on what is a happening at each step. It may be useful to emphasize what is important and what is not important to focus on. This is a strategy that one can employ whenever a video or diagram is shown that includes a complicated molecular or cellular process. Can also tell students ahead of time what they will see and what they need to focus on.

Make sure the students understand the following:

i. A special protein machine binds to DNA and makes an RNA copy of the gene.
ii. One important difference between DNA and RNA is the instead of Thymine (T), RNA uses Uracil (U) which can pair with A.
iii. The RNA is moved to the cytoplasm where the ribosome “translates” the instructions from the genes into a sequence of amino acids to make a protein
iv. The sequence of DNA bases determines the order of bases in the RNA strand, and consequently the order of amino acids in a protein. (Ultimately, the order of the amino acid sequence is determined by the DNA sequence).

Model for the students how to go through the process of reading the instructions in a gene that is made up of DNA.

Ask the students to keep track of the steps in their student reader.

STEP 1 - Start with a gene written in DNA. One is written below as an example, however, using an assembled DNA model for your starting sequence (or assembling it to match this one) will help students to make the connection between the model they made and the activity they are doing now.

```
TACAAAGGACGAATA
|||||||||||||||
ATGTTTCCTGCTTAT
```

STEP 2 - Split the DNA so that the RNA copy can be made

ATGTTTCCTGCTTAT

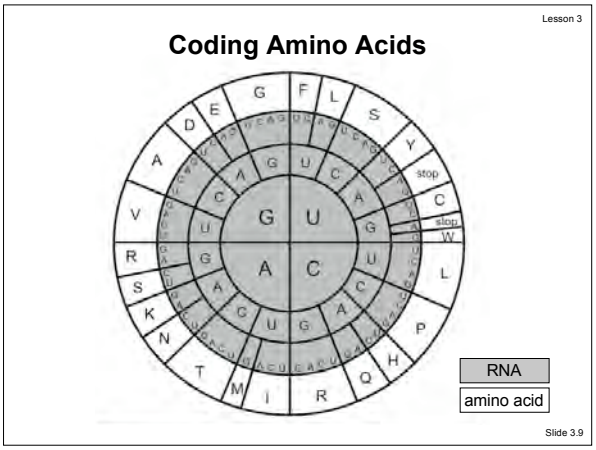
STEP 3 - Make the RNA copy of the gene match As to T, Gs to C, Cs to G, and Us to A.

UACAAAGGACGAAUA

STEP 4 - The ribosome looks at RNA three letters at a time so it is helpful for us to break it up in the same way:

UAC|AAA|GGA|CGA|AUA

Explain to students that the code is read in a series of 3 bases. Go over chart and amino acids that are coded by each triplet. Students need to understand that.



STEP 5 - Use the circular “decoder” to figure out what amino acids to use and in what order:
Y - K - G - R - I

There are specific sequences of bases in the code that mark the end of a protein sequence. These are the sequences that are marked STOP on the decoder. If your RNA has one of these, that is the end of the protein

Group activity - Making a model of transcription and translation - Reader pgs. 63-64

Shift back to the LDL Receptor and point out where the genes for the LDL Receptor is located. Before letting students determine the LDL Receptor amino acid sequence, show the image of chromosome 19 and the location of the LDL Receptor gene. This is to emphasize that a gene is one segment of a chromosome, but make sure students do not confuse genes with whole chromosomes because this is a point of confusion for some students. Students need to realize that genes are only tiny segments of whole chromosomes.

Break students into groups so that can begin the process of modeling how to build the LDL Receptor protein models. Tell students the LDL Receptor is really big (800 amino acid long), and this would take too long to make in class, so we will only make part. We will make the part that binds the LDL molecule.

Depending on the layout of your classroom, groups can model on a large table top or desk pushed together. Each table top will be a 2-D model of a cell and the students will work the parts of the cells.

Ask the class to generate a list of all the parts their model will need to model a liver cell making an LDL receptor protein:

> cell membrane (the edge of the tables), nucleus (a string or a piece of paper), DNA with a gene (to be passed out), RNA (blank paper that can be written to match DNA sequence), ribosome (the students themselves) amino acids (thumbtacks), LDL receptor (to be made with Toobers)

Make sure that each group has the appropriate materials.

Tell the students that you will give them a sequence of part of a gene and they should help the cells work and do the jobs of transcription and translation. They should be careful to make sure that all the processes take place in the right place.

Where does transcription (DNA to RNA) take place? (Nucleus)

Where does translation (RNA to protein) take place? (cytoplasm)

Give each group the following DNA sequence:

```
TGGCGCTGTGATGGTGGCCCCGACTGCAAGGACAAATCTGACGAG
||||||||||||||||||||||||||||||||||||||||||||
ACCGCGACACTACCACCGGGGCTGACGTTCCTGTTTAGACTGCTC
```

Check in with the groups on the following points:

Is the DNA in the nucleus? Is it staying there?

Does the RNA use Us instead of Ts?

Are they using the decoder in the reader in the correct way?

Each group should record what the RNA sequence is, what the protein sequence is, what the Toober looks like in their Student Reader. In groups students determine the RNA sequence corresponding to the DNA sequence.

Students should come up with the following mRNA sequence:

UGG CGC UGU GAU GGU GGC CCC GAC UGC AAG GAC AAA UCU GAC GAG

Note that since this sequence is from the middle of the protein there is no stop

Students should come up with the following amino acid sequence corresponding the mRNA sequence determined from above.

W R C D G G P D C K D K S D E

(amino acids 213-227) Sequence for the full length LDL receptor can be found in the appendix.

Discuss as a class the main points of this exercise. First, ask students what they just did in class and how was this different than in lesson 2 where they made the lactase protein? Then ask the questions raised in the checkpoint box below. Guide students to suggested answers in checkpoint box, if do not

come up with them immediately, by pressing them with additional questions. Students should record answers to discussion questions in student guides. Can add box with lesson 3 to poster with driving question.

Checkpoint:

Ask the following questions to assess student understanding of genes and how they are used to code for proteins. Discuss in class and have students record in student readers..

1. Given what you have learned from the activity with the LDL Receptor, how would you now define a gene:

A gene is a segment of DNA that determines the amino acid sequence of a protein.

2. From activities in this section, describe how genes are used as instructions to make proteins?

An RNA copy of is made of a DNA sequence, the RNA is moved to the cytoplasm, where it is read in groups of three bases. The order of the bases determines the order of the amino acids in a protein.

Section IV. How two people have different versions of the same protein: the effect of gene mutations.

Purpose: Introduce students to notions of mutation and types of mutation. Link mutations in a gene to changes in protein structure and function. Explore nucleotide substitutions, deletions, and additions.

Student Reader - Mutations - Reader pgs. 65-67

Ask the students what they think a mutation is. Assign the reading about mutations and explain they will read more about mutations. This text will help students learn about the various mutations they will encounter in the next activity. This reading contains some new vocabulary for the students (mutation, deletion, insertion, substitution.) Consider using a Semantic Features chart to help student understand these ideas.

Group activity - Determining the effect of mutations - Reader pgs. 68-71

In groups, students determine the effect of specific mutation on the LDL Receptor protein. Tell students they will know use their knowledge of genes and proteins to predict who might have FH?

Tell students that the DNA sequence for the LDL Receptor was determined for 5 individuals. Each of the individuals is a young person who has high cholesterol. The doctor is unsure of whether it is FH or another disease. The students will determine the likelihood that it is FH based on the sequence of the LDL receptor.

Ask the students what they will need to do to determine this?

Have students identify what is different in each of the sequences, then convert the sequences to mRNA sequence to determine what affect the sequence will have on the proteins, and what is the health status of the individual. Students will see addition, deletion and substitution mutations most of which result in an amino acid sequence difference. Assign each student or group of students one of the mutations to focus on. Each student or group will be responsible for reporting back their results to the group.

When students report their findings, make sure they answer the following questions:

- What was the nucleotide change for the mutant sequence?
- What effect did the mutation have on the amino acid sequence? (First, convert the DNA sequences to RNA sequences, then determine the amino acid sequences)
- What affect might each mutation have on function of the protein encoded? (Could the changed protein still carry out it's function of binding LDL and taking it into the cell)?
- Is the person with each mutation likely to have FH?

Answers

UGG CGC UGU GAU GGU GGC CCC GAC UGC AAG GAC AAA UCU GAC GAG

healthy

UGG CGC UGU GAU GGU GGC CCC CAC UGC AAG GAC AAA UCU GAC GAG

Substitution, C for G in 1st GAC, substitute aspartate for histidine (neg to pos), LDL Receptor probably does not work, likely has FH

UGG CGC UGU GAU GGU GGC CCC GAU UGC AAG GAC AAA UCU GAC GAG

Substitution, U for C in 1st GAC, no change in amino acid, LDL Receptor should work okay, does not have FH

UGG CGC UGU GAU GGU GGC CCC GGA CUG CAA GGA CAA AUC UGA CGA G

Insertion (frameshift), G added in front of 1st GAC, many amino acids changed, LDL Receptor probably does not work, likely has FH

UGG CGC UGU GAU GGU GGC CCC ACU GCA AGG ACA AAU CUG ACG AG

Deletion mutation (frameshift), G deleted in 1st GAC, many amino acids changed, LDL Receptor probably does not work, likely has FH

UGG CGC UGU GAU GGU GGC CCC GAC UGA AAG GAC AAA UCU GAC GAG

Substitution mutation, A substituted for C in UGC, stop codon, short protein, LDL Receptor probably does not work, likely has FH

Reviewing Discussion - How do mutations affect proteins?

Review the changes as a whole class and students label type of mutations. Obtain class consensus on the types of changes and identify these changes as nucleotide addition, substitutions, and deletion mutations. Can also label types of changes to proteins as no change, amino acid substitution, new amino acid sequence, or short proteins (due to the formation of a stop codon).

Discussion Rationale: The idea of this discussion is for students to talk about the process of transcription and translation. It also a chance for the students to talk about how mutations can change, or not change the amino acid sequence of a protein, and resulting in the trait of a person. Be sure to allow students to talk through the process they went through and the reasonings for the decisions they made. Make sure that students use complete sentences in their responses.

Discussion Strategies: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

Here are some points/questions to guide you:

What would the students report back to the doctor about the FH status of each patient? How did they come to that conclusion?

Do all mutations in DNA change the amino acid sequence?

What do they think would happen if the mutation caused a change that replaced a hydrophobic amino acid with another hydrophobic amino acid?

When students give answers, here are some things you can do:
Think/Pair/Share: Have student try it on their neighbor, then share with the class.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”

- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.
  For example: Student: “Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together into one process that explains how proteins are made? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
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- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

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For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Optional: Explain briefly how mutations can occur. Explain that mutations can be caused by radiation, a chemical agent in our environment, or on rare occasion can occur spontaneously (spontaneous mutations are essentially typos that occur when the DNA is being copied before cell division occurs). Ask students if they have heard of the term “mutagen.” This refers to an agent that causes DNA mutations. Can mention that these mutations can be passed on to future generations if they exist in sperm or egg cells. As we noticed above, some mutations could be harmful to the organism and some may not be. FH is an example of what can happen if a mutation in a gene is harmful.

Checkpoint:

As a check point ask students how would they define what a mutation is to a friend and how does it relate to people with different protein sequences.

A mutation is any change in a DNA sequence that is different from the normal sequence you would find. Mutations in genes can lead to different amino acid sequences of proteins.

Section VI. Review lesson and connect to driving question

Purpose: In class discussion review main point of the lesson and connect to the driving question.

Video - From Cells to DNA

Use this video to remind students of everything they learned and help them synthesize the information. (Note: this movie is available in the PowerPoint slides for this lesson and must be in view mode of the PowerPoint to play the video; note must also have movie file on computer labeled 3D copy.mov as well as Quicktime. Video is also available on-line at the following website)

http://www.genome.gov/Pages/EducationKit/video/qt/3D.mov

Or use the following website for cartoon animation that steps through one step at a time

http://www.pbs.org/wgbh/nova/genome/dna.html

Research project - Exploring a specific trait or career

One of the main activities that students will do in this unit is a research project on a specific disease or trait. A collection of diseases or traits to choose from can be found in the Research Project Packet at the end of the Reader, pgs. 112-130. It is up to your discretion to decide to let students to choose diseases or traits or careers outside of these.

Students will choose one trait or career to research. Each trait has a little bit of information about it and some websites with some information about the trait. Students main goal is to make a brochure or a poster about the trait they choose. They will share these products with their peers and possibly their communities.

To help students with the final product, several steps are included:
Step 1- Students pick a topics and reflect on why they are interested and what they already know
Step 2- Students use provided websites to help answer provided questions.
Step 3- Students use a provided template and the answers they have researched to generate a final product.

Additionally a rubric for scoring the projects is included. If you wish, students can receive a copy of the rubric so that they understand the criteria on which they will be scored.

It is up to your discretion to establish a time line and to use class time to research and work on the projects..

C. Circle chart

Ask students to return to the circle chart at the beginning of the students reader. Guide students to fill out section of it with the trait relating to high cholesterol.

- What did we learn about the biology of cholesterol?

  There is a protein called LDL receptor which moves cholesterol from outside liver cells to inside to be processed. A gene has the instructions for making the protein. If there is a mistake in the directions, the protein does not get made correctly and the cholesterol cannot be moved and processed.

- Do you think there is an environmental component to having high cholesterol?

  Students might have some ideas about how diet might affect high cholesterol. If so, ask them how it relates to what they learned about the LDL receptor. If not, push them to think about where cholesterol comes from.

Lesson 4: Gene Expression

Overview

Objective

The intent of this lesson is for students to explore similarities and difference at the level of whether or not a gene is being transcribed. They should understand that one of the ways similarities and differences manifest is through differences in gene transcribing. Students will get the opportunity to use data to draw a conclusion about how genes might be turned on or off. The understanding of genes turning on and off provides the foundation for thinking about how the environment might play a role in some of our traits. Students will practice using their understanding of genetics to make ethical decisions.

Connection

The students will connect to what they have learned about gene transcription and translation. Additionally they will revisit the trait of lactose-intolerance.

Description

- *Students learn about gel electrophoresis as a technique for examining proteins, RNA and DNA*
- *Students explore the case of lactase, where the gene is there, but the protein is not.*
- *Students read about the effect of the environment on skin color.*
- *Students discuss how the environment and genes both play a role in their traits.*
- *Students have an ethical discussion to make a decision about how athletes should be allowed to alter their levels of the protein EPO.*

Learning Goals

National Standards

LG2 Biochemical basis for traits - An organism's traits reflect the actions (and inactions) of its proteins. (AAAS considering this but has not published yet)

LG7 Different cells use different genes - The many body cells in an individual can be very different from one another even though they are all descended from a single cell and thus have essentially identical genetic instructions. Different parts of the instructions are used in different types of cells, influenced by the cell's environment and past history (AAAS, pg. 109, 5B:9-12#6).

LG8 Environment and genes - Most physical and behavioral characteristics that an individual possess are the combination of both genes and environment. (AAAS considering this but not published yet)

Michigan Standards

B2.2g Propose how moving an organism to a new environment may influence its ability to survive and predict the possible impact of this type of transfer.

B2.6x Internal/External Cell Regulation - Cellular processes are regulated both internally and externally by environments in which cells exist, including local environments that lead to cell differentiation during the development of multicellular organisms. During the development of complex multicellular organisms, cell differentiation is regulated through the expression of different genes.

B4.1 Genetics and Inherited Traits - Hereditary information is contained in genes, located in the chromosomes of each cell. Cells contain many thousands of different genes. One or many genes can determine an inherited trait of an individual, and a single gene can influence more than one trait. Before a cell divides, this genetic information must be copied and apportioned evenly into the daughter cells.

L4.p2A Explain that the traits of an individual are influenced by both the environment and the genetics of the individual. Acquired traits are not inherited; only genetic traits are inherited. (prerequisite)

B4.2C Describe the structure and function of DNA.

[The learning goals addressed in this lesson are darkened.]

Learning Performance(s)
Students can explain how turning genes on or off can make a specific type of cell like a red blood cell or a melanocyte.
Students understand that the environment and their genes both affect their traits.
Students can use a decision-making framework to make an ethical decision.

Prior Knowledge

Students should understand that cells in different part of the body look different and do different jobs.

Students should have completed the previous lessons and understand the process of transcription and translation.

PREPARATION

Time

3 days

Materials

PowerPoint slides and projector

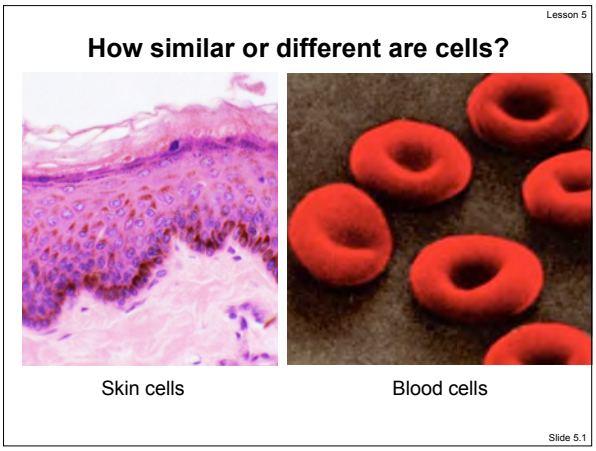
Student readers

Instructional Sequence

Section I: How similar or different are red blood cells and skin cells?

Purpose: The purpose of this section is to introduce students to the idea that while all of our cells have the same DNA and therefore the same genes, they do no have the same proteins. Students should begin to understand that genes can be turned off or on. Cells control the amount of RNA made and thereby control the amount of protein made.

Generating discussion - How are different cells different



Discussion Rationale: Students should realize the genes have switches and can be turned on or off. They should also realize that done difference between cells is that their proteins are different because that have different genes turned on or off. The idea is for students to learn that genes can be turned on or off. For all genes there are “switches” near genes that allow cells to control how much RNA is made. If the cells are making a lot of RNA for a specific gene, they can also make a lot of protein. If the cells are not making any RNA they can’t make that protein.

Also, this discussion is to help students share ideas openly without fearing evaluation.

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

Here are some points/questions to guide you:

Slide 4.1 - Show student the pictures of cells that they have seen before: skin cells and blood cells. Ask them what types of work these cells do? If they do different types of work, do they need to have different types of proteins?

Do they think there is hemoglobin in the skin cells? Is there tyrosinase in blood cells?

Help students understand that different cells have different proteins to accomplish their different jobs. A blood cell doesn't need to make melanin so it doesn't have tyrosinase. A skin cell doesn't need to transport oxygen so it doesn't have hemoglobin. There are some jobs that all cells do: maintain all the parts of the cell, respire, have a membrane. So there are some proteins that you would find in all cells.

Ask the students if all the cells in their bodies have the same genes. To the extent necessary, review mitosis and explain that since all of our cells originated from a single cell, they all have the same DNA. Hopefully, this connects to their previous understanding of mitosis and human development.

How can your cells have all the same genes but not all the same proteins?

How much RNA from the tyrosinase gene they would expect to find in a melanocyte as compared to a red blood cell? Do they think that all people make the same amount of RNA from their tyrosinase gene? What would happen if they made more tyrosinase RNA? Less? Would melanin levels change?

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

For example: Student: "Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too."

- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: "Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as "WHY" and "HOW DO YOU KNOW THAT" when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- What have you observed or experienced?
- What else is on your group's list?
- What do you/other people think about when they hear the word ___?
- Who has a different idea/response/way of thinking about this?
- What do you know about [topic X]?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Student reader - Gene Expression: Genes Can Be Turned On and Off - pgs. 76

In this text, student read that genes can be expressed (transcribed and translated into proteins) based on whether they are turned on or off. There is an explanation of the use of gel electrophoresis and how this technique is used to detect the presence of proteins. Students can use a variety of reading strategies. The suggested strategies are underlining unfamiliar words, outlining the text, or concept cards.

Section II: How do genes get turned off or on? – Exploring the biology of lactase non-persistence or lactose intolerance

Purpose: The purpose of this section is to allow the students to use their understanding of the relationship between genes and proteins to analyze a set of data about a family with some occurrence of lactose intolerance. Students will explore how a mutation near a gene affects the levels of RNA and protein. Additionally students will have the opportunity to connect their molecular understanding of genetics to their classical understanding of genetics.

Generating discussion - Why is Jason lactose intolerant?

Discussion Rationale: Students should be able to think about reasons Jason might be lactose intolerant based on what they have learned about genes and proteins. Additionally they should start to think about finding ways to analyze genes and proteins. Also, this discussion is to help students share ideas openly without fearing evaluation.

Discussion Strategies: Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

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- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: “Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- What have you observed or experienced?
- What else is on your group’s list?
- What do you/other people think about when they hear the word ___?
- Who has a different idea/response/way of thinking about this?
- What do you know about [topic X]?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Here are some points/questions to guide you:

Ask the students to recall Jason's story – Please Don't Pass the Milk, from the Student Reader - Lesson 2. If the students did not read the story or do not remember the story, provide them time to read the story. Ask the students to explain what is happening to Jason in the story. Make sure to discuss the following points:

- Jason doesn't have the ability to break down lactose
- Does Jason have a gene for the lactase protein?
- Does the gene have mutations in it?
- Could Jason's lactase gene be turned off?

Ask students how they would like to go about figuring out why Jason is lactose intolerant? Do they want to look at his genes, his RNA, his proteins, or all of them?

Hopefully students want to look at all of these things to try to figure out why Jason is lactose intolerant.

Ask the students if they have any ideas about how scientist might look at proteins.

> The answer to this question is hard because there are not a lot of good ways to look at proteins since they are too small to be seen with a microscope. Scientists are still looking for good ways to look at proteins. Current techniques focus on taking large samples of proteins and analyzing them in indirect ways - such as gel electrophoresis. The students will read about gel electrophoresis next in the reader.

Where should scientists look if they want to study tyrosinase? What about lactase?

> Hopefully students think to look in the skin and the intestine respectively, if not prompting to recall where their functions are needed might be necessary.

Ask the student to imagine that we have samples of both tyrosinase and lactase and that we are going to use a technique called gel electrophoresis to analyze them. Explain that we can learn two types of information about our samples:

> What size each molecule of protein is
>
> How many molecules of protein we have (relatively)

Student reader - A Closer Look into Gels - pgs. 76-77

This text goes into more depth about what gel electrophoresis is. It explains the process and how they can be used to tell if a gene has been turned on or off. Some of the suggested strategies for this reading are underlining unfamiliar words, outlining the text, or concept cards.

Reviewing discussion - Understanding gel electrophoresis

Discussion Rationale: Students should be able to think about reasons Jason might be lactose intolerant based on what they have learned about genes and proteins. Additionally they should start to think about finding ways to analyze genes and proteins. Also, this discussion is to help students share ideas openly without fearing evaluation.

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

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- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: "Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as "WHY" and "HOW DO YOU KNOW THAT" when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together into one process that explains how proteins are made? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today's activity help us think about ___?
- How does this connect to ____?

Supporting Communication

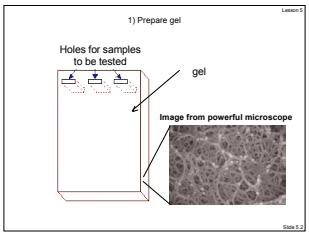
Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

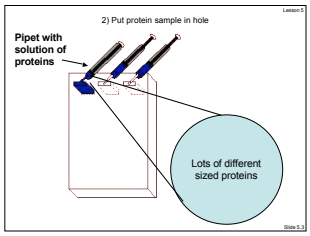
Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

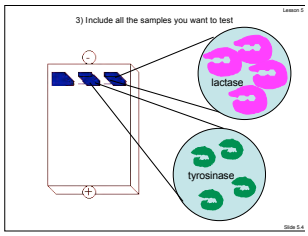
For example: Suzie, “How come DNA is passed to the offspring?”

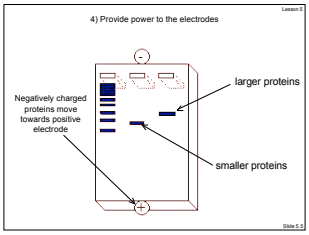
Teacher, “Why do YOU think DNA is passed to the offspring?”

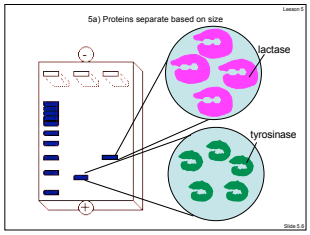
Use the following slides to review how gel electrophoresis works. After reviewing the slides, ask students to explain the various steps.

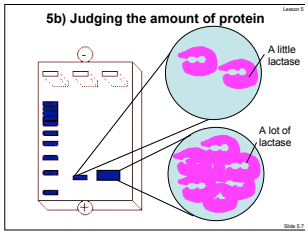


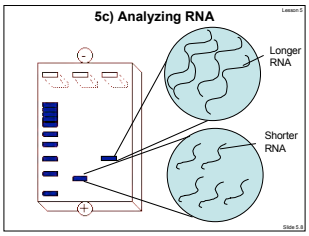


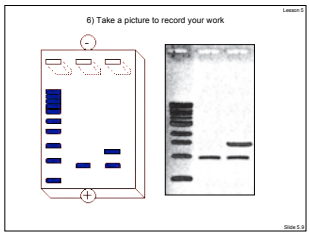












Slide 4.2 - This slide is for a tour of a gel. A gel is a thin rectangular square that roughly has the consistency of a thick Jell-O. If one looked at the gel under a very powerful microscope they would see a thick jungle- like mesh for fibers. There are holes where we are going to add our samples.

Slide 4.3 - We start to add our samples to our gel. The first sample is a solution of lots of different proteins. This will give us something to compare our samples of lactase and tyrosinase to.

Slide 4.4 - We put our samples of lactase and tyrosinase in the holes in the gel. Each sample has billions of lactase and tyrosinase proteins even though only a few are shown.

Slide 4.5 - We turn on the gel by putting a positive electrode at the bottom and a negative electrode at the other end, creating an electric current that runs through the gel. Our proteins are negatively charged so they want to move towards the positive electrode. Ask the students whether they think the small or the big protein can move through the Jell-O like substance more easily? It is easier for small proteins to move through the gel so they move faster than the big proteins.

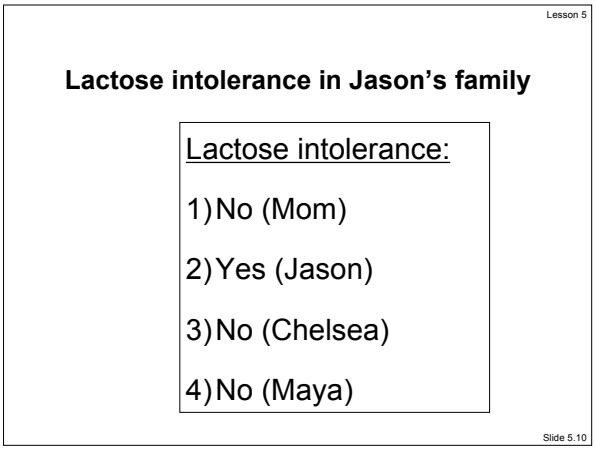
Slide 4.6 - Demonstrate the previous point on the next slide.

Slide 4.7 - Not only can we separate proteins based on size, we can make estimates about how much protein there is. A really dark, fat spot on the gel indicates a lot of protein. A light skinny spot indicates less protein.

Slide 4.8 - RNA gels - We can look at RNA on a gel in the same way that we can look at protein on a gel. In the same way that proteins separate by size, RNA separates by size.

Slide 4.9 - Good scientists always keep a record of their work so we need a picture of the gel. The picture captures all the places where the proteins have moved.

Group work - Exploring data about lactose intolerance - Reader pgs. 78-82



Slide 4.10 - Tell the students that we are going to learn what they already know about genes and proteins and the newly learned gel electrophoresis to try to figure out why Jason is lactose intolerant The first data we have is information about Jason's family - his mom and his two sisters, Chelsea and Maya.

Ask the students why they think Jason might be lactose intolerant? Why does the rest of his family not have lactose intolerance? Have the students record their explanation in their student readers and then share them with the class.

Expected answers hopefully include:

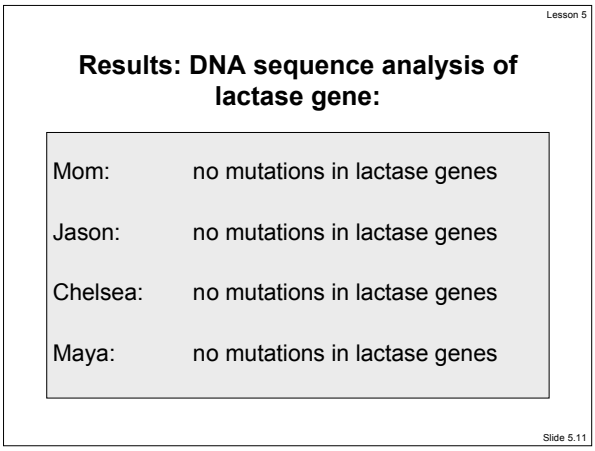
- Jason has a mutated protein
- Jason's missing both copies of the gene for lactase, Chelsea and Mom have 1, Maya has 2
- Jason has a mutation in both copies of the gene for lactase, Chelsea and Mom have a mutation in one of their genes and Maya has no mutations
- Jason doesn't make the RNA for lactase, Chelsea and Mom make some RNA
- Jason makes the protein, but it goes away quickly (degrades) Chelsea's and Mom make a protein that goes away less quickly
- Jason has a gene that is turned off, Chelsea and Mom have genes that not all the way off

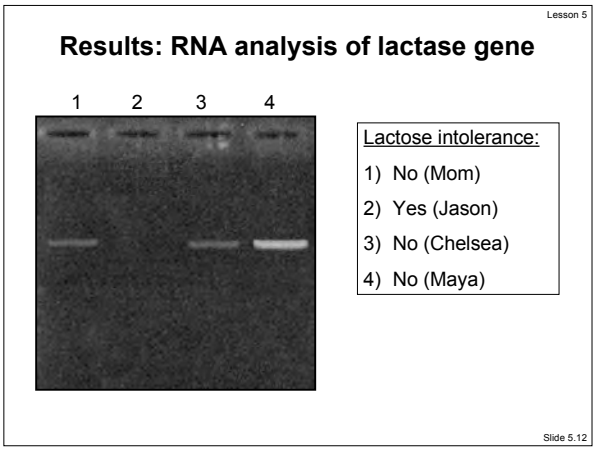
Ask students what type of information or data they would like to look at to determine if their explanation is correct? If the students get stuck here, remind them about what type of data they have looked at before: gel electrophoresis for looking at proteins and DNA sequence for looking at genes.

Divide the students in to groups to analyze data and draw conclusions.

Using the data in their student readers and/or on the slides the students will determine if their explanation is still reasonable. If necessary, they will develop a new explanation that makes sense with the conclusions they will draw from the data. Students will record their analysis in a table provided in the students reader.

(Depending on your class, the student groups could analyze one piece of data and then the whole class could discuss the conclusion, or the student groups could analyze all the data at once and then the whole class could discuss the conclusion or some combination of these two possibilities.)





Slide 4.11 - DNA sequence - All four family members have the same DNA sequence.

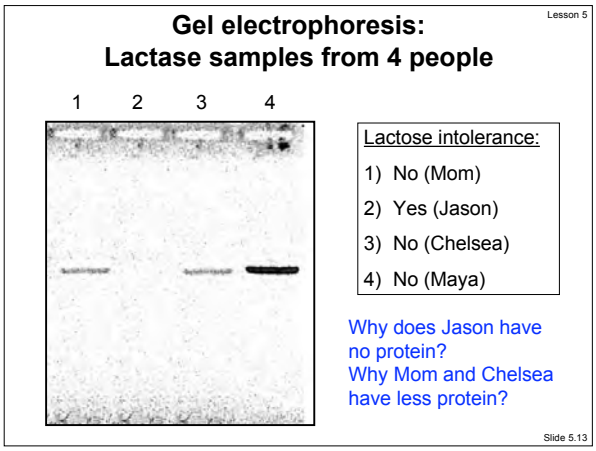
Guiding questions:
- Would their RNA be the same?
- Would their proteins be the same?

Students should conclude that mutations in the gene are not a good explanation.

Slide 4.12- RNA analysis - Jason doesn't have RNA. Mom and Chelsea have less RNA. Maya has the most RNA. All of the RNAs are the same size which is consistent with the results that there are no mutations in the genes.

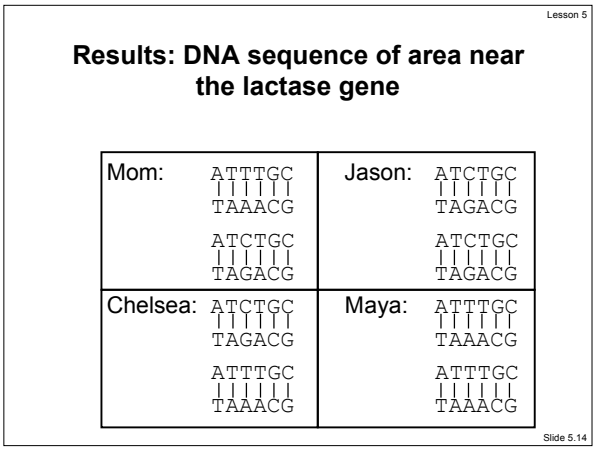
Guiding questions:
- Does Jason have any lactase RNA? Without RNA could he make lactase?
- Do Mom and Chelsea have RNA?
- How much RNA does someone need to make enough protein to digest lactose?
- What is not happening in Jason's cells? Transcription? Translation?
- Do they think that Jason's cells are still making other proteins? Is he still able to digest other foods? Does he need proteins to digest food?

Hopefully students conclude that Jason is not making RNA. Mom and Chelsea are making some RNA which is enough to be able to digest the lactose in their diets. Since Jason is likely to be otherwise healthy, we can assume that all other proteins are being made normally and that there is not a general problem with transcription or translation.



Slide 4.13 - The gel on this slide shows how much lactase each of these people have. These results are similar to the RNA results.

- Does Jason have any lactase? Without lactase could he break down lactose?
- Do Mom and Chelsea have protein? Is this the amount of protein you would expect based on the amount of RNA they have?
- How much lactase does a person need to digest lactose?
- What is not happening in Jason's cells? Transcription? Translation?
- Do they think that Jason's cells are still making other proteins? Is he still able to digest other foods? Does he need proteins to digest food?



Slide 4.14 - Examining DNA sequence - This slide shows a brief 6 basepair segment of DNA that is near the lactase gene. Explain to the students that this region of the DNA is a potentially a switch for controlling whether or not RNA gets made from the nearby lactase gene. Their job is to determine if it could be a switch.

Ask the students why they think there are two different sequences for each person? If necessary, prompt the students to remember where the DNA came from. Like all of their DNA they have two copies, one from their father and one from their mother. When scientists determine the sequence of DNA they can't tell which is which, but they can tell when there is a difference between the two copies. That is what has happened here.

Ask the students if they notice any differences in the sequence of these short segments of DNA? (The 3 basepair is either a C-G or a T-A.)

Do all of the family members have the same set of DNA?

(No, Mom and Chelsea have one of each kind. Jason has two C-Gs and Maya has two T-As.)

If your students have already studied classical genetics, you could prompt them to think about who is a homozygous and who is heterozygous.

Make sure the students fill in the table as they work. The last column can be filled in the discussion that follows.

	Lactose Intolerance	DNA mutations	RNA amount	Protein amount	Switch	Gene on or off
Mom	*no*	*no*	*some*	*some*	*C-G, T-A*	*1 on, 1 off*
Jason	*yes*	*no*	*none*	*none*	*C-G, C-G*	*both off*
Chelsea	*no*	*no*	*some*	*some*	*C-G, T-A*	*1on, 1 off*
Maya	*no*	*no*	*lots*	*lots*	*T-A, T-A*	*both on*

Reviewing discussion - Drawing conclusions from the data

Discussion Rationale: Students should use the data and their understanding of genes and proteins to draw a conclusion about the on/off switch for lactose intolerance. In this discussion, students should also be putting ideas together. Student can be making connections to personal experiences, the driving question, to another lesson, or to knowledge just gained.

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

  For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.
  For example: Student: “Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together into one process that explains how proteins are made? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Here are some points/questions to guide you:

Ask the students to examine their table for patterns. Do they recognize a pattern between the DNA sequences and whether or not a person is lactose intolerant?

Both Mom, Chelsea and Maya have at least on T-A and they do not have lactose intolerance. Jason has C-Gs and he is lactose intolerant.

Walk students through the data in the following way as necessary:

- Focus on the data for Maya - How much RNA is she making? How much protein? It seems like lots. What DNA bases does she have in the switch area? If she has a lot of RNA and a lot of protein, does it seem like a T-A switch is usually off or is it usually on? (It seems to usually be on)
- Focus on Jason - How much RNA is he making? How much protein? (None) What DNA bases does he have in the switch area? If he has no RNA and no protein, does it seem like the C-G switch is usually off or usually on? (It seems to usually be off)
- Focus on Mom and Chelsea - If we take what we learned from Maya and Jason: the T-A switch is usually on and the C-G switch is usually off, what would you expect from a person who has one T-A switch and one C-G switch? Would they make the same amount of RNA as a person with two on switches? What about the amount of protein? Hopefully students realize that with only one on switch, Chelsea and Mom can't make as much RNA and therefore protein as Maya, but they do make some.

Ask students write their explanation of the relationship between the sequence of the DNA near the lactase gene and whether or not RNA is made from the lactase gene?

For students who have studied classical genetics: Ask them if they think lactose tolerance is dominant or recessive? Prompt them to think about Mom the heterozygote, is she lactose tolerant? Ask the students to explain why lactose intolerance is recessive?

(People just need to make the RNA from one of their copies of the lactase gene to make enough protein to digest lactase.)

For students who have studied classical genetics: Ask students to predict what's Dad's DNA would look like (he would be heterozygous) and whether or not he is lactose intolerant (probably not).

Ask the students if they think that Jason ever made lactase? Explain that almost all humans digest milk early in their life. For many people all over the world their genes turn off at some point and they can no longer digest lactose. Scientist have figured out that people with a lactase gene with the C-G near are more likely to turn of the gene than people with genes that have an A-T near.

Ask the students why they think the genes might turn off? Why would we want to know? Scientists don't yet know the answer to why they turn off. But if we knew how they because turned off, perhaps we could keep them from turning off and people could drink more milk.

Section III: How does the environment affect genes?

Purpose: The purpose of this section is for students to consider how the environment they live in can affect them. Students should realize that the environment (for the most part) does not change their genes and therefore their proteins. Generally the environment affects what genes get turned "on and off".

Student reader - The Environment Can Turn Genes On and Off - pgs. 83-85

This text explains how the environment plays a role in gene expression. Some of the suggested strategies are: Underlining unfamiliar words, outlining the text, concept cards.

Student reader - Circle model

Ask students to reconsider the environment circle in their model. Are there new ideas that should be considered here? How will they represent the effect that the sun has on skin color? See sample in Appendix.

Reviewing discussion - Genes and Environment

Discussion Rationale: Students should reconsider that our genes **and** our environments play a role in determining who we are. While we can't control our genes, we can control elements of our environment to help improve our health. In this discussion, students should also be putting ideas together. Student can be making connections to personal experiences, the driving question, to another lesson, or to knowledge just gained.

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

  For example: Student: "Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too."
- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.
  For example: Student: "Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together into one process that explains how proteins are made? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Here are some points/questions to guide you:

Remind students about the different examples they have learned about in this unit: skin color, Familial hypercholesterolemia, lactose intolerance, and sickle-cell disease.

Prompt the students to begin to think how the environment might play a role in these traits:

- How do our genes affect our skin color?
- How does our environment affect our skin color?
- What do we mean by environment? Where we live? What we eat? What kind of air we breath? Is there a lot of stress?
- Does the environment affect our genes?
- What about FH, what affects our cholesterol levels, our genes or our environments?
- What about sickle cell and lactose intolerance, do they have environment components?

Push students to take the discussion outside of what they have learned:

- Do your genes have any effect on whether or not you catch a cold or the flu?
- What about diabetes or heart disease?

- Can you change your genes? What about your environment?
- If both of your parents had a specific disease, like diabetes or heart disease, what does that mean for you? What can you do about it?

Student Reader - Ethical Problem - Erythropoietin - pgs. 86-88

Assign students to read the section of the reader about erythropoietin and how athletes might try to use it to their advantage.

After students have read about erythropoietin, review the science of how it works using slide 4.15. Make sure that students know that different parts of the country have different amounts of oxygen depending on their elevation.

Ethical problem - Altering genes for athletic performance

In this discussion, students will consider four different ways in which athletes can alter their levels of erythropoietin (EPO) - a protein that affects the number of red blood cells. The four scenarios are hypothetically proposed to them by the International Olympic Committee. They will consider the biology of each scenario and then use the decision making framework used in Lesson 2 to make a recommendation to the Committee.

If necessary, review the rules of an ethical discussion and remind the students that there is not a wrong and a right answer for these scenarios. However, they should use what they have learned to try to come up with a fair solution.

Divide the students into groups. Ask each group to work through the initial steps of the process and make a decision about whether or not they agree with each of the four scenarios. Keep track of how each group decides using public documents in the classroom.

As a class review how the groups decided on each of the scenarios. Ask groups to offer evidence and rationale about their decision.

Students probably have a lot of ideas about this subject already, but ask them to consider the following during the course of the discussion:
- Will all athletes have equal access to this technology? What if they do not have as much money?
- What criteria are you using to make your decision?
- Do you think your decision would be different if you didn't understand the science of EPO?

LESSON 5: GENOMES

OVERVIEW

Objective

The purpose of this unit is to help students understand what a genome is and how similar any two people are to each other on the genetic level.

Connection

This lesson should help students develop a richer understanding of our genetic make up beyond just single genes as discussed in lessons 3-4, and now consider the entire genome (the entire genetic make up of a person). With this insight, students should be able to better respond to the question of how similar or different we are (the driving question introduced at the beginning of the unit).

Description

- *Students explore what chromosomes are in, what is in chromosomes, and how many we have in order to understand what the genome is.*
- *Students engage in a scavenger hunt in the genome to find the specific diseases linked to specific chromosomal regions.*
- *This sets the stage for examining the map of disease that scientists have linked to specific chromosomal locations.*

Learning Goals

National Standards

LG9 Constituents of a genome - A genome consists of all of the DNA found inside a single cell or virus. The genome contains all the genes required to build, maintain and propagate the cell, or a multicellular organism. For humans the genome includes all the DNA within both 23 pairs of chromosomes within the nucleus and the DNA in the mitochondria. The human genome consists of about 3 billion base pairs and is estimated to have 25,000 genes. Most of the genome is noncoding DNA, while only a small fraction is protein coding. The non-coding DNA includes some small parts that are highly variable DNA, which can be used to identify people. The genomes of any two humans are highly similar (99.9% identical to be exact). (Written by Aaron Rogat with the help of genomic experts)

Michigan Standards

B2.4A Explain that living things can be classified based on structural, embryological, and molecular (relatedness of DNA sequence) evidence.

B2.4d Analyze the relationships among organisms based on their shared physical, biochemical, genetic, and cellular characteristics and functional processes.

B4.1 Genetics and Inherited Traits - Hereditary information is contained in genes, located in the chromosomes of each cell. Cells contain many thousands of different genes. One or many genes can determine an inherited trait of an individual, and a single gene can influence more than one trait. Before a cell divides, this genetic information must be copied and apportioned evenly into the daughter cells.

B4.2B Recognize that every species has its own characteristic DNA sequence.

B4.4x Genetic Variation - Genetic variation is essential to biodiversity and the stability of a population. Genetic variation is ensured by the formation of gametes and their combination to form a zygote. Opportunities for genetic variation also occur during cell division when chromosomes exchange genetic material causing permanent changes in the DNA sequences of the chromosomes. Random mutations in DNA structure caused by the environment are another source of genetic variation.

[The learning goal addressed in this lesson is darkened.]

Learning Performance(s)
Students define the human genome.
Students identify how many genes and base pairs are in the human genome.
Students identify genes that others have be linked to disease

Prior Knowledge

- LG3 (Nature and function of DNA) from Lesson 3: DNA is a long chain that contains four different types of nucleotides (Adenine, Guanine, Cytosine, and Thymine). The order of these nucleotides determines the order of amino acids in a protein.
- LG4 (Genes as information for proteins) from lesson 3: Students should have been introduced to the notion that genes are segments of DNA that provide information on how to assemble protein. Students should be familiar using an DNA strand to make to make an RNA sequence and use that RNA sequence to decode an amino acid sequence.
- LG3 (molecular nature of DNA) from lesson 4 and 5. An organism's traits reflect the actions (and inactions) of its proteins.
- Students should be familiar with the nucleus of a cell and the mitochondria and chloroplasts and the function of these organelles. They should know mitochondria are found in both plants and animals, but not bacteria. In addition students should know chloroplasts are not found in animal cells and typically are in plant cells.
- Students should be familiar with bacteria and know they are the smallest-free living organisms.
- Students must have a decent understanding of the relationship between genes and DNA to understand this lesson.

Student Misconceptions

- Some students think that DNA is everywhere in the cells of animals like the cytoplasm (not just in the nucleus).
- Students frequently confuse chromosomes and genes. Some misidentify genes as chromosomes.

Time

3-4 days

Materials

PowerPoint slides and projector

Student readers

Print out of aligned sequences – one for human vs human, and one for human vs chimp

Human genome maps (set of 23)

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INSTRUCTIONAL SEQUENCE

Section I: What is a genome?

Purpose: Understand what makes up a genome, understand how big the human genome is, and understand what some general characteristics of the genome are (very little of it is actually protein coding DNA, regions in between DNA are the variable regions which do not code for DNA.

Student reader - Priya Should Find Out If She Inherited a Fatal Disease (or should she?) pgs. 93

http://www.ornl.gov/sci/techresources/Human_Genome/publicat/genechoice/2_priya.html

Assign students to read about Priya and answer questions. This reading has an ethical question, but students should be comfortable with ethical questions by now.

Problem Solving discussion - What is a genome? Making a map

Discussion Rationale: Students should have a preliminary idea of what a genome is and how large and complex it is. They should connect their understanding of what a gene is to the idea that it is just a small part of the genome. This type of discussion is see how students are making sense of things.

You are trying to press students for their understanding and try to get the student to respond with more elaborate and below the surface responses.

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

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For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”

- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: “Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does X compare with Y?
- How can . . .? How might . . . ?
- How do you know? What evidence supports that idea?
- What does it mean to say …?
- Why doesn’t our old model work to explain this new phenomenon?
- Why can’t …?
- How could we figure this out?
- What new questions do you have?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will

encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Here are some points/questions to guide you:

Ask students who are comfortable sharing their response to the story to share their answers as to whether or not they would choose to be tested and why.

Ask students how they think the test for Huntington’s Disease? Would they look at the sequence of the gene? What would they expect to find.

Helping students make connections:

Remind students of all the other proteins and genes they have studies so far: tyrosinase, lactase, LDL receptor, and hemoglobin. Remind them of the exercise they did at the beginning of lesson 2 where they thought about all the different work that proteins need to do.

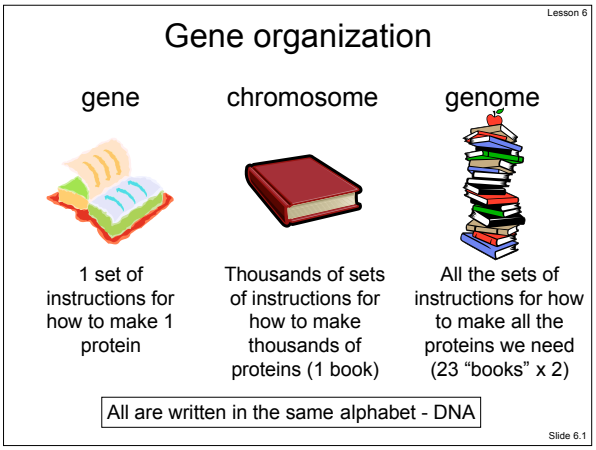
Ask the students how many different genes they think that they need to make all the proteins they need to keep their bodies running?

Help students understand that we have about 25,000 genes on one set of chromosomes. That is about 50,000 total in each cell. That is more genes than there are seats at Comerica Field, or most other Major League Ball parks. That is a lot of genes, but maybe not too many when you think of how complex humans are.

Ask students: If you wanted to understand more about humans, how many of the 25,000 genes should we study?

Hopefully, students think that it is probably important to study most of them. Even if they have very little effect on anything we are interested in, we will not know that until we study them.

Explain to the students that all of the genes are organized into a genome. If we want to study most of the genes, we are going to have to figure out how they are organized. Create a map so that we know where to find a specific gene.



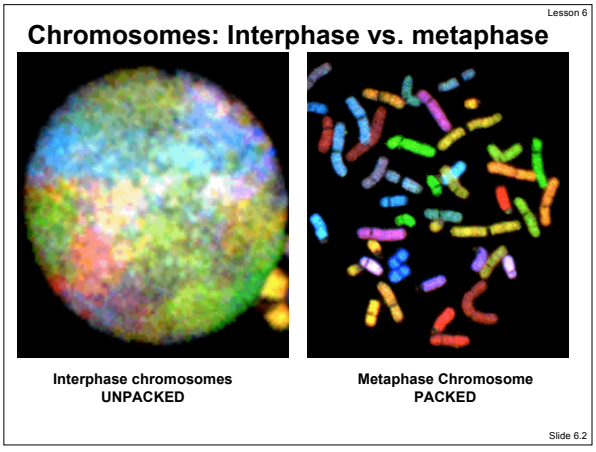
Slide 5.1 - Explain to students that if we looked at all the DNA in one cell of our body we would find all the genes (or instructions) for making all the proteins in all the cells of our bodies.

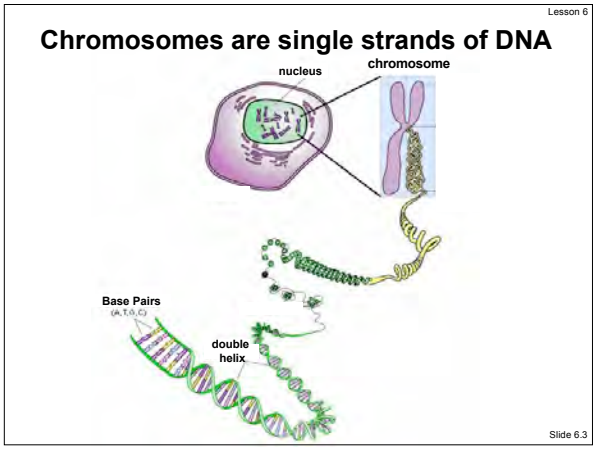
All that DNA contained within one cell has all the information necessary to make a human being in other words: all the DNA found in a cell contains the blueprint to make a human being.

All this DNA is organized in a special way. Remind them of the food recipe or directions analogy. If we took those recipes or sets of directions and started binding a bunch of them together, we would have a chromosome. We need the directions in two copies of 23 different books to make a human. This is how are genes are organized at the most basic level. Remind students that we still need to be able to find specific genes. We need to know what book to look in (which chromosome) and what page (which gene).

Ask students where they would find DNA? Answer: nuclei

Ask students if they remember how DNA is stored in side of a nucleus. Should remember is packed tightly into chromosomes inside of a nucleus.





Slide 5.2 - Show image of packed and unpacked DNA . Ask students if they remember the images of chromosomes from an earlier lesson.

Slide 5.3 - Remind students that chromosomes are one long strand of DNA folded wrapped and folded tightly. Show cartoon image of chromosome that shows how it is one long strand of DNA folded and wrapped tightly. Remind students that images of chromosomes in “X’s are actually two chromosomes that are prepared to divide for mitosis.

Ask the students if they could stretch out the DNA in just one of their cells, how long do they think it would be?

Student reader - Human Genome - pgs. 94-95

This text is a review of what the genome is in the human body.

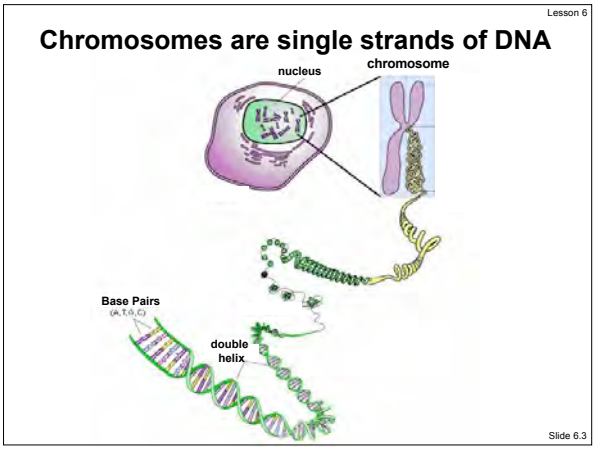
Teacher Explanation - How much DNA is there in every cell?

Activity objective: Students should have and expanded idea of what a genome is.

Show the students a 2 meter long piece of string, yarn, ribbon or tape. Explain that this is the length of DNA in almost all of their cells if we lined up each of our chromosomes. Of course, the DNA would be so skinny you wouldn’t be able to see it.

Ask students to imagine that they could see their DNA all stretched out and ask them what they think it would look like?

Hopefully students will think of the double helix structure they created in lesson 3. Remind them of what the pieces in the middle were: bases. Tell the students that scientists have counted up all the pairs of bases and figured out which base is where. There are a total of 3 billion pairs of bases in one set of human chromosomes.



Slide 5.4 - (You could also use one the DNA kits and your string to model this.) To help students get

an idea of how the model they built in lesson 3 compares to the size of chromosomes and genomes, show them this slide. Explain that the model that they built of DNA represents a very small piece of a chromosome; smaller than we could see on our string. Chromosome 11 is an average size chromosome and it has 135 million pairs of bases. The student model only has 12 pairs of bases. If the students wanted to model a whole chromosome, it would take over 10 million sets!

Ask the students if they remember how many genes are in the human genome? Answer: 25,000.

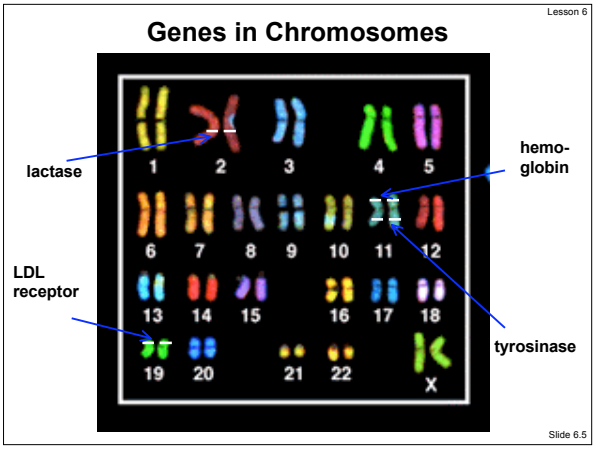
Ask students to estimate the number of genes on a chromosome in there are 23 chromosomes and 25,000 genes? Answer: ~1000 genes per chromosome.

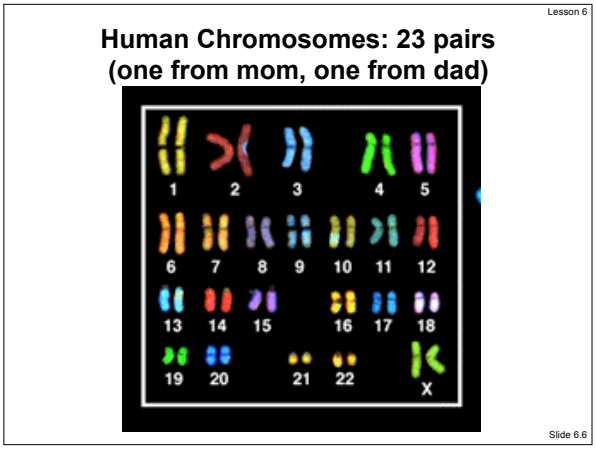
Tell the students that the average gene length in 3000 pairs of bases. Ask them to do the math: If we have 25,000 genes and they are on average 30000 pairs of bases each, how many pairs of bases total? Answer: 25,000 x 3000 = 75,000,000.

Go back to your string model of all the DNA in the genome. Remind the students that this represents all the pairs of DNA in one of their cells. That is 6,000,000,000 pairs. Genes only make up 75,000,000 of the pairs. Measure out 50 millimeter (5 cm). Of the 2 meters of DNA, that is how much of it is genes.

Ask the students what they think the rest of the DNA might be? One answer that they could guess is that is the switches that they learned about in Lesson 5. Explain that some of it is genes that worked in our ancestors and no longer work, some of it came from viruses that our ancestors had, some of it is junk and a lot of it, scientists still don't completely understand.

Explain that the genes are all spread out on the chromosomes. Although the entire chromosome is DNA, only 2% of it has directions for making proteins.





Slide 5.5 - Point out were all the genes discussed in the unit so far are located in the genome (this includes genes that encode proteins which were discussed earlier such as lactase to reinforce the idea that all protein have a gene that corresponds to it. This serves to emphasize what genes are provide an opportunity to connect ideas already learned about to this new idea of the genome and server to reinforce the relationship between genes and chromosome

Slide 5.6 - Show colored karyotype of genome and point out includes all 23 pairs of chromosomes. Note that this genome is the same in every single cell of our bodies. Therefore a skin cell from you has the exact same genome as a brain cell from you. Have students record in student guide what makes up the human genome.

Group activity - Scavenger hunt - filling out the map - pgs. 96

Divide the students into groups to go on a scavenger hunt to put more “landmarks” on our map of the human genome. They are going to look for genes that are linked to disease.

Explain that to a “link” between a gene and disease means certain characteristics such as diseases (like sickle cell disease) or physical appearances (like muscle mass) have been associated with a mutation in a specific gene. Likely the protein that is made from the directions in the gene does work in the development of that trait. For example, the lactase gene is linked to lactose intolerance. The protein lactase does work in the digestion of lactose.

Explain how having a sequenced genome helps link genes to traits using the analogy of our 23 books filled with directions for how to make proteins. Explain that because we have a master map (having sequence the human genome) we can compare the master map to the individuals with a disease and find out where the mutations are quickly. The bottom line is we can find mutations linked to disease quickly.

Explain that thanks to the sequenced genome scientists have quickly linked a large number of mutations in specific genes to different diseases. Ask groups to go on a scavenger hunt to find where disease genes are located in the human genome. Students must find a number of diseases by using the genome map. Each group of students will be given a few of the chromosomes to search. Ask students to identify the chromosomes and the regions on each chromosome where each of the following diseases have been linked:

a. Deafness (find 5)

b. Dyslexia (find 1)

c. Schizophrenia (find 1)

d. Alzheimer’s disease (find 1).

e. Obesity (find 1)

f. Breast Cancer (find 2)

g. Facial anomalies Syndrome (find 1)

h. Duchenne Muscular Dystrophy (MS) (find 1)

Students should list where these are located on the chromosome using terms like top of chromosome 1, middle of chromosome 1, bottom or chromosome 1.

It may be useful to go over maps before students do the scavenger hunt. Focus on one chromosome from the map with the whole class and talk about what is in the map and emphasize what is meant by placing a disease next to specific section on a chromosome.

For example, at the top of chromosome 1 one finds cataracts (an eye disease) this means a mutation, which has been found in people with cataracts, was found in a gene at this location on chromosome 1.

To view maps online or print more copies:

http://www.ornl.gov/sci/techresources/Human_Genome/posters/chromosome/chooser.shtml

(Note: can do a query search for disease and it will identify all regions in the genome associated with that disease- then click on the chromosome number from the graphic to view chromosome)

Following this activity have students answer the following question individually— then discuss the questions, and allow students to revise ideas:

a. A region at the bottom of chromosome 12 is linked to Diabetes. What does this mean and what is being linked to the disease?
b. Often the new reports on breakthroughs in medicine, for example you might hear a report that states “scientist have found a gene for Dyslexia.” What do you think this means?
c. What might be the difference in the genomes of a person with Dyslexia and a person with out dyslexia?
d. Why would several genes be linked to a single trait? In other words, why are there 5 genes linked to deafness?

Extra credit activity - exploring genomes of other organisms

As an option, you can have students go to website below which allows students to examine the genome of different species http://www.ncbi.nlm.nih.gov/mapview/ and have students identify the number of chromosomes, the number nucleotides, and the number of genes for each organism listed in the table above. Then have students determine if there are any patterns between complexity of organism— e.g. number of nucleotides of genes related to the complexity of the organism— answer is amazingly no! This means we still have to learn how complexity is encoded in our genes, knowing all the genes is not quite enough (can see video by Nova –Cracking the code which talks about this but this optional video will probably add about 20-30 minutes)

Instructional note walking through maps (for extra credit activity)

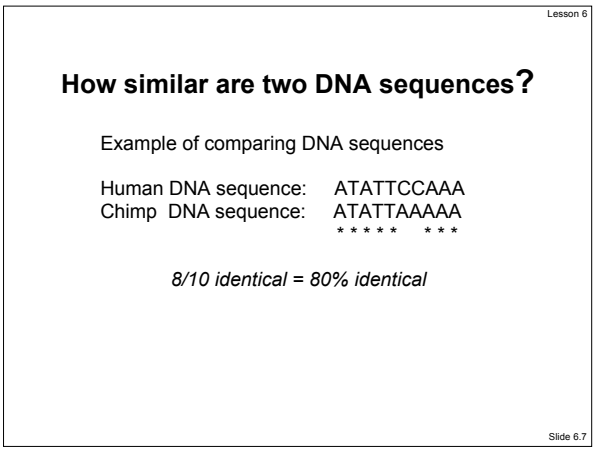
Once at main page go to http://www.ncbi.nlm.nih.gov/mapview/ then go to scroll bar window that says “select group or organism” (circled below), then pick the organism you are interested in (model with Mus musculus which is a mouse). Then click “go” to the right. Will see images of all the chromosomes found in that organism. Note the total number of chromosomes (there are 22 for the mouse which includes the mitochondrial chromosome, which is labeled as “mt”). Then click on the number under the chromosome (e.g. 1 under the first chromosome image). Then point out where the number of nucleotides are presented for each chromosome (this is located at the top under “region displayed” and includes the number of base pairs (e.g. 0-195 M bp means there are 195 million base pairs). Students will need to identify these numbers in their own searches. Then scroll down and see the number of genes at the bottom under “total genes on chromosome.” Next, go to the next chromosome and do the same thing to find out the number of base pairs and genes on the next chromosome. Repeat for every chromosome in the organism and add up the base pairs and genes from each chromosome to get the totals. Students will do this with all the organisms in the table and determine.

Section II - How similar or different are our genomes?

Purpose: The students will get the opportunity to compare parts of two different genomes and calculate how similar and different genomes are from each other.

Review of Driving Question - How similar are our genomes? - Reader pgs. 97-98

Return to driving question “How similar or different are we from each other?” and ask students: Given what you know about the genome, what must you do to understand how similar two people are at the genetic level or how similar two organisms are? Students should realize the need to compare entire genomes?



Slide 5.8 - Suggest to students that they can compare DNA sequence by comparing them side-by-side. By determining how many bases are identical, one can get a measure of how similar two DNA sequences are. Show the hypothetical example below to illustrate this point.

Example of comparing DNA sequences

Human DNA sequence: ATATTCCAAA

Chimp DNA sequence: ATATTAAAAA

* * * * * * * *

8/10 nucleotides are identical, therefore is 80% identical

Then ask students to predict the degree of similarity for the following at the DNA level:

- Two humans
- A human and chimp.

Ask students if they were to compare two sequence what % of the nucleotide would be identical (e.g. 10%, 80%, 90%, 100%)? Have students record their predictions in the student reader.

2. Group activity - Comparing 2 humans, comparing a human and a chimp

Tell students that we are going to further explore how similar and different we are by comparing sequences of 2 humans and a chimp.

Explain that we could try to align the entire genomic sequence of two individuals or two different species to find how similar they are at the DNA level, but this is a lot of data (3 billion base pairs for the human genome) and requires several computers.

Instead we will begin to explore the question of “How similar are we at the DNA level” by looking at a small part of DNA from different individuals.

Break students up into groups and give each student group some of the DNA sequences. The one labelled A and B are comparisons of two people. The ones labeled A and C are human and chimp. Don’t reveal this to the students yet.

Help students make sense of the sequence comparisons with the following points:

- We need several pages of sequence to be able to compare more DNA
- We are not looking at both strands of DNA, just one strand and comparing it to the same strand of another person
- The numbers on the right indicate what pair of bases the last letter on the line is. Using these numbers the students should be able to figure out the number of comparisons on the page without counting.
- Bases that are the same have a dot underneath them. Bases that are different do not.
- Some of this sequence is a gene, some of it is not. Cells would be able to tell the difference, but human eyes cannot.

Have the students figure out the number of identical bases:

total # bases identical = total # of bases - total # of different bases

Ask students to calculate the percentage identical using the following formula:

% bases identical = (total # bases identical / total # of bases) X 100%

Divide the task by giving each student in the group a few pages to work on; then, they can all combine their numbers to get total number of nucleotides identical.

Ask student to record their result in the student reader.

Reviewing discussion - How much variation is there?

Discussion Rationale: This discussion is meant to help students realize that humans are over 99% similar to each other. This is also meant to help the students make connections to the driving question. The reviewing discussion is to help students put together ideas and make connections to different parts of the unit thus far; such as the driving question, other lessons, personal experiences, and knowledge gained.

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

For example: Student: "Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too."

- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: "Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as "WHY" and "HOW DO YOU KNOW THAT" when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these ideas together into one process that explains how proteins are made? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today's activity help us think about ___?
- How does this connect to ____?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, "How come DNA is passed to the offspring?"

Teacher, "Why do YOU think DNA is passed to the offspring?"

Here are some points/questions to guide you:

What does it mean to have a certain percentage identical nucleotides, what do these letters represent again?

Was your group was comparing 2 humans or a human and a chimp? Why do they think that?

Helping students make connections:

Mention that if one took any two humans in the world, they would find the same degree of similarity (e.g. a person from Asia and a person from Africa, or a person from the middle East and a person from South America).

If looked at other animals that are more different, like flies or worms, would find many more differences. Thus, the degree of DNA sequence similarity is also a measure of how close or distant species are in time.

Introduce these ideas to student:

Note that this is just one part of the genome (and a small one at that), but it is larger than one gene sequence so it gives us more information than looking at one gene. Ask students if they think it is possible to have some genes highly similar and other very different. In fact this is the case. Thus we have to look at entire genome to understand just how similar or different we are. Scientists are doing this now. They have determined, and are currently determining, the DNA sequence of the entire genome of many organisms – from mice, human, dogs and pigs, to flies, worms, mold, corn, and soybean (note, this is just a small list of all the organisms whose genomes have been sequenced and the list grows every day).

Introduce the evidence from science investigations to what the students did in the last activity. In the last activity, students compared human genomes and human/chimp genomes. In this case, scientists have compared the whole genomes of humans and a number of different organisms and here is what they have found:

a. The genome of any two humans are in the world are 99.9% identical. This includes both genes and non-gene regions. Explain that even though 0.1% difference is a small number it translates into 3 million base pair differences because the human genome is 3 billion base pairs; therefore, we can still find unique differences between people.
b. The chimpanzee and a human genomes are 95% identical. This includes both gene and non-gene regions, but this is still 40 million base pair differences. However, if just look at the protein coding regions of DNA find they are 99% identical.
c. An average the mouse and human coding regions are 85% identical. Some genes are as low as 60% but some are as high as 99%, there is much less similarity in non-gene regions.
d. Some gene regions in flies are as much as 90% identical to those in humans. However the over all genomes of flies and humans are much less similar than mice and humans.

Ask students to consider these findings in light of the driving question. In an informal discussion, ask students how these findings might change their thinking about how similar we are biologically? No need to write down thoughts now, will come back to this in the end of the unit.

Checkpoint:

By the end of this section, students should understand the following about the human genome:

- The human genome is comprised of 23 pairs of chromosomes in the nucleus and DNA in the mitochondria.
- There are 3 billion base pairs in the human genome and there 25,000 genes.
- There are regions that have genes and regions that do not have genes and that the gene regions are few and sparse in the genome.
- Any two humans in the world are 99.9% identical at the DNA level.

Lesson 6: Why do some people have diseases like Sickle Cell and others do not?

Overview

Objective

Through this example of sickle cell anemia, students get another chance to learn about the idea of genes as information for building proteins. Students also get to revisit the ideas of mutations and the effect of gene mutation on proteins— which in some cases can cause disease. Finally students have the option of learning that not all mutations are bad— some can confer a benefit. In the case of sickle cells, students can learn about the benefit of resistance against malaria. We chose sickle cell anemia in this unit because it is particularly frequent in African American and Hispanic populations, thus those classrooms with a high proportion of these students should find this lesson personally relevant.

Connection

This lesson serves to reinforce the connection between genes, proteins, and health introduced in lesson 3. It also provides opportunities to develop a deeper understanding of mutations introduced in lesson 3 by discussing the beneficial aspects of some mutations.

Description

- *Students are introduced to the symptoms of sickle cell anemia through videos and images and learn about the link between sickle cell anemia and the Hemoglobin protein and the mutation in the Hemoglobin gene.*
- *Students construct molecular explanations for disease that include descriptions of what is different between healthy and disease individuals at the all biological levels (including the protein and DNA level).*
- *Students learn about the connection between malaria resistance and the sickle cell mutation.*

Learning Goals

National Standards

LG2 Biochemical basis for traits - An organism's traits reflect the actions (and inactions) of its proteins. (AAAS considering this but has not published yet)

LG3 Nature and function of DNA - In all organisms, the instructions for specifying the characteristics of the organism are carried in DNA, a large polymer formed from subunits of four kids (A, G, C, and T). The chemical and structural properties of DNA explain how the genetic information that underlies heredity is both encoded in genes (as a string of molecular "letters) and replicated (by a templating mechanism). Each DNA molecule in a cell forms a single chromosome. (NRC, pg 185, 9-12:C2#1)

LG4 Genes as information for proteins - The genetic information in DNA molecules provide the instructions on assembling protein molecules. The code is virtually the same for all life forms. (AAAS, pg. 114, 5C:9-12#4)

LG5 Molecular nature of genes and mutations - Genes are segments of DNA molecules. Inserting, deleting, or substituting DNA segments can alter genes. An altered gene may be passed on to every cell that develops from it. The resulting features may help, harm, or have little or no effect on the offspring's success in its environment. (AAAS, pg. 109, 5B:9-12#4)

LG6 Heritable material - The information passed from parents to offspring is coded in DNA molecules. (AAAS, pg 108, 5B:9-12#3)

Michigan Standards

B2.2f Explain the role of enzymes and other proteins in biochemical functions (e.g., the protein hemoglobin carries oxygen in some organisms, digestive enzymes, and hormones).

L4.p2 Heredity and Environment (prerequisite) - The characteristics of organisms are influenced by heredity and environment. For some characteristics, inheritance is more important. For other characteristics, interactions with the environment are more important. (prerequisite)

B4.1 Genetics and Inherited Traits - Hereditary information is contained in genes, located in the chromosomes of each cell. Cells contain many thousands of different genes. One or many genes can determine an inherited trait of an individual, and a single gene can influence more than one trait. Before a cell divides, this genetic information must be copied and apportioned evenly into the daughter cells.

B4.2 DNA - The genetic information encoded in DNA molecules provides instructions for assembling protein molecules. Genes are segments of DNA molecules. Inserting, deleting, or substituting DNA segments can alter genes. An altered gene may be passed on to every cell that develops from it. The resulting features may help, harm, or have little or no effect on the offspring's success in its environment.

B4.2C Describe the structure and function of DNA.

B4.2D Predict the consequences that changes in the DNA composition of particular genes may have on an organism (e.g., sickle cell anemia, other).

B4.2x DNA, RNA, and Protein Synthesis - Protein synthesis begins with the information in a sequence of DNA bases being copied onto messenger RNA. This molecule moves from the nucleus to the ribosome in the cytoplasm where it is "read." Transfer RNA brings amino acids to the ribosome, where they are connected in the correct sequence to form a specific protein.

B4.2f Demonstrate how the genetic information in DNA molecules provides instructions for assembling protein molecules and that this is virtually the same mechanism for all life forms.

B4.2g Describe the processes of replication, transcription, and translation and how they relate to each other in molecular biology.

B4.4a Describe how inserting, deleting, or substituting DNA segments can alter a gene. Recognize that an altered gene may be passed on to every cell that develops from it and that the resulting features may help, harm, or have little or no effect on the offspring's success in its environment.

B4.4c Explain how mutations in the DNA sequence of a gene may be silent or result in phenotypic change in an organism and in its offspring.

[The learning goals addressed in this lesson are darkened.]

Learning Performance(s)
Students determine what the amino acid sequence of a protein given a DNA sequence.
Students predict the affect of changing the DNA sequence on protein structure and function.
Students explain that the affect of genes on health is mediated by the proteins they encode.

Prior Knowledge

- LG 1 (Nature and function of proteins from Lesson 2A and 2B): Proteins are long folded chains of amino acids and the amino acids sequence determines the protein shape, which in turn determines the protein function. If students were not exposed to Hemoglobin earlier in lesson 2B, they will have to spend more time talking about the function of the protein in this lesson.
- LG3 (Nature and function of DNA) from Lesson 3: DNA is a long chain that contains four different types of nucleotides (Adenine, Guanine, Cytosine, and Thymine). The order of these nucleotides determines the order of amino acids in a protein.
- LG4 (Genes as information for proteins) from lesson 3: Students should have been introduced to the notion that genes are segments of DNA that provide information on how to assemble protein. Students should be familiar using an DNA strand to make to make an RNA sequence and use that RNA sequence to decode an amino acid sequence. Note that this lesson is meant to give students an another opportunity to understand this content so it is not necessary that students are completely proficient with this content prior to this lesson.

Student Misconceptions

1. Some students are unaware of central role proteins play in biological processes.
2. Some students sometimes are unclear as to where genes are found -- some students think genes are found in places other than the nucleus of every cell (i.e. “the blood” or “the brain”).
3. Some students don’t always realize genes exclusively code for proteins or that a gene produces a product. Students sometimes think genes can also code for cells and cell function (something beyond proteins).
4. Some students have difficulty making connections between gene and protein.
5. Some students have difficulty understanding the function of RNA.

Time

3-4 days

Materials

PowerPoint slides and projector

Student readers

Blood smear pre-made slides from healthy and Sickle Cell individuals (Carolina Biological)

Microscope (with at least 40X lens)

Instructional Sequence

Section I. How do gene mutations cause disease?: Lessons from hemoglobin

Purpose: Students review again what is a gene, this time using a different example, hemoglobin, and identifying the mutation that causes sickle cell anemia. Students explore in more depth how a mutation in a gene can affect protein structure and can destroy the function of a protein, which leads to changes in cell function and the health of the organism.

Student reader - pgs. 101-102

Assign students to read “One-eyed cat, No Hoax”. The questions after this reading can be used as an assessment of students’s understanding of many of the topics covered in this unit.

Group work - Examining blood cells in a microscope - pgs. 103

Divide students into groups to look at microscope slides of normal and sickle cells and report differences. Without revealing the types of cells, have the students examine pre-made slide of blood smears from healthy individuals and those with sickle-cell. You will have the best result with at least a 40 X lens.

Have students report on what they observe in student reader.

What differences do they notice? Are there similarities?

Note: Ask students to focus on differences in shape. The differences in color are due to the differences in the preparation of the samples, not to differences in the blood.

Generating discussion - Sickle cell disease

Discussion Rationale: Students should get the opportunity to share what they already know about sickle cell disease and start to think about it as it relates to the other genetic diseases they have learned about. This discussion to allow students to share their ideas without fear of evaluation

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”

- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: “Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- What have you observed or experienced?
- What else is on your group’s list?
- What do you/other people think about when they hear the word ___?
- Who has a different idea/response/way of thinking about this?
- What do you know about [topic X]?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Here are some points/questions to guide you:

Ask the students to describe what they saw in the microscope. Do they think the people with those blood cells are healthy or not?

Tell the students that one of the samples was from a healthy person and one was from a person with sickle cell disease. Ask them which they think was which?

Explain which was which if students do not know?

Ask students what they know about sickle cell disease? Do they already know it is a genetic disease? What are the symptoms?

Ask students if they think a gene could be involved in sickle cell disease? How do they think it might be involved?

Optional: Point out that a person of any race can have the disease, but it is more frequent in some population of humans, for example the rate of sickle cell disease is higher in some African and Asian populations than it is in some European populations. Approximately 1 in every 500 African-American's has sickle-cell disease. It is also frequent in Hispanic populations – effecting every 1 in 1000- 1400 Hispanics. It is also frequent in people of Mediterranean, Middle Eastern and South Asian decent. So if the class has a significant number African Americans or Hispanics, you can ask how many in the class know someone who has the disease (chances high that are someone in the class will know someone who has it).

Student reader - Sickle Cell Disease: The crooked red blood cells; Red Blood Cells Supply Oxygen, Can I Run a Marathon With Sickle Cell Disease? The affect of Sickle Cell Disease on Oxygen Intake, and Why is it called Sickle Cell Disease? - pgs. 104-105

These texts review Sickle Cell Disease. The texts discuss the physical manifestations of sickle cell and why it is difficult for someone that may have the disorder. Some suggested strategies are Concept mapping, Vocabulary cards, Underlining unfamiliar words.

Slide 6.1 -Make sure the students understand the following points.

Red blood cells become banana shaped when oxygen is low in the blood.
The oddly shaped cells cause blockages.
The blockages cause pain, damage to tissue and organs, even death.

Video - More information about sickle-cell disease

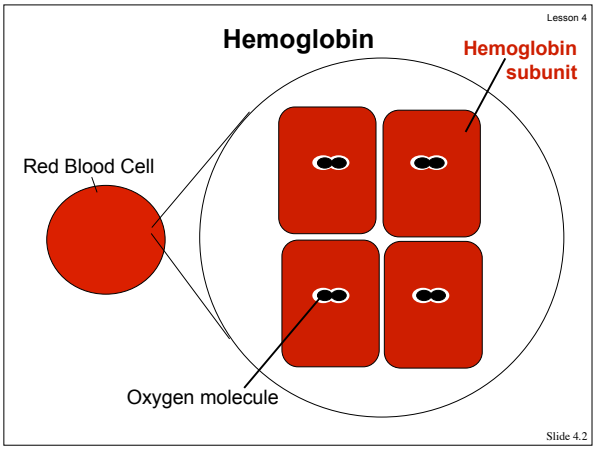
The following video shows an interview with a Sickle Cell patient who describes the pain:

http://www.yourgenesyourhealth.org/sickle/have.htm

In the view mode of PowerPoint, click on “interview with Sickle Cell patient: pain.” Once at the site click on “pain” on the left hand side (you may need Quicktime for this as well). A girl talks about the type of pain she suffers from. This video puts a human face on the disease.

Introducing New Information - Hemoglobin and its role in sickle-cell disease

Objective: Students should connect what they learned about genetic diseases in the form FH with sickle cell disease. They should also review some of the relevant information about sickle cell disease.



Slide 6.2 - Revisit the function of hemoglobin from students exercise at the end of Lesson 2. . Tell students hemoglobin is a protein in red blood cells. Ask students if they remember what its function is—may have to provide hints. Show cartoon image of the protein in a cell (from lesson 2— see below) and ask students to describe what is going on in this image and what hemoglobin does.

Point out hemoglobin is made of four subunits. Each subunit is a single chain of amino acids. But, unlike the other proteins they've studied, in order for hemoglobin to function it needs three partner proteins. Carrying oxygen is a four protein job. Each individual protein chain is called a subunit.

Instructional note: Definition of subunit

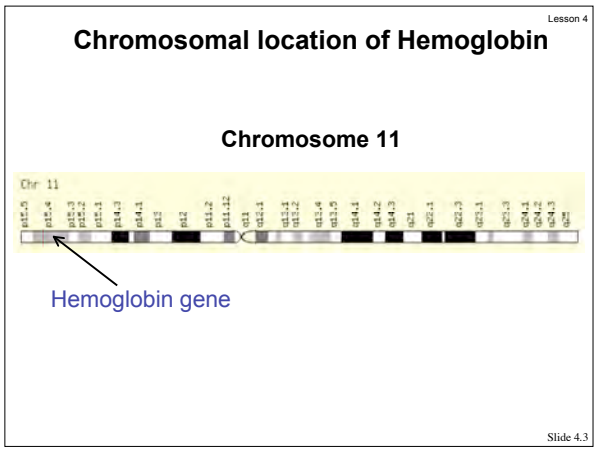
If students do not know what subunit means explain that "sub" means below as in a level below, so subunit, means a small part of a larger complex. For example, a bicycle chain link could be considered a subunit of a chain. However not all subunits have to be identical—for example a nucleotide in DNA could be considered a subunit of DNA.

Mention to students that scientists have discovered an association between hemoglobin and sickle cell disease.

Ask students what information they need to find out if there is a link between hemoglobin and sickle cell disease?

If students do not come up with what information they would need to determine if hemoglobin is associated with sickle cell, provide guiding questions such as: what was done to diagnosis people with FH? or based on how genes work what might we look for?

From the previous readings about FH and the activity with the LDL Receptor, hopefully students will mention examining the hemoglobin protein or the hemoglobin gene in patients that have sickle cell.



Slide 6.3 - Point out to students that if we are going to examine the hemoglobin gene, we need to know where it is. Point out the location of one of the hemoglobin genes on chromosome 11.

Group work - Analyzing hemoglobin - pgs. 105

Divide students into groups

Post the following DNA sequence from the hemoglobin gene and have students determine the RNA sequence and amino acid sequence for this DNA sequence (like done in lesson 3).

Part of hemoglobin gene from healthy person

```
ATGGTGCACCTGACTCCTGAGGAGAAGTCTGCCGTTACTGCCCTG
||||||||||||||||||||||||||||||||||||||||||||||
TACCACGTGGACTGAGGACTCCTCTTCAGACGGCAATGACGGGAC
```

Answer

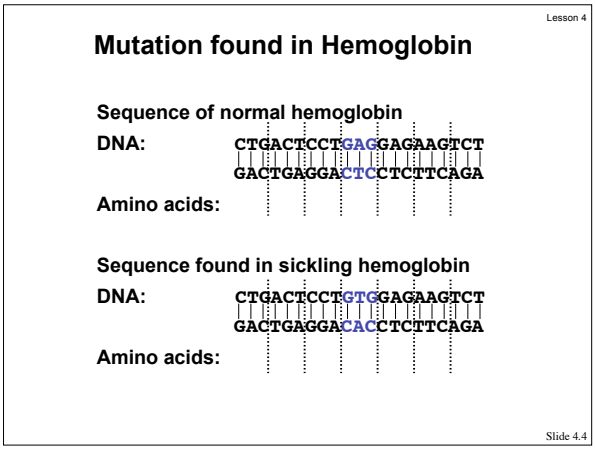
mRNA sequence

```
AUG GUG CAC CUG ACU CCU GAG GAG AAG UCU GCC GUU ACU GCC CUG
```

amino acid sequence

M V H L T P E E K S A V T A L

Full gene and protein sequences can be found in the appendix.



Give students a new genetic code with the sickle cell mutation (part of this is on slide 6.4).

```
ATGGTGCACCTGACTCCTGTGGAGAAGTCTGCCGTTACTGCCCTG
||||||||||||||||||||||||||||||||||||||||||||||
TACCACGTGGACTGAGGACACCTCTTCAGACGGCAATGACGGGAC
```

Ask students to predict what will happen to the protein structure and function. If they have trouble imagining what a change in amino acids will do, have them build it with their Toobers.

Discuss results as a class. In whole class discussion. Ask students if the still think the hemoglobin will function properly in cells. Ask the students if they think there could be an association between hemoglobin and sickle-cell?

Teacher Note: However, the sickle cell hemoglobin proteins can function somewhat, in the sense that they can still bind oxygen. But they do display other abnormal behaviors and function as will be discussed below.

Reviewing discussion - How does the mutation in the hemoglobin gene affect red blood cells?

Discussion Rationale: Students should understand how changes to the hemoglobin gene lead to change in the hemoglobin protein and how change sin the proteins lead to changes in the cells and changes in the blood cells lead to health problems. In this discussion, students put ideas together and make connections between information learned.

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”

- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: “Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does _____ help us think about other times when _____?
- How can we put these 4 ideas together into one process that we might call “the water cycle”? What happens 1st, 2nd . . . ?
- What do we know about _____ so far?
- How does this help us think about the driving question?
- Yesterday we talked about ___; how does today’s activity help us think about ___?
- How does this connect to ____?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

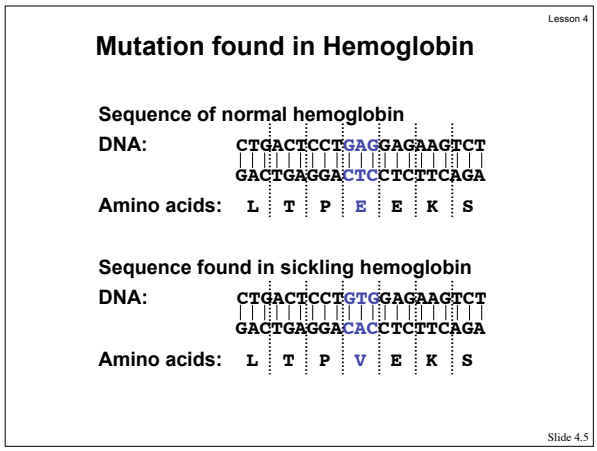
For example: Suzie, “How come DNA is passed to the offspring?”

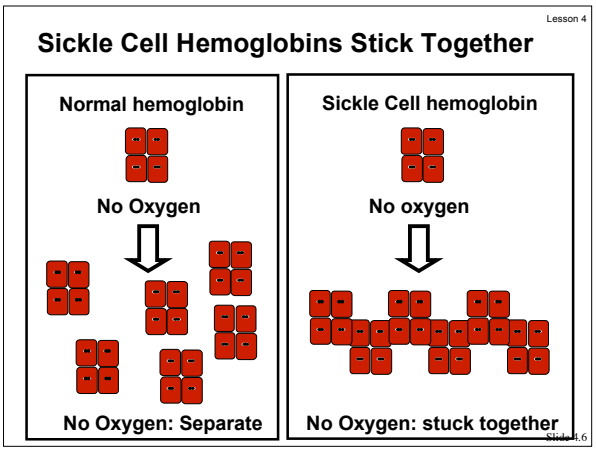
Teacher, “Why do YOU think DNA is passed to the offspring?”

Here are some points/questions to guide you:

Ask students what was the property of the amino acid before and after the swap on the model. Should realize a charged amino acid was swapped for a hydrophobic amino acid.

Explain that this mutation causes a hydrophobic patch to form on the surface of the protein that normally is not there. Ask students, what might happen to a hydrophobic patch (note that there would be other hemoglobin protein with neighboring it that would have a similar patch)

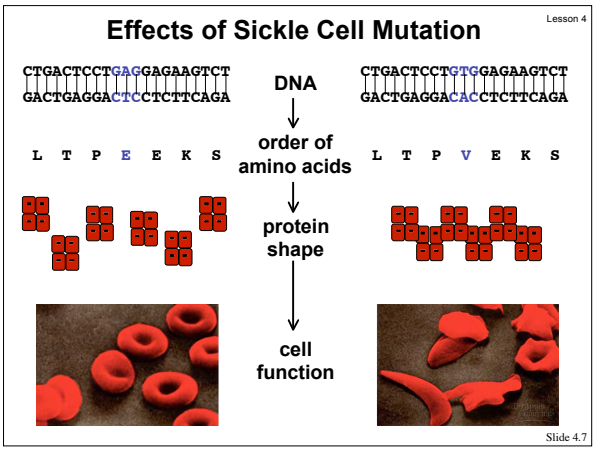




Slide 6.5 and 6.6 - Explain that scientists have explored this mutation and its affect on hemoglobin and have determined there is a problem. Hemoglobin forms long chains inside red blood cells. Then show cartoon images showing this.

Explain to students that the hydrophobic parts of proteins like to clump together (like hydrophobic amino acids). In this case the abnormal hydrophobic patch on the outside of the protein, can interact with other nearby sickle cell hemoglobins when no oxygen is present forming long crystals of hemoglobin inside of the red blood cells. In contrast normal hemoglobin proteins stay separated when no oxygen is present.

The long chains in of sickle cell hemoglobin stretch the red blood cell so that it looks banana shaped.



Slide 6.7 - Students struggle to make connections from genes to traits so use this slide to walk through the steps from gene to protein to trait. Make connections to content from lesson 4 by asking students if they think that the hemoglobin gene is on in all cells? Why or why not? Hopefully they remember that genes are the same in all cells and that the difference between cells is what genes are turned on.

Section II: Connection molecular genetics to classical genetics

The purpose of this section is for students to make connections between their understanding of classical genetics (homozygous, heterozygous, recessive, dominant, etc.) and what they have learned in this unit.

Problem Solving discussion - What is a genetic disease?

Discussion Rationale: Students should realize that since genes are contained in DNA, that DNA is what is passed on from generation to generation—this therefore means that mutations can be passed on from one generation to another. In this discussion, students go beyond surface answers. They making sense out of information.

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

Addressing Other Students:

- Encourage students to address other students in the classroom.

For example: Student: “Suzie said that protein shape would stay the same. I disagree. I think that if amino acids change, then the protein shape changes too.”

- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and similarities and differences.

For example: Student: “Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT”

when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- How does X compare with Y?
- How can . . .? How might . . . ?
- How do you know? What evidence supports that idea?
- What does it mean to say …?
- Why doesn't our old model work to explain this new phenomenon?
- Why can't …?
- How could we figure this out?
- What new questions do you have?

Supporting Communication

Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, "How come DNA is passed to the offspring?"

Teacher, "Why do YOU think DNA is passed to the offspring?"

Here are some points/questions to guide you:

Through class discussion about the meaning of "genetic disease" introduce the idea that DNA is the material that is passed from one generation to another and in doing so can pass on mutations. Ask students if they have ever heard of the word "genetic" or have they every heard a disease be called genetic. Ask students what they think that means? Based on their understanding of genes what do they think that means. Focus on root of word "gene" in "genetic" and encourage students to consider what they have thus far learned about genes.

Students should realize this genetic disease must involve genes and perhaps mutations that cause disease.

Ask students how many copies of each type of gene they have? Where did they get their genes?

Genes are passed from parents to children.

Ask students, if genes are passed on from parents to children what does that mean about DNA and the types of mutations modeled earlier in the lesson? Does someone who has sickle cell disease have a parent with the mutation?

Student Reader - How can sickle cell disease be passed to me? And How Do Children Receive Their Parents' Genes? Mendel Activity - pgs. 107-109

Assign students to read answer questions in the appropriate part of the student reader. Students read about Mendelian genetics and do an activity that shows how genes can be passed from parents to offspring. If your students have covered Mendelian genetics, push them to make connections between what they learned in that unit and what they have learned here. If a trait is recessive, what do they think that means about the protein? (Half the amount is enough is a reasonable answer but students could have other plausible ideas.) What does it mean to be a homozygote at the DNA level? (The DNA sequence is the same in both copies of the gene.)

Section III - Are all mutations bad? Selective pressures on sickle cell trait

Purpose: Describe story of malaria resistance and sickle cell mutation to show how some mutations are actually beneficial, not always bad. Additionally assign the reading on pgs. 110-111.

Generating discussion - The protective effects of sickle cell trait

Discussion Rationale: Students should understand that not all mutations are bad. In this case, a mutation protects people from malaria. In this discussion, students can share their ideas without fear of being evaluated.

Discussion Strategies:

Think/Pair/Share: You can have the students first try it on their neighbor, then reconvene as a class and share their explanations.

When students give answers, here are some things you can do:

Encourage students to use complete sentences.

Make Knowledge Explicit:

- Evidence: What evidence did they use to explain their answers?

Student Centered: Encourage the STUDENTS to initiate the discussion questions, follow-up questions, challenging of evidence, etc. Try to GUIDE the discussion rather than lead the discussion.

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- Ask students to consider a previous response while formulating their own. (See above example in quotes).
- Encourage students to ask other students questions about their predictions and

similarities and differences.

For example: Student: “Why do you think that this disease can be passed to offspring?

Follow-up Questions: Use follow-up questions, such as “WHY” and “HOW DO YOU KNOW THAT” when students give answers (claims). This can push them to think deeper about why they think they know something.

Additional follow-up questions include:

- What have you observed or experienced?
- What else is on your group’s list?
- What do you/other people think about when they hear the word ___?
- Who has a different idea/response/way of thinking about this?
- What do you know about [topic X]?

Supporting Communication

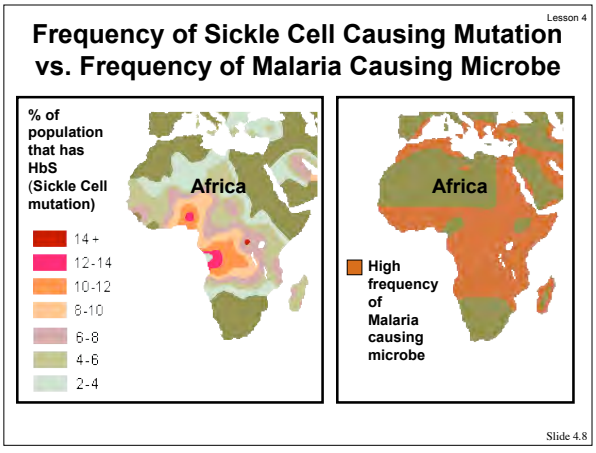
Public Documents: On the board, create a public document of what the students say, so that everyone can keep track of what has been said. You can ask a student to do this. This will encourage the students to listen to one another and use other responses to reflect on their own responses.

Reflective toss: Throw back the students response/question to the students, rather than evaluating. This will encourage them to think about what was just stated/asked.

For example: Suzie, “How come DNA is passed to the offspring?”

Teacher, “Why do YOU think DNA is passed to the offspring?”

Here are some points/questions to guide you:



Slide 6.8 - Present maps of malaria and sickle cell to introduce an interesting finding. Present the interesting finding that malaria frequency and the frequency of the sickle cell mutation are correlated in geographic areas of the world.

Have students identify overlap in areas. Ask question such as do you see an overlap, what do you

think this means, do you think there could be some benefit to having sickle cell in these areas or perhaps one is causing the other. Explain that scientist have looked into this case and have found surprising results.

Show video on malaria resistance.

http://science.education.nih.gov/supplements/nih1/genetic/activities/activit2.htm

Ask students to summarize what just saw in maps and video of sickle cell. Correct any misconceptions student might that might emerge from discussion..

Section IV - Research projects

Purpose: The purpose of this section os for students to share their work with their classmates and to learn about what their classmates have studied.

Teacher Explanation - Instructions for sharing work

Depending on your class size, it is likely impractical for each student to share his or her work individually. Instead, you may divide your class into two groups. One group will be with their project while the other group walks around and asks individuals questions about their project. Then students will exchange places.

Ask each student to talk to at least three other students and write what they learned using the following questions:

- Whose project did you look at?
- What trait did the project report on?
- If your friend had this trait, what do you think they would like to know about it?

Class Activity - Sharing research projects

Have the first group stay with their projects while the second group asks them questions. Then have the groups switch.

If you choose to score students on their ability to present their project, this is your opportunity to talk to each student.

At the end of class have the students turn in their projects to be scored. A rubric for scoring both a poster and a brochure is included in the Appendix.

Section V - Student Reader Circle Chart

Purpose: The purpose of this section is for students to finish their circle charts and draw connections from environment to genes to proteins to traits.

If the students have not already filled in all of the areas for the specific traits, have them work in groups or alone to finish filling in the chart.

Ask the students to look at their charts across the circles.

- Are there things they notice that are similar across the environment circle? the biology circle
- What similarities can they see for these genetic traits? Do they all have a different gene sequence? Do the genes all have instructions for proteins? Do the proteins all do work?
- If they were going to describe any genetic trait what information would they need to know on the gene level? the protein level? the trait level?

Appendix

Sequences

Note: DNA sequences reported here are the sequences of the mRNA with the Us turned into Ts. If you choose to use these sequences, it is recommended that you provide the students both strands of sequence. To be consistent with the rest of the unit and with convention, use the provided sequence as the top strand. The predicted RNA sequence should match the provided sequence (only with Us instead of Ts).

Tyrosinase

Protein aequence:

```
MLLAVLYCLL WSFQTSAGHF PRACVSSKNL MEKECCPPWS GDRSPCGQLS
GRGSCQNILL SNAPLGPQFP FTGVDDRESW PSVFYNRTCQ CSGNFMGFNC 100
GNCKFGFWGP NCTERRLLVR RNIFDLSAPE KDKFFAYLTL AKHTISSDYV
IPIGTYGQMK NGSTPMFNDI NIYDLFVWMH YYVSMDALLG GYEIWRDIDF 200
AHEAPAFLPW HRLFLLRWEQ EIQKLTGDEN FTIPYWDWRD AEKCDICTDE
YMGGQHPTNP NLLSPASFFS SWQIVCSRLE EYNSHQSLCN GTPEGPLRRN 300
PGNHDKSRTP RLPSSADVEF CLSLTQYESG SMDKAANFSF RNTLEGFASP
LTGIADASQS SMHNALHIYM NGTMSQVQGS ANDPIFLLHH AFVDSIFEQW 400
LRRHRPLQEV YPEANAPIGH NRESYMVPFI PLYRNGDFFI SSKDLGYDYS
YLQDSDPDSF QDYIKSYLEQ ASRIWSWLLG AAMVGAVLTA LLAGLVSLLC 500
RHKRKQLPEE KQPLLMEKED YHSLYQSHL 529
```

Lactase

Protein sequence:

```
MELSWHVVFI ALLSFSCWGS DWESDRNFIS TAGPLTNDLL HNLSGLLGDQ
SSNFVAGDKD MYVCHQPLPT FLPEYFSSLH ASQITHYKVF LSWAQLLPAG 100
STQNPDEKTV QCYRRLLKAL KTARLQPMVI LHHQTLPAST LRRTEAFADL
FADYATFAFH SFGDLVGIWF TFSDLEEVIK ELPHQESRAS QLQTLSDAHR 200
KAYEIYHESY AFQGGKLSVV LRAEDIPELL LEPPISALAQ DTVDFLSLDL
SYECQNEASL RQKLSKLQTI EPKVKVFIFN LKLPDCPSTM KNPASLLFSL 300
FEAINKDQVL TIGFDINEFL SCSSSSKKSM SCSLTGSLAL QPDQQQDHET
TDSSPASAYQ RVWEAFANQS RAERDAFLQD TFPEGFLWGA STGAFNVEGG 400
WAEGGRGVSI WDPRRPLNTT EGQATLEVAS DSYHKVASDV ALLCGLRAQV
YKFSISWSRI FPMGHGSSPS LPGVAYYNKL IDRLQDAGIE PMATLFHWDL 500
PQALQDHGGW QNESVVDAFL DYAAFCFSTF GDRVKLWVTF HEPWVMSYAG
YGTGQHPPGI SDPGVASFKV AHLVLKAHAR TWHHYNSHHR PQQQGHVGIV 600
LNSDWAEPLS PERPEDLRAS ERFLHFMLGW FAHPVFVDGD YPATLRTQIQ
QMNRQCSHPV AQLPEFTEAE KQLLKGSADF LGLSHYTSRL ISNAPQNTCI 700
PSYDTIGGFS QHVNHVWPQT SSSWIRVVPW GIRRLLQFVS LEYTRGKVPI
YLAGNGMPIG ESENLFDDSL RVDYFNQYIN EVLKAIKEDS VDVRSYIARS 800
LIDGFEGPSG YSQRFGLHHV NFSDSSKSRT PRKSAYFFTS IIEKNGFLTK
GAKRLLPPNT VNLPSKVRAF TFPSEVPSKA KVVWEKFSSQ PKFERDLFYH 900
```

GTFRDDFLWG VSSSAYQIEG AWDADGKGPS IWDNFTHTPG SNVKDNATGD
IACDSYHQLD ADLNMLRALK VKAYRFSISW SRIFPTGRNS SINSHGVDYY 1000
NRLINGLVAS NIFPMVTLFH WDLPQALQDI GGWENPALID LFDSYADFCF
QTFGDRVKFW MTFNEPMYLA WLGYGSGEFP PGVKDPGWAP YRIAHTVIKA 1100
HARVYHTYDE KYRQEQKGVI SLSLSTHWAE PKSPGVPRDV EAADRMLQFS
LGWFAHPIFR NGDYPDTMKW KVGNRSELQH LATSRLPSFT EEEKRFIRAT 1200
ADVFCLNTYY SRIVQHKTPR LNPPSYEDDQ EMAEEEDPSW PSTAMNRAAP
WGTRRLLNWI KEEYGDIPIY ITENGVGLTN PNTEDTDRIF YHKTYINEAL 1300
KAYRLDGIDL RGYVAWSLMD NFEWLNGYTV KFGLYHVDFN NTNRPRTARA
SARYYTEVIT NNGMPLARED EFLYGRFPEG FIWSAASAAY QIEGAWRADG 1400
KGLSIWDTFS HTPLRVENDA IGDVACDSYH KIAEDLVTLQ NLGVSHYRFS
ISWSRILPDG TTRYINEAGL NYYVRLIDTL LAASIQPQVT IYHWDLPQTL 1500
QDVGGWENET IVQRFKEYAD VLFQRLGDKV KFWITLNEPF VIAYQGYGYG
TAAPGVSNRP GTAPYIVGHN LIKAHAEAWH LYNDVYRASQ GGVISITISS 1600
DWAEPRDPSN QEDVEAARRY VQFMGGWFAH PIFKNGDYNE VMKTRIRDRS
LAAGLNKSRL PEFTESEKRR INGTYDFFGF NHYTTVLAYN LNYATAISSF 1700
DADRGVASIA DRSWPDSGSF WLKMTPFGFR RILNWLKEEY NDPPIYVTEN
GVSQREETDL NDTARIYYLR TYINEALKAV QDKVDLRGYT VWSAMDNFEW 1800
ATGFSERFGL HFVNYSDPSL PRIPKASAKF YASVVRCNGF PDPATGPHAC
LHQPDAGPTI SPVRQEEVQF LGLMLGTTEA QTALYVLFSL VLLGVCGLAF 1900
LSYKYCKRSK QGKTQRSQQE LSPVSSF

LDL receptor

Protein sequence:

(The bolded letters represent part of the ligand-binding domain (i.e. the domain that binds LDL). There are 292 amino acids that make of the domain that binds the LDL Receptor. The region selected to model (underlined) is also part of this ligand-binding domain. This region that was modeled also binds to a calcium ion—this calcium binding appears to be important for binding to LDL. People with the genetic disease familial hypercholesterolemia (FH) have have mutations in this region 2/3rds of the time - with a preponderance in the region selected to model in class.)

MGPWGWKLRW TVALLLAAAG TAVGDRCERN EFQCQDGKCI SYKWVCDGSA
ECQDGSDESQ ETCLSVTCKS GDFSCGGRVN RCIPQFWRCD GQVDCDNGSD 100
EQGCPPKTCS QDEFRCHDGK CISRQFVCDS DRDCLDGSDE ASCPVLTCGP
ASFQCNSSTC IPQLWACDND PDCEDGSDEW PQRCRGLYVF QGDSSPCSAF 200
EFHCLSGECI HSSWRCDGGP DCKDKSDEEN CAVATCRPDE FQCSDGNCIH
GSRQCDREYD CKDMSDEVGC VNVTLCEGPN KFKCHSGECI TLDKVCNMAR 300
DCRDWSDEPI KECGTNECLD NNGGCSHVCN DLKIGYECLC PDGFQLVAQR
RCEDIDECQD PDTCSQLCVN LEGGYKCQCE EGFQLDPHTK ACKAVGSIAY 400
LFFTNRHEVR KMTLDRSEYT SLIPNLRNVV ALDTEVASNR IYWSDLSQRM
ICSTQLDRAH GVSSYDTVIS RDIQAPDGLA VDWIHSNIYW TDSVLGTVSV 500
ADTKGVKRKT LFRENGSKPR AIVVDPVHGF MYWTDWGTPA KIKKGGLNGV

DIYSLVTENI QWPNGITLDL LSGRLYWVDS KLHSISSIDV NGGNRKTILE 600
DEKRLAHPFS LAVFEDKVFW TDIINEAIFS ANRLTGSDVN LLAENLLSPE
DMVLFHNLTQ PRGVNWCERT TLSNGGCQYL CLPAPQINPH SPKFTCACPD 700
GMLLARDMRS CLTEAEAAVA TQETSTVRLK VSSTAVRTQH TTTRPVPDTS
RLPGATPGLT TVEIVTMSHQ ALGDVAGRGN EKKPSSVRAL SIVLPIVLLV 800
FLCLGVFLLW KNWRLKNINS INFDNPVYQK TTEDEVHICH NQDGYSYPSR
QMVSLEDDV 860

DNA sequence:

(The sequence used in class is underlined)

ATGGGGCCCTGGGGCTGGAAATTGCGCTGGACCGTCGCCTTGCTCCTCGCCGCGGCGGGGACTGCAGTGG
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TGGCAGCGCTGAGTGCCAGGATGGCTCTGATGAGTCCCAGGAGACGTGCTTGTCTGTCACCTGCAAATCC
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GCCTCCTGCCCGGTGCTCACCTGTGGTCCCGCCAGCTTCCAGTGCAACAGCTCCACCTGCATCCCCCAGC
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TTACGTGTTCCAAGGGGACAGTAGCCCCTGCTCGGCCTTCGAGTTCCACTGCCTAAGTGGCGAGTGCATC
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CGTCTGCAATGACCTTAAGATCGGCTACGAGTGCCTGTGCCCCGACGGCTTCCAGCTGGTGGCCCAGCGA
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CATCGCCTACCTCTTCTTCACCAACCGGCACGAGGTCAGGAAGATGACGCTGGACCGGAGCGAGTACACC
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TCTTCCACAACCTCACCCAGCCAAGAGGAGTGAACTGGTGTGAGAGGACCACCCTGAGCAATGGCGGCTG
CCAGTATCTGTGCCTCCCTGCCCCGCAGATCAACCCCCACTCGCCCAAGTTTACCTGCGCCTGCCCGGAC
GGCATGCTGCTGGCCAGGGACATGAGGAGCTGCCTCACAGAGGCTGAGGCTGCAGTGGCCACCCAGGAGA
CATCCACCGTCAGGCTAAAGGTCAGCTCCACAGCCGTAAGGACACAGCACACAACCACCCGGCCTGTTCC

CGACACCTCCCGGCTGCCTGGGGCCACCCCTGGGCTCACCACGGTGGAGATAGTGACAATGTCTCACCAA
GCTCTGGGCGACGTTGCTGGCAGAGGAAATGAGAAGAAGCCCAGTAGCGTGAGGGCTCTGTCCATTGTCC
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AACCAGGACGGCTACAGCTACCCCTCGAGACAGATGGTCAGTCTGGAGGATGACGTGGCGTGAACATCTG
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GGCCCGGGGGGACCAGGATGACACCTCCATTTCTCTCCAGGAAGTTTTGAGTTTCTCTCCACCGTGACAC
AATCCTCAAACATGGAAGATGAAAGGGCAGGGGATGTCAGGCCCAGAGAAGCAAGTGGCTTTCAACACAC
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ACCTTGGCCGTGAGGACACGTGGCCTGCACCCAGGTGTGGCTGTCAGGACACCAGCCTGGTGCCCATCCT
CCCGACCCCTACCCACTTCCATTCCCGTGGTCTCCTTGCACTTTCTCAGTTCAGAGTTGTACACTGTGTA
AA

Beta-Hemoglobin

DNA sequence:

ATG GTG CAC CTG ACT CCT GAG GAG AAG TCT GCC GTT ACT GCC CTG TGG GGC AAG GTG
AAC GTG GAT GAA GTT GGT GGT GAG GCC CTG GGC AGG CTG CTG GTG GTC TAC CCT TGG
ACC CAG AGG TTC TTT GAG TCC TTT GGG GAT CTG TCC ACC CCT GAT GCT GTT ATG GGC
AAC CCT AAG GTG AAG GCT CAT GGC AAG AAA GTG CTC GGT GCC TTT AGT GAT GGC CTG
GCT CAC CTG GAC AAC CTC AAG GGC ACC TTT GCC ACA CTG AGT GAG CTG CAC TGT GAC
AAG CTG CAC GTG GAT CCT GAG AAC TTC AGG CTC CTG GGC AAC GTG CTG GTC TGT GTG
CTG GCC CAT CAC TTT GGC AAA GAA TTC ACC CCA CCA GTG CAG GCT GCC TAT CAG AAA
GTG GTG GCT GGT GTG GCT AAT GCC CTG GCC CAC AAG TAT CAC TAA

Protein sequence:

MVHLTPEEKSAVTALWGKV

NVDEVGGEALGRLLVVYPW

TQRFFESFGDLSTPDAVMG

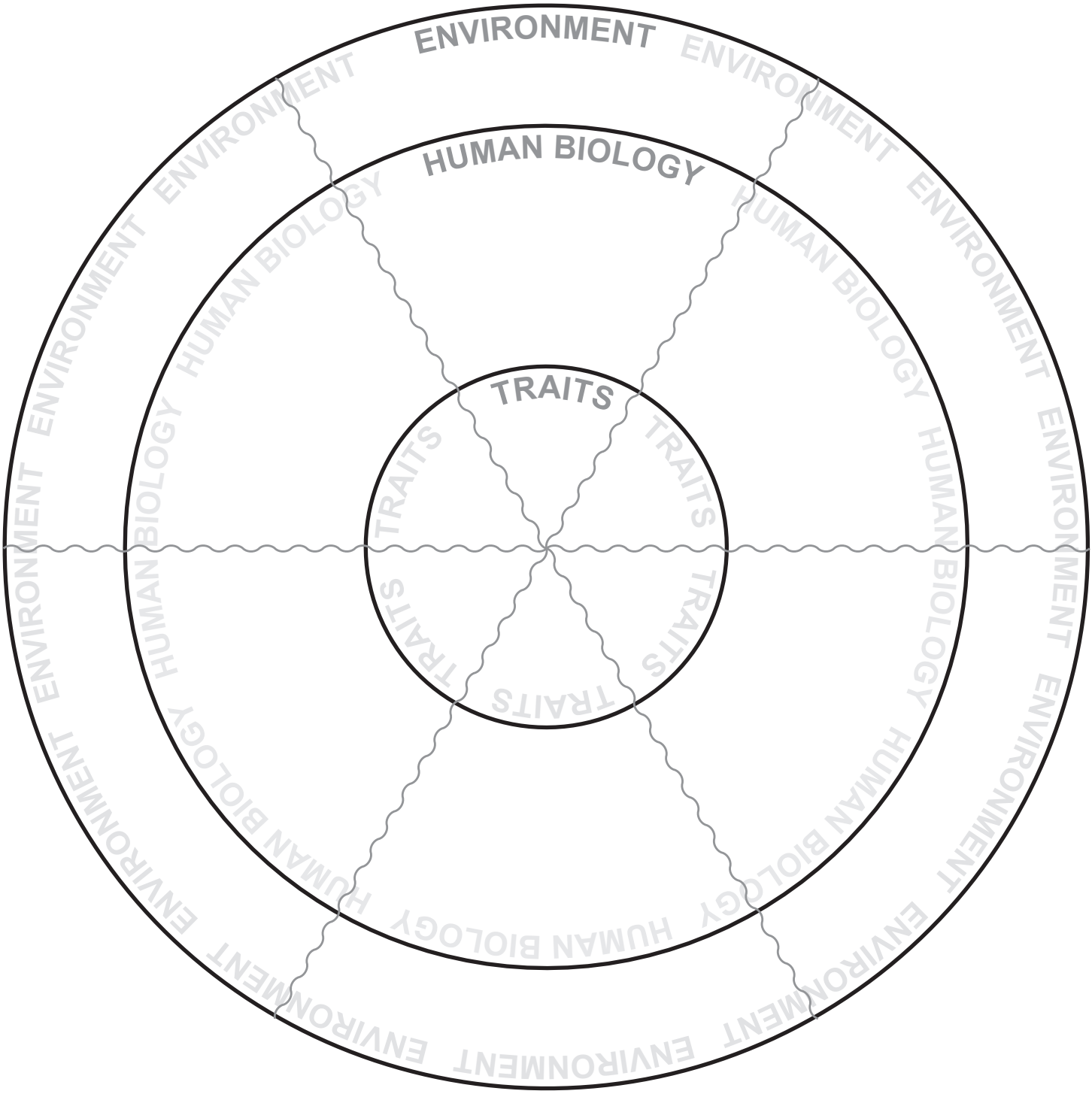
NPKVKAHGKKVLGAFSDGL

AHLDNLKGTFATLSELHCD

KLHVDPENFRLLGNVLVCV

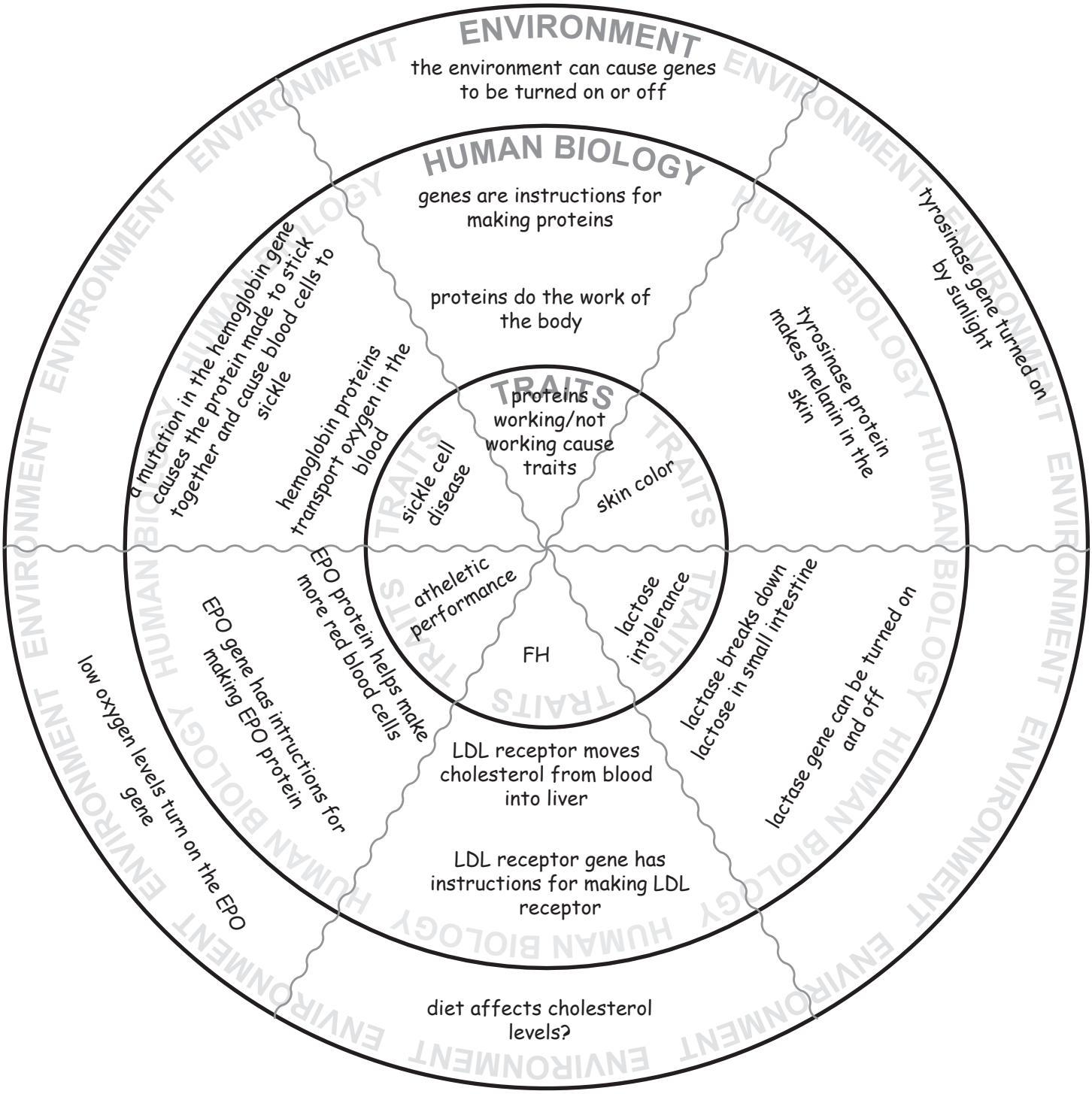
LAHHFGKEFTPPVQAAYQK

VVAGVANALAHKYH


ENVIRONMENT
HUMAN BIOLOGY
TRAITS

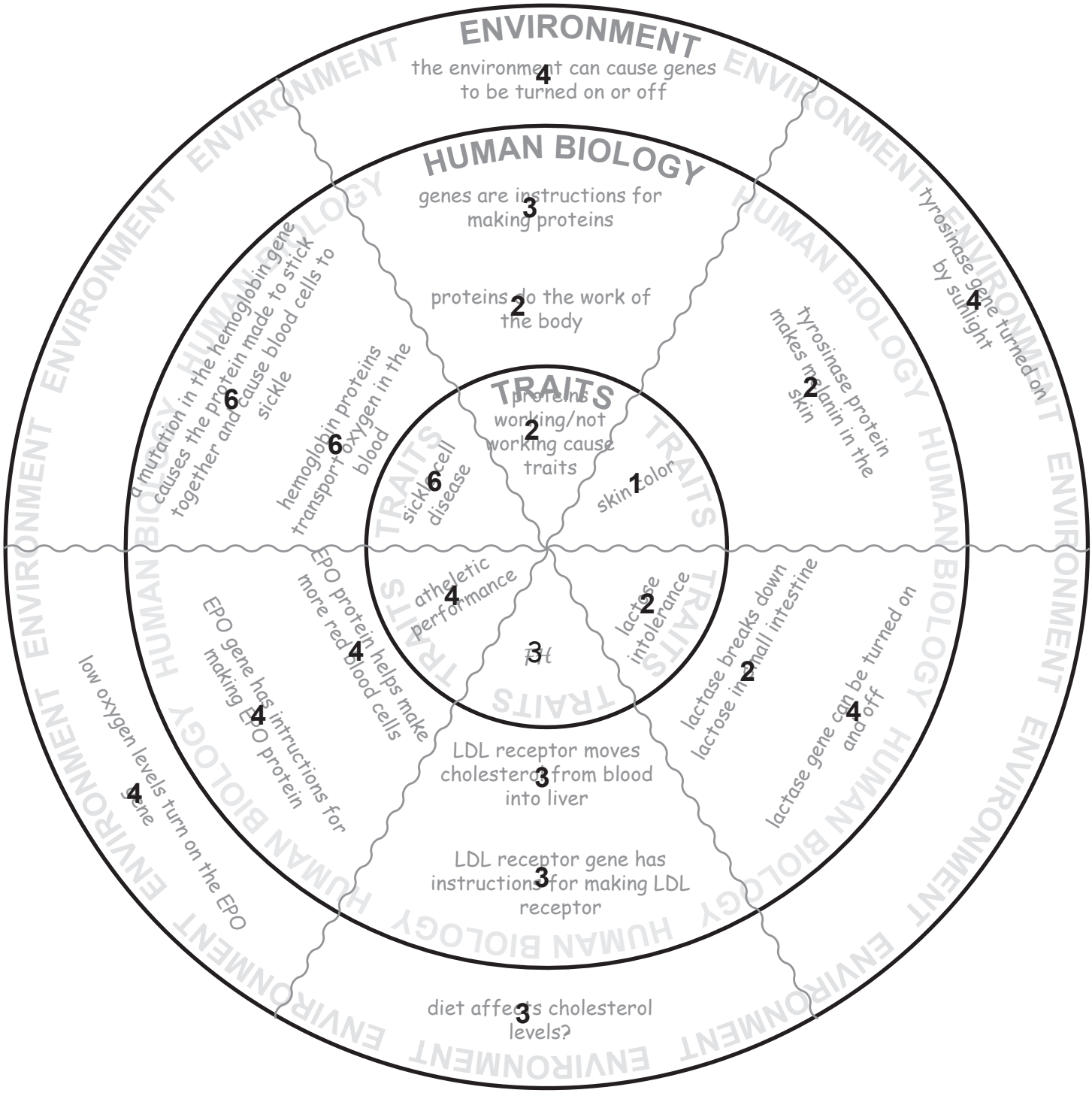
This is one example of how the circle chart might look upon completion. It is not as important to get all the details in as it is to start to see the trends that the major learning goals of the unit:

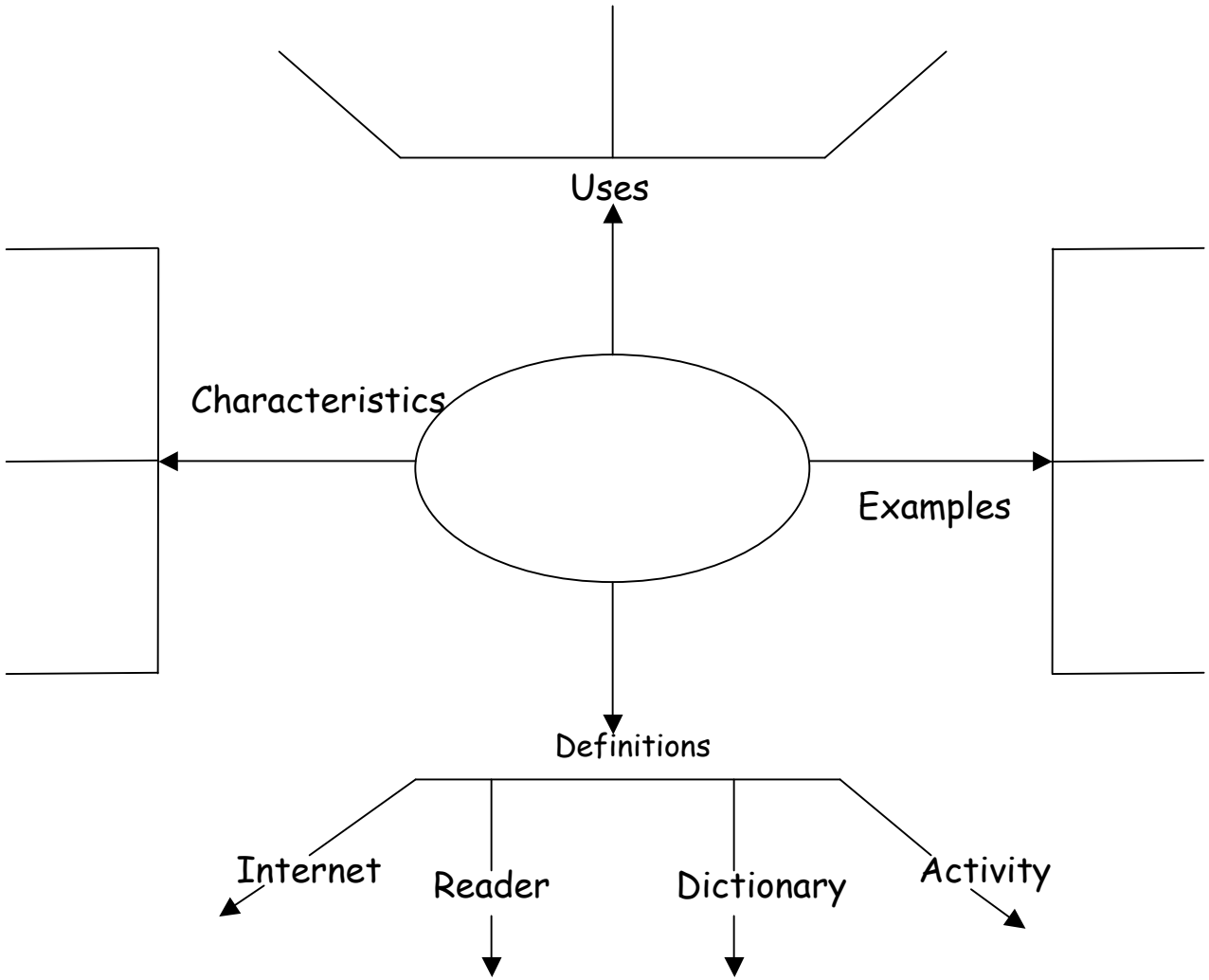
- proteins do the work of the body
- proteins working/not working cause traits
- genes are instructions for making proteins
- the environment can cause genes to be turned on or off

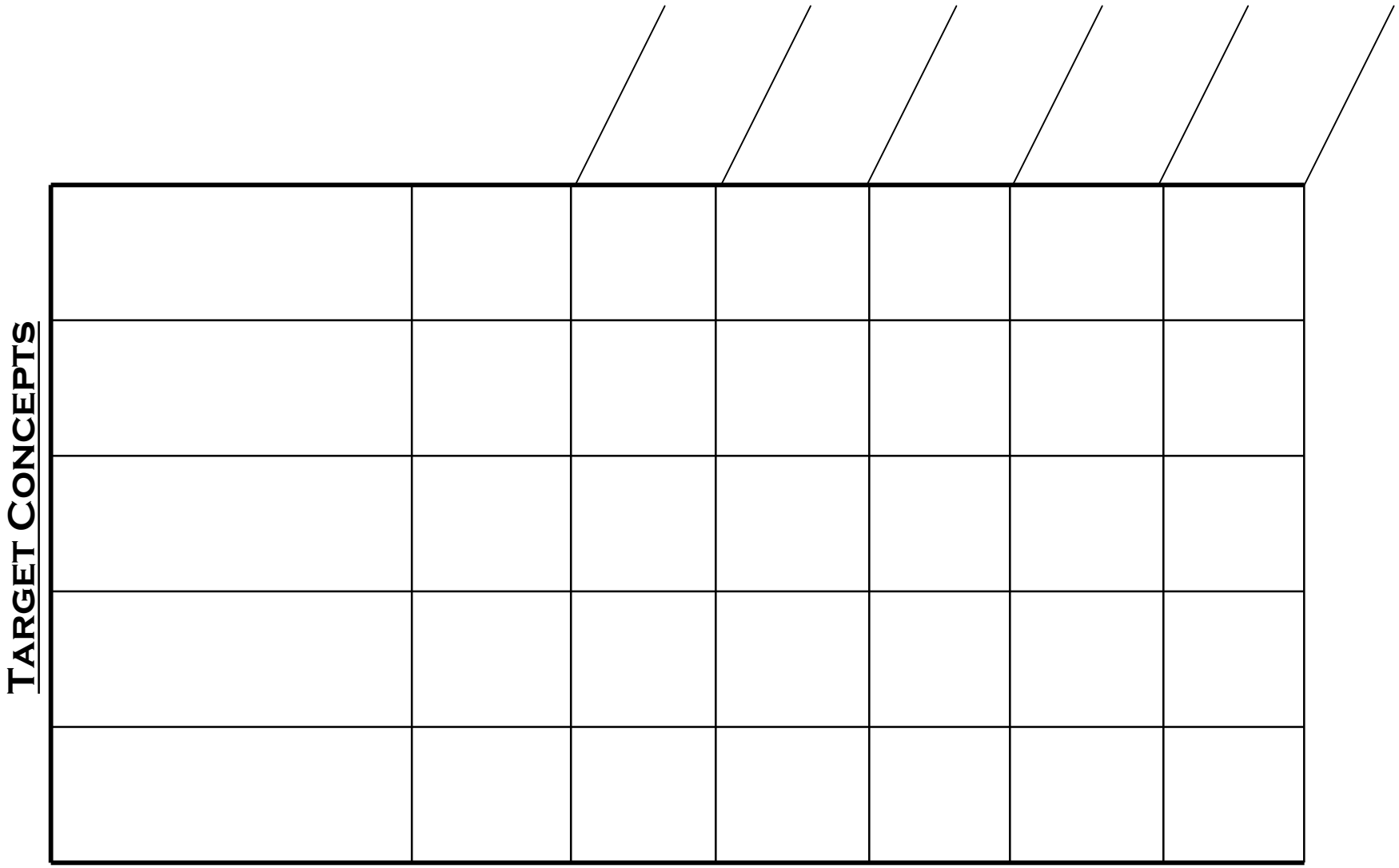


Consider making a large version of this model to keep on the wall in your classroom or making an overhead version that you can add to as a class over the course of the unit.

The numbers here indicate in which lesson the students will be ready to add this information to the chart.




Uses
Characteristics
Examples
Definitions
Internet
Reader
Dictionary
Activity


Features of the object/phenomenon
Target Concepts

Question	Before Reading	After Reading

	Before Reading	After Reading	
Questions	What do you think?	What does the author think?	What do you think now?

263 million bases

Cataracts
Malignant transformation suppression
Ehlers-Danlos syndrome, type VI
Glaucoma, primary infantile
Hirschsprung disease, cardiac defects
Schwartz-Jampel syndrome
Hypophosphatasia, infantile, childhood
Breast cancer, ductal
Cutaneous malignant melanoma/dysplastic nevus
p53-related protein
Serotonin receptors
Schnyder crystalline corneal dystrophy
Kostmann neutropenia
Oncogene MYC, lung carcinoma-derived
Deafness, autosomal dominant
Porphyria
Epiphyseal dysplasia, multiple, type 2
Intervertebral disc disease
Lymphoma, non-Hodgkin
Breast cancer, invasive intraductal
Colon adenocarcinoma
Maple syrup urine disease, type II
Atrioventricular canal defect
Fluorouracil toxicity, sensitivity to
Zellweger syndrome
Stickler syndrome, type III
Marshall syndrome
Stargardt disease
Retinitis pigmentosa
Cone-rod dystrophy
Macular dystrophy, age-related
Fundus flavimaculatus
Hypothyroidism, nongoitrous
Exostoses, multiple
Pheochromocytoma
Psoriasis susceptibility
Limb-girdle muscular dystrophy, autosomal dominant
Pycnodysostosis
Vohwinkel syndrome with ichthyosis
Erythrokeratoderma, progressive symmetric
Anemia, hemolytic
Elliptocytosis
Pyropoikilocytosis
Spherocytosis, recessive
Schizophrenia
Lupus nephritis, susceptibility to
Migraine, familial hemiplegic
Emery-Dreifuss muscular dystrophy
Cardiomyopathy, dilated
Lipodystrophy, familial partial
Dejerine-Sottas disease, myelin P-related
Hypomyelination, congenital
Nemaline myopathy, autosomal dominant
Lupus erythematosus, systemic, susceptibility
Neutropenia, alloimmune neonatal
Viral infections, recurrent
Antithrombin III deficiency
Atherosclerosis, susceptibility to
Glaucoma
Tumor potentiating region
Nephrotic syndrome
Sjogren syndrome
Coagulation factor deficiency
Alzheimer disease
Cardiomyopathy
Factor H deficiency
Membroproliferative glomerulonephritis
Hemolytic-uremic syndrome
Nephropathy, chronic hypocomplementemic
Epidermolysis bullosa
Popliteala pterygium syndrome
Ectodermal dysplasia/skin fragility syndrome
Usher syndrome, type 2A
Kenny-Caffey syndrome
Diphenylhydantoin toxicity

Homocystinuria
Neuroblastoma (neuroblastoma suppressor)
Rhabdomyosarcoma, alveolar
Neuroblastoma, aberrant in some
Exostoses, multiple-like
Opioid receptor
Hyperprolinemia, type II
Bartter syndrome, type 3
Prostate cancer
Brain cancer
Charcot-Marie-Tooth neuropathy
Muscular dystrophy, congenital
Erythrokeratodermia variabilis
Deafness, autosomal dominant and recessive
Glucose transport defect, blood-brain barrier
Hypercholesterolemia, familial
Neuropathy, paraneoplastic sensory
Muscle-eye-brain disease
Medulloblastoma
Basal cell carcinoma
Corneal dystrophy, gelatinous drop-like
Leber congenital amaurosis
Retinal dystrophy
B-cell leukemia/lymphoma
Lymphoma, MALT and follicular
Mesothelioma
Germ cell tumor
Sezary syndrome
Colon cancer
Neuroblastoma
Glycogen storage disease
Osteopetrosis, autosomal dominant, type II
Waardenburg syndrome, type 2B
Vesicoureteral reflux
Choreoathetosis/spasticity, episodic (paroxysmal)
Hemochromatosis, type 2
Leukemia, acute
Gaucher disease
Medullary cystic kidney disease, autosomal dominant
Renal cell carcinoma, papillary
Insensitivity to pain, congenital, with anhidrosis
Medullary thyroid carcinoma
Hyperlipidemia, familial combined
Hyperparathyroidism
Lymphoma, progression of
Porphyria variegata
Hemorrhagic diathesis
Thromboembolism susceptibility
Systemic lupus erythematosus, susceptibility
Fish-odor syndrome
Prostate cancer, hereditary
Chronic granulomatous disease
Macular degeneration, age-related
Epidermolysis bullosa
Chitotriosidase deficiency
Pseudohypoaldosteronism, type II
Hypokalemic periodic paralysis
Malignant hyperthermia susceptibility
Glomerulopathy with fibronectin deposits
Metastasis suppressor
Measles, susceptibility to
van der Woude syndrome (lip pit syndrome)
Rippling muscle disease
Hypoparathyroidism-retardation-dysmorphism syndrome
Ventricular tachycardia, stress-induced polymorphic
Fumarase deficiency
Chediak-Higashi syndrome
Muckle-Wells syndrome
Zellweger syndrome
Adrenoleukodystrophy, neonatal
Endometrial bleeding-associated factor
Left-right axis malformation
Prostate cancer, hereditary
Chondrodysplasia punctata, rhizomelic, type 2

255 million bases

2

Melanoma-associated gene
Thyroid iodine peroxidase deficiency
Goiter, congenital
Hypothyroidism, congenital
Lipoproteinemia, hypobeta, abeta-, hyperbeta-, and apo-
ACTH deficiency
Obesity, adrenal insufficiency, and red hair
LCHAD deficiency
Trifunctional protein deficiency, type 1
HELLP syndrome, maternal, of pregnancy
Fatty liver, acute, of pregnancy
Deafness, autosomal recessive
Glaucoma, primary infantile
Spastic paraplegia
Gingival fibromatosis, hereditary
Holoprosencephaly
Ovarian dysgenesis
Carney complexes
Endometrial carcinoma
Zellweger syndrome
Adrenoleukodystrophy, neonatal
Alstrom syndrome
Preeclampsia/eclampsia
Welander distal myopathy
Kappa light chain deficiency
Pancreatic stone protein
Lissencephaly
Renal tubular acidosis with deafness
BRCA1-associated RING domain (breast cancer)
Achromatopsia
Rhabdomyosarcoma, down-regulated in
Diazepam-binding inhibitor
Thrombophilia due to protein C deficiency
Purpura fulminans, neonatal
Liver cancer oncogene
Xeroderma pigmentosum, group B
Trichothiodystrophy
Nemaline myopathy, autosomal recessive
Convulsions, familial febrile
Progressive intrahepatic cholestasis
Edstrom myopathy
Mesomelic dysplasia, Kantaputra type
Cardiomyopathy, familial hypertrophic
Bardet-Biedl syndrome
Ehlers-Danlos syndromes
Aneurysm, familial arterial
Diabetes mellitus, insulin-dependent
Primary pulmonary hypertension (familial primary)
Cleft palate, isolated
Wrinkly skin syndrome
Amyotrophic lateral sclerosis, juvenile recessive
Lactic acidosis due to defect in iron-sulfur cluster of complex I
Ichthyosis
Finnish lethal neonatal metabolic syndrome
T-cell leukemia or lymphoma
Bjornstad syndrome (pili torti and deafness)
Myopathy, desmin-related, cardioskeletal
Cardiomyopathy, dilated
Natural resistance-associated macrophage protein
Hyperoxaluria, primary, type 1
Alport syndrome, autosomal recessive
Hematuria, familial benign
Brachydactyly-mental retardation syndrome
Oguchi disease
Epidermolysis bullosa

SRY (sex-determining region Y)
Tremor, familial essential
Oculodigitoesophagoduodenal syndrome
Anaplastic lymphoma kinase (Ki-1)
Pseudovaginal perineoscrotal hypospadias
Xanthinuria, type I
Colorectal cancer, hereditary, nonpolyposis, type 1
Ovarian cancer
Muir-Torre syndrome
Human T-cell leukemia virus enhancer factor
Precocious puberty, male
Pseudohermaphroditism, male, with Leydig cell hypoplasia
Hypogonadotropic hypogonadism
Micropenis
Leydig cell adenoma, with precocious puberty
Sitosterolemia
Cystinuria
Doyne honeycomb degeneration of retina
Dyslexia, specific
Muscular dystrophy
Miyoshi myopathy
Myopathy, distal, with anterior tibial onset
Orofacial cleft
Parkinson disease, type 3
Vitamin K-dependent coagulation defect
Pancreatitis-associated protein
Pulmonary alveolar proteinosis, congenital
Glaucoma, open angle, B (adult-onset)
Diabetes mellitus, non-insulin-dependent
Ectodermal dysplasia, autosomal dominant and recessive
Hypothyroidism, congenital
Nephronophthisis
Colorectal cancer
Cardiomyopathy, dilated
Spastic cerebral palsy, symmetric, autosomal recessive
Epilepsy
Ataxia, episodic
Deafness, autosomal dominant
Myasthenic syndrome, slow-channel congenital
Rhizomelic chondrodysplasia punctata, type 3
Cardiomyopathy, dilated
Duane retraction syndrome
Synpolydactyly, type II
Colorectal cancer, hereditary nonpolyposis, type 3
Neurogenic differentiation
Arrhythmogenic right ventricular dysplasia
Myasthenia gravis, neonatal transient
Cataracts
Paroxysmal nonkinesiogenic dyskinesia
Choreoathetosis, familial paroxysmal
Cerebrotendinous xanthomatosis
Acyl-Coenzyme A dehydrogenase
Carbamoylphosphate synthetase I
Waardenburg syndrome, types I and III
Rhabdomyosarcoma, alveolar
Craniofacial-deafness-hand syndrome
Brachydactyly, type A1
Goodpasture antigen
Serotonin receptor
Bethlem myopathy
Programmed cell death
Leigh syndrome, French-Canadian type
Ultraviolet damage, repair of
Crigler-Najjar syndrome, type I

214 million bases

von Hippel-Lindau syndrome
Renal cell carcinoma
Fanconi anemia, complementation group D
Biotinidase deficiency
Xeroderma pigmentosum, complementation group C
Cardiomyopathy, dilated, autosomal dominant
Endplate acetylcholinesterase deficiency
Arrhythmogenic right ventricular dysplasia
Teratocarcinoma-derived growth factor
Hepatoblastoma
Pilomatricoma
Ovarian carcinoma, endometrioid type
Hypobetalipoproteinemia, familial
GM1-gangliosidosis
Mucopolysaccharidosis
BRCA1 associated protein (breast cancer)
Hemolytic anemia
Septooptic dysplasia
Progressive external ophthalmoplegia, type 2
Larsen syndrome, autosomal dominant
HIV infection, susceptibility/resistance to
Ichthyosiform erythroderma, congenital
Long QT syndrome
Brugada syndrome
Heart block, progressive and nonprogressive
Deafness, autosomal recessive
Waardenburg syndrome
Tietz syndrome
Glycogen storage disease
Dementia, familial, nonspecific
Pituitary hormone deficiency, combined
Thyrotropin-releasing hormone deficiency
Deafness, autosomal recessive
Hypomagnesemia, primary
Tremor, familial essential
Charcot-Marie-Tooth neuropathy
Malignant hyperthermia susceptibility
Hypocalciuric hypercalcemia, type I
Neonatal hyperparathyroidism
Hypocalcemia, autosomal dominant
Atransferrinemia
Propionicacidemia, type II or pccB
Hailey-Hailey disease
Retinitis pigmentosa, autosomal dominant and recessive
Night blindness, congenital stationery, rhodopsin-related
Cataracts, juvenile-onset and congenital
Common acute lymphocytic leukemia antigen
Blepharophimosis, epicanthus inversus and ptosis type 1
Hemosiderosis, systemic
Sucrose intolerance
Cerebral cavernous malformations
Myelodysplasia syndrome
Apnea, postanesthetic
Ovarian cancer
Megakaryocyte growth and development factor
Thrombocythemia, essential
Peroxisomal bifunctional enzyme deficiency
Thrombophilia due to HRG deficiency
Leukoencephalopathy with vanishing white matter
Lipoma-preferred-partner gene fused with HMGIC

Moyamoya disease
Muscular dystrophy, limb-girdle, type IC
Obesity, severe
Diabetes mellitus, insulin-resistant
Marfan-like connective tissue disorder
Thyroid hormone resistance
Usher syndrome, type IIB
Pseudo-Zellweger syndrome
Lung cancer, small-cell
Colon cancer
Deleted in lung and esophageal cancer
Metaphyseal chondrodysplasia, Murk Jansen type
Carnitine-acylcarnitine translocase (deficiency)
Epidermolysis bullosa
Colorectal cancer, hereditary nonpolyposis, type 2
Turcot syndrome with glioblastoma
Muir-Torre family cancer syndrome
Hyperglycinemia, nonketotic
Pancreatic cancer
Spinocerebellar ataxia
Pituitary ACTH-secreting adenoma
Ventricular tachycardia, idiopathic
Night blindness, congenital stationary
T-cell leukemia translocation altered gene
Wernicke-Korsakoff syndrome, susceptibility to
Bardet-Biedl syndrome
Nonpapillary renal carcinoma
Protein S deficiency
Ventricular, skeletal, slow
Cardiomopathy, hypertrophic
Myotonic dystrophy
Coproporphyria
Harderoporphyrinuria
Oroticaciduria
Neuropathy, hereditary motor and sensory, Okinawa type
Dopamine receptor
Psoriasis susceptibility
Moebius syndrome
Alkaptonuria
Glaucoma, primary open angle
Hypertension, essential
Usher syndrome (Finland)
Nephronophthisis, adolescent
Ataxia telangiectasia
Short stature
Myeloid leukemia factor, acute
Ectropic viral integration site (oncogene EVI1)
3q21q26 syndrome
Encephalopathy, familial, with neuroserpin inclusion bodies
Diabetes mellitus, noninsulin-dependent
Fanconi-Bickel syndrome
SRY (sex determining region Y)
Lymphomas
Eukaryotic translation initiation factor (squamous cell lung cancer)
Limb-mammary syndrome
Tumor protein p63
Ectrodactyly, ectodermal dysplasia, and cleft lip/palate syndrome
Optic atrophy
Lipoma
Bernard-Soulier syndrome, type C melanoma-associated

203 million bases

Cherubism (familial benign giant-cell tumor of the jaw)
Dopamine receptor
Huntington disease
Night blindness, congenital stationary, type 3
Retinitis pigmentosa, autosomal recessive
Retinal degeneration, autosomal recessive
Wolfram syndrome
Craniosynostosis, Adelaide type
Phenylketonuria
Parkinson disease, familial
Pituitary tumor-transforming gene
Stargardt disease
Dentin dysplasia, Shields type II
Leukemia, acute myeloid
Periodontitis, juvenile
Muscular dystrophy, limb-girdle, type 2E
Melanoma growth-stimulating activity
Hyper-IgE syndrome
Renal tubular acidosis
Mucolipidosis
Lymphocytic leukemia, acute T-cell
Alcoholism, susceptibility to
Wolfram syndrome
Sclerotylosis
Huriez syndrome
Rieger syndrome
Iridogoniodysgenesis syndrome
Severe combined immunodeficiency
Afibrinogenemia
Anterior segment mesenchymal dysgenesis
Tryptophan oxygenase
Aspartylglucosaminuria
Hepatitis B virus integration site
Hepatocellular carcinoma
Progressive external ophthalmoplegia, type 3
Coagulation factor XI
Facioscapulohumeral muscular dystrophy
Eutropenia, neonatal alloimmune
Fletcher factor

Deafness, autosomal dominant
Achondroplasia
Hypochondroplasia
Thanatophoric dysplasia, types I and II
Crouzon syndrome with acanthosis nigricans
Muencke syndrome
Mucopolysaccharidosis
Wolf-Hirschhorn syndrome
Hypodontia
Dopamine receptor
Ellis-van Creveld syndrome
Weyers acrodental dysostosis
Huntington-like neurodegenerative disorder
Retinitis pigmentosa, autosomal recessive
Psoriasis susceptibility
Analbuminemia
Amelogenesis imperfecta
Piebaldism
Mast cell leukemia
Mastocytosis with associated hematologic disorder
Germ cell tumors
Dentinogenesis imperfecta
Myeloid/lymphoid or mixed-lineage leukemia
Parkinson disease, type 1
Polycystic kidney disease, adult, type II
Hypogonadotropic hypogonadism
Abetalipoproteinemia
Mannosidosis, beta
C3b inactivator deficiency
Long QT syndrome with sinus bradycardia
Fibrodysplasia ossificans progressiva
Fibrinogenemia
Amyloidosis, hereditary renal
Hair color, red
Pseudohypoaldosteronism type I, autosomal dominant
Glutaricaciduria, type IIC
Hypercalciuria
Beukes familial hip dysplasia
Facioscapulohumeral muscular dystrophy region

194 million bases

5

Dopamine transporter
Attention-deficit hyperactivity disorder, susceptibility to
Cri-du-chat syndrome, mental retardation in
Chondrocalcinosis
Taste receptor
Alpha-methylacyl-CoA racemase deficiency
Differentially expressed in ovarian cancer
Ketoacidosis
Leukemia inhibitory factor receptor
Myopathy, distal, with vocal cord and pharyngeal weakness
Molybdenum cofactor deficiency, type B
Endometrial carcinoma
Klippel-Feil syndrome
Anemia, megaloblastic
Sandhoff disease
Spinal muscular atrophy, juvenile
X-ray repair
Convulsions, familial febrile
Adenomatous polyposis coli
Gardner syndrome
Colorectal cancer
Desmoid disease
Turcot syndrome
Ehlers-Danlos syndromes
Neonatal alloimmune thrombocytopenia
Myelodysplastic syndrome
Limb-girdle muscular dystrophy, autosomal dominant
Deafness
Bronchial hyperresponsiveness (bronchial asthma)
Hemangioma, capillary infantile
Spinocerebellar ataxia
Macrocytic anemia
Gastric cancer
Non small-cell lung cancer
Retinitis pigmentosa, autosomal recessive
Charcot-Marie-Tooth neuropathy
Netherton syndrome
Treacher Collins-Franceschetti syndrome
Pituitary tumor-transforming gene
Coagulation factor XII (Hageman factor)
Myeloid malignancy, predisposition to
Craniosynostosis, type 2
Parietal foramina
Leukotriene C4 synthase deficiency
Dopamine receptor
Hermansky-Pudlak syndrome

Homocystinuria-megaloblastic anemia, cbl E type
Craniometaphyseal dysplasia
Leigh syndrome
Polycystic ovary syndrome
Hirschsprung disease
Severe combined immunodeficiency
Dwarfism
Malignant hyperthermia susceptibility
Pituitary hormone deficiency
Cytotoxic T-lymphocyte-associated serine esterase
Hanukah factor serine protease
Maroteaux-Lamy syndrome
Serotonin receptor
Schizophrenia susceptibility locus
Wagner syndrome
Erosive vitreoretinopathy
Basal cell carcinoma
Obesity with impaired prohormone processing
Diphtheria toxin receptor
Contractural arachnodactyly, congenital
Cutis laxa, recessive, type I
Deafness
Cortisol resistance
Corneal dystrophy
Eosinophilia, familial
Serotonin receptor
Schistosoma mansoni infection, susceptibility/resistance to
Natural killer cell stimulatory factor-2
GM2-gangliosidosis, AB variant
Startle disease, autosomal dominant and recessive
Diastrophic dysplasia
Atelosteogenesis
Achondrogenesis
Epiphyseal dysplasia, multiple
Asthma, nocturnal, susceptibility to
Obesity, susceptibility to
Muscular dystrophy, limb-girdle, type 2F
Carnitine deficiency, systemic primary
Atrial septal defect with atrioventricular conduction defects
Arthrogryposis multiplex congenital, neurogenic
Leukemia, acute promyelocytic, NPM/RARA type
Vascular endothelial growth factor receptor
Lymphedema, hereditary
Cockayne syndrome
Pancreatitis, hereditary

6

183 million bases

Iridogoniodysgenesis
Anterior segment mesenchymal dysgenesis
Rieger anomaly
Axenfeld anomaly
Coagulation factor XIII
Keratosis palmoplantaris striata
Spinocerebellar ataxia
Schizophrenia susceptibility locus
Maple syrup urine disease, type Ib
Bare lymphocyte syndrome, type I
Atrial septal defect, secundum type
Adrenal hyperplasia, congenital
Renal glucosuria
Beryllium disease, chronic, susceptibility to
Leukemia, pre-B-cell transcription factor
Tumor necrosis factor (cachectin)
Malaria, cerebral, susceptibility to
Retinitis pigmentosa
Platelet-activating factor
Asthma and atopy, susceptibility to
Peroxisomal biogenesis disorder
Anemia, hemolytic, Rh-null, suppressor type
Methylmalonicaciduria, mutase deficiency type
Hemolytic anemia
Char syndrome
Gluten-sensitive enteropathy (celiac disease)
Cone-rod dystrophy
Inflammatory bowel disease
Mixed polyposis syndrome, hereditary
Leber congenital amaurosis, type V
Serotonin receptors
Macular dystrophy, retinal, North Carolina type
Obesity, severe
Diabetes mellitus, insulin-dependent
Muscular dystrophy, congenital merosin-deficient
Arthropathy, progressive pseudorheumatoid, of childhood
Rhizomelic chondrodysplasia punctata, type 1
Deafness
Cardiomyopathy, dilated, autosomal dominant
Human immunodeficiency virus type I susceptibility
Epilepsy, myoclonic, Lafora type
Opioid receptor
Estrogen receptor
Breast cancer
Estrogen resistance
Insulin-like growth factor-2 receptor
Hepatocellular carcinoma
Tumorigenicity, suppression of
Loss of heterozygosity, ovarian
Ovarian cancer, serous
Myeloid/lymphoid or mixed-lineage leukemia
Pancreatic beta cell, agenesis of
uniparental disomy
Conjunctivitis, ligneous
Coronary artery disease, susceptibility to
Complex neurologic disorder
Xeroderma pigmentosum, variant type

Multiple myeloma oncogene
Orofacial cleft
Leukemia, acute nonlymphocytic
SRY (sex determining region Y)
Fanconi anemia, complementation group E
Ankylosing spondylitis
Stickler syndrome, type II
OSMED syndrome
Weissenbacher-Zweymuller syndrome
Deafness, nonsyndromic sensorineural
Dyslexia
Hemochromatosis
Porphyria variegata
Pemphigoid, susceptibility to
Immune suppression to streptococcal antigen
Sialidosis, types I and II
Panbronchiolitis, diffuse
Psoriasis susceptibility
Ehlers-Danlos-like syndrome
Cone dystrophy
Polycystic kidney and hepatic disease, autosomal recessive
Retinal degeneration, slow (peripherin)
Retinitis pigmentosa, peripherin-related and punctata albescens
Macular dystrophy
Butterfly dystrophy, retinal
Cleidocranial dysplasia
Dental anomalies, isolated
Nystagmus, autosomal dominant
Bullous pemphigoid antigen 1
Pelviureteric junction obstruction
Stargardt disease, autosomal dominant
Epilepsy, juvenile myoclonic
Brain-specific angiogenesis inhibitor
Diazepam-binding inhibitor
Schizophrenia susceptibility locus
Salla disease
Sialic acid storage disorder, infantile
Chorioretinal atrophy, progressive bifocal
Melanoma, absent in
Metaphyseal chondrodysplasia, Schmid type
Spondylometaphyseal dysplasia, Japanese type
Hepatic fibrosis susceptibility
Oculodentodigital dysplasia (Syndactyly type III)
Hereditary persistence of fetal hemoglobin, heterocellular
Argininemia
Leukemia
Immune interferon, receptor for
Mycobacterial infection, atypical, familial disseminated
BCG infection, generalized familial
Tuberculosis, susceptibility to
Diabetes mellitus, transient neonatal
Pleomorphic adenoma (ZAC tumor supressor)
Parkinson disease, juvenile, type 2
Plasminogen Tochigi disease
Thrombophilia, dysplasminogenemic
Plasminogen deficiency, types I and II

171 million bases

Ewing sarcoma
Turcot syndrome with glioblastoma
Colorectal cancer, hereditary nonpolyposis, type 4
Osteopenia/osteoporosis
Macular dystrophy, dominant cystoid
Retinitis pigmentosa
Growth hormone deficient dwarfism
Hand-foot-uterus syndrome
Hyperinsulinism, familial
Charcot-Marie-Tooth neuropathy, neuronal type D
Alpha-ketoglutarate dehydrogenase deficiency
Myopathy
T-cell tumor invasion and metastasis
Argininosuccinicaciduria
Hyperreflexia
Clostridium perfringens enterotoxin receptor
Supravalvar aortic stenosis
Williams-Beuren syndrome
Cutis laxa
Cytoplasmic linker
Williams-Beuren syndrome chromosome region 4
Chronic granulomatous disease
Malignant hyperthermia susceptibility
P-glycoprotein/multiple drug resistance
Colchicine resistance
Cholestasis
Split hand/foot malformation (ectrodactyly) type 1
Paraoxonase
Coronary artery disease, susceptibility to
Plasminogen activator inhibitor, type I
Thrombophilia
Hemorrhagic diathesis
Hemochromotosis
Osteogenesis imperfecta
Ehlers-Danlos syndrome, type VIIA2
Osteoporosis, idiopathic
Marfan syndrome, atypical
Deafness, autosomal recessive
Pendred syndrome
Deafness, autosomal recessive
Enlarged vestibular aqueduct
Lipoamide dehydrogenase deficiency
Hemolytic anemia
Suppression of tumorigenicity (breast)
Obesity
Taste receptors
Renal tubular acidosis, distal, autosomal recessive
Deafness, autosomal recessive
Trypsinogen deficiency
Pancreatitis, hereditary
Glaucoma-related pigment dispersion syndrome

Lunatic fringe
Craniosynostosis, type 1
Saethre-Chotzen syndrome
Blepharophimosis, epicanthus inversus, and ptosis
Deafness, autosomal dominant
Myeloid leukemia
Cerebral cavernous malformations
Wilms tumor suppressor locus
Amphiphysin (Stiff-Man syndrome)
Greig cephalopolysyndactyly syndrome
Pallister-Hall syndrome
Polydactyly
Glioblastoma amplified sequence
Spinal muscular atrophy, distal
Autism, susceptibility to
Limb-girdle muscular dystrophy, autosomal dominant
Platelet glycoprotein IV deficiency
Cerebral cavernous malformations
Colon cancer
Zellweger syndrome
Adrenoleukodystrophy, neonatal
Refsum disease, infantile
Mucopolysaccharidosis
Osteoporosis, postmenopausal, susceptibility
Citrullinemia, adult-onset type II
Ulcerative colitis, susceptibility to
Adenoma, down-regulated in
Chloride diarrhea, congenital, Finnish type
Cardiomyopathy, familial hypertrophic
Renal cell carcinoma, papillary, familial and sporadic
Hepatocellular carcinoma, childhood type
Speech-language disorder
Basal cell carcinoma, sporadic
Retinitis pigmentosa, autosomal dominant
Cystic fibrosis
Congenital bilateral absence of vas deferens
Sweat chloride elevation without CF
Colorblindness, blue cone pigment
Myotonia
Glaucoma, open angle
Human ether-a-go-go-related gene
Long QT syndrome
Preeclampsia, susceptibility to
Coronary spasm, susceptibility to
Holoprosencephaly
Serotonin receptor
Growth rate controlling factor
Currarino syndrome
Sacral agenesis
Triphalangeal thumb-polysyndactyly syndrome
X-ray repair

155 million bases

Epilepsy, progressive, with mental retardation
Keratolytic winter erythema
Prostate cancer tumor suppressor, putative
Liver cancer, deleted in
Alopecia universalis
Atrichia with papular lesions
Scurvy
Schizophrenia susceptibility locus
Plasminogen activator deficiency
Spastic paraplegia, autosomal recessive
Lipoid adrenal hyperplasia
Monocytic leukemia
Retinitis pigmentosa
Pleomorphic adenoma
ACTH deficiency
Convulsions, familial febrile
Ataxia with isolated vitamin E deficiency
Achromatopsia
CMO II deficiency
Zellweger syndrome
Refsum disease, infantile form
Lymphoma, non-Hodgkin
Colon adenocarcinoma
Dihydropyrimidinuria
Cohen syndrome
Glaucoma, open angle
Epidermolysis bullosa simplex, Ogna type
Neuropathy, hereditary motor and sensory
Epilepsy
Oncogene PVT (MYC activator)
Nephroblastoma overexpressed gene
Exostoses, multiple, type 1
Chondrosarcoma
Trichorhinophalangeal syndrome type I
Prostate stem cell antigen
Rothmund-Thomson syndrome
Meleda disease

Microcephaly, primary autosomal recessive
Hyperlipoproteinemia
Chylomicronemia syndrome, familial
Combined hyperlipemia, familial
Farber lipogranulomatosis
Hepatocellular cancer
Colorectal cancer
Hemolytic anemia
Hypotrichosis, Marie Unna type
Torsion dystonia, adult onset, of mixed type
Werner syndrome
Spherocytosis
Pfeiffer syndrome
Chondrocalcinosis, with early-onset osteoarthritis
Opiate receptor, kappa
Salivary gland pleomorphic adenoma
Duane retraction syndrome
Charcot-Marie-Tooth neuropathy, autosomal recessive
Branchiootorenal syndromes
Branchiootic syndrome
Adrenal hyperplasia, congenital
Aldosteronism
Nijmegen breakage syndrome
Giant cell hepatitis, neonatal
Renal tubular acidosis-osteopetrosis syndrome
Segmentation syndrome
Spastic paraplegia
Brain-specific angiogenesis inhibitor
Papillomavirus type 18 integration site
Muscular dystrophy with epidermolysis bullosa
Macular dystrophy, atypical vitelliform
Renal cell carcinoma
Langer-Giedion syndrome
Burkitt lymphoma
Hypothyroidism, hereditary congenital
Goiter, adolescent multinodular and nonendemic

9

145 million bases

Sex-reversal, autosomal
Hyperglycinemia, nonketotic
Suppression of tumorigenicity, pancreas
Diaphyseal medullary stenosis
Melanoma
Trichoepithelioma, multiple familial
Immotile cilia syndrome
Cartilage-hair hypoplasia
X-ray repair
Fanconi anemia, complementation group G
Sialuria
Hyperoxaluria, primary, type II
Cardiomyopathy
Deafness, autosomal recessive
Choreoacanthocytosis
Prostate-specific gene
Bamforth-Lazarus syndrome
Tyrosine kinase-like orphan receptor
Brachydactyly, type B1
Nephronophthisis (infantile)
Neuropathy, sensory and autonomic, type 1
Fructose intolerance
Basal cell carcinoma, sporadic
Muscular dystrophy, Fukuyama congenital
Basal cell nevus syndrome
Dysautonomia (Riley-Day syndrome)
Esophageal cancer
Endotoxin hyporesponsiveness
Amyotrophic lateral sclerosis, juvenile dominant
Berardinelli-Seip congenital lipodystrophy
Dystonia, torsion, autosomal dominant
Lethal congenital contracture syndrome
Leukemia, acute undifferentiated
Tuberous sclerosis
Hemolytic anemia
Telangiectasia, hereditary hemorrhagic
Ehlers-Danlos syndrome, types I and II
Joubert syndrome
Leukemia, T-cell acute lymphoblastic

Ovarian cancer
Albinism, brown and rufous
Interferon, alpha, deficiency
Leukemia
Cyclin-dependent kinase inhibitor
Venous malformations, multiple cutaneous and mucosal
Arthrogryposis multiplex congenita, distal, type 1
Galactosemia
Acromesomelic dysplasia, Maroteaux type
Myopathy, inclusion body, autosomal recessive
Hypomagnesemia with secondary hypocalcemia
Friedreich ataxia
Geniospasm
Bleeding diathesis
Hemophagocytic lymphohistiocytosis, familial
Chondrosarcoma, extraskeletal myxoid
Pseudohermaphroditism, male, with gynecomastia
Tangier disease
HDL deficiency, familial
Fanconi anemia, type C
Xeroderma pigmentosum
Epithelioma, self-healing, squamous
Leukemia, T-cell acute lymphoblastic
Muscular dystrophy, limb-girdle, type 2H
Bladder cancer
Sex reversal, XY, with adrenal failure
Leukemia transcription factor, pre-B-cell
Porphyria, acute hepatic
Lead poisoning, susceptibility to
Citrullinemia
Dopamine-beta-hydroxylase deficiency
Amyloidosis, Finnish type
Microcephaly, primary autosomal recessive
Leigh syndrome
Leukemia
Nail-patella syndrome
Prostaglandin D2 synthase (brain)
Pituitary hormone deficiency

10

144 million bases

Refsum disease, adult
Hypoparathyroidism, deafness, renal dysplasia
DiGeorge syndrome/velocardiofacial syndrome
Leukemia
Thrombocytopenia
Osaka thyroid oncogene
Ewing Sarcoma
Obesity, susceptibility to
Multiple endocrine neoplasia
Medullary thyroid carcinoma
Hirschsprung disease
Thyroid papillary carcinoma
Deafness, autosomal recessive
Serotonin receptor
Moebius syndrome
Hemolytic anemia
Hyperphenylalaninemia
Metachromatic leukodystrophy
Gaucher disease, variant form
SEMD, Pakistani type
Hermansky-Pudlak syndrome
Breast cancer
Multiple advanced cancers
Cowden disease
Lhermitte-Duclos syndrome
Bannayan-Zonana syndrome
Endometrial carcinoma
Polyposis, juvenile intestinal
Prostate cancer
Progressive external ophthalmoplegia
Corneal dystrophy, Thiel-Behnke type
Leukemia, T-cell acute lymphocytic
Spinocerebellar ataxia, infantile-onset
Split hand/foot malformation, type 3
Polycystic kidney disease
Meningioma-expressed antigen
Adrenal hyperplasia, congenital
Diabetes mellitus, insulin-dependent
Anterior segment mesenchymal dysgenesis
Cataract, congenital
Malignant brain tumors
Glioblastoma multiforme
Medulloblastoma
Crouzon syndrome
Jackson-Weiss syndrome
Beare-Stevenson cutis gyrata syndrome

Suppression of tumorigenicity, prostate
Prostate adenocarcinoma
Interleukin receptor, alpha chain, deficiency of
Arrhythmogenic right ventricular dysplasia
Myasthenic antigen B
Lambert-Eaton syndrome
Megaloblastic anemia
Diabetes mellitus, insulin-dependent
Severe combined immunodeficiency disease, Athabascan
Cockayne syndrome, type B
Cerebrooculofacioskeletal syndrome
Opsonic defect
Chronic infections
Retinal nonattachment, nonsyndromic congenital
Cardiomyopathy, dilated, autosomal dominant
Neuropathy, congenital hypomyelinating
Graves disease autoantigen
Hypermethioninemia, persistent, autosomal dominant
Hemophagocytic lymphohistiocytosis, familial
Retinitis pigmentosa, autosomal recessive and dominant
Urofacial syndrome (Ochoa syndrome)
Hypoglobulinemia and absent B cells
Hyperinsulinism-hyperammonemia syndrome
Spastic paraplegia
Dubin-Johnson syndrome
Warfarin sensitivity
Wolman disease
Cholesteryl ester storage disease
Tumor necrosis factor receptor superfamily, member 6
Autoimmune lymphoproliferative syndrome
Epidermolysis bullosa, generalized atrophic benign
Optic nerve coloboma with renal disease
Prostate cancer
Neurofibrosarcoma
Porphyria, congenital erythropoietic
Endometrial carcinoma
Gyrate atrophy of choroid and retina
Pancreatic lipase deficiency
Glaucoma
Pfeiffer syndrome
Apert syndrome
Saethre-Chotzen syndrome
Schizencephaly
Polykaryocytosis inducer (promoter)
Usher syndrome, autosomal recessive, severe

144 million bases

Beckwith-Wiedemann syndrome
Cyclin-dependent kinase inhibitor
Dopamine receptor
Autonomic nervous system dysfunction
Long QT syndrome
Jervell and Lange-Nielsen syndrome
Thalassemia
Diabetes mellitus, rare form
Hyperproinsulinemia, familial
Breast cancer
Rhabdomyosarcoma
Lung cancer
Segawa syndrome, recessive
Hypoparathyroidism, dominant and recessive
Tumor susceptibility gene
Breast cancer
Usher syndrome
Atrophia areata
Fanconi anemia, complementation group F
Leukemia, myeloid and lymphocytic
Acatalasemia
Aniridia
Peters anomaly
Cataract, congenital
Foveal hypoplasia, isolated
Keratitis
Severe combined immunodeficiency, B cell-negative
Reticulosis, familial histiocytic
Omenn syndrome
Wilms tumor, type 1
Denys-Drash syndrome
Frasier syndrome
Foramina parietalia permagna (Catlin marks)
Exostoses, multiple
Suppression of tumorigenicity, prostate
Prostate cancer
Spinocerebellar ataxia
Hyperlipidemia, combined
Osteoarthritis susceptibility, female-specific
Xeroderma pigmentosum, group E, subtype 2
High bone mass
Osteoporosis-pseudoglioma syndrome
Parathyroid adenomatosis
Centrocytic lymphoma
Multiple myeloma
Mammary tumor and squamous cell carcinoma
Anemia, pernicious, congenital
Multiple endocrine neoplasia
Hyperparathyroidism
Prolactinoma, carcinoid syndrome
Asthma, atopic, susceptibility to
Leukemia, acute promyelocytic
Retinitis pigmentosa, digenic
Cervical carcinoma
Macular dystrophy, vitelliform type (Best disease)
Spinal muscular atrophy with respiratory distress
Paraganglioma or familial glomus tumors
Folate receptor, adult
T-cell immune regulator
Osteopetrosis, recessive
Leukemia, acute myeloid and T-cell lymphoblastic
Ataxia-telangiectasia-like disorder
Apoptosis inhibitor
Deafness, autosomal dominant and recessive
Phenylketonuria
Hypertriglyceridemia
Immunodeficiency
Erythrocytosis, autosomal recessive benign
Glycogen storage disease
Jacobsen syndrome
Paragangliomas, familial nonchromaffin
Herpes virus entry mediator
Epstein-Barr virus modification site
Serotonin receptor
Porphyria, acute intermittent

Freeman-Sheldon syndrome variant
Jansky-Bielschowsky disease
Diabetes mellitus, insulin-dependent
Sickle cell anemia
Thalassemias, beta
Erythremias, beta
Heinz body anemias, beta
HPFH, deletion type
Bladder cancer
Wilms tumor, type 2
Adrenocortical carcinoma, hereditary
Sjogren syndrome antigen
Niemann-Pick disease, types A and B
Osteoporosis
Persistent hyperinsulinemic hypoglycemia of infancy
Deafness, autosomal recessive
Charcot-Marie-Tooth disease, type 4B
Leukemia, T-cell acute lymphoblastic
Hepatitis B virus integration site
Hepatocellular carcinoma
Lacticacidemia
T-cell leukemia/lymphoma
Diabetes mellitus, noninsulin-dependent
Xeroderma pigmentosum, group E
Cardiomyopathy, familial hypertrophic
Prostate cancer overexpressed gene
Coagulation factor II (thrombin)
Hypoprothrombinemia
Dysprothrombinemia
Complement component inhibitor
Angioedema, hereditary
Smith-Lemli-Opitz syndrome, types I and II
IgE responsiveness, atopic
Bardet-Biedl syndrome
Kaposi sarcoma
Diabetes mellitus, insulin-dependent
Meckel syndrome, type 2
Leigh syndrome
Alexander disease
McArdle disease
Somatotrophinoma
UV radiation resistance-associated gene
Vitreoretinopathy
Leukemia/lymphoma, B-cell
Pyruvate carboxylase deficiency
Usher syndrome, type 1B
Papillon-Lefevre syndrome
Albinism, oculocutaneous, type IA
Waardenburg syndrome
Glomerulosclerosis
Lung cancer
Ataxia-telangiectasia
T-cell prolymphocytic leukemia, sporadic
Lymphoma, B-cell non-Hodgkin
Breast cancer
Myopathy, desmin-related, cardioskeletal
ApoA-I and apoC-III deficiency
Hypertriglyceridemia
Hypoalphalipoproteinemia
Corneal clouding, autosomal recessive
Amyloidosis
Dopamine receptor
Dystonia, myoclonic
Ectodermal dysplasia, type 4 (Margarita type)
Hypomagnesemia, renal
Leukemia, myeloid/lymphoid or mixed-lineage
Lung cancer, non small-cell
Hydrolethalus syndrome
Porphyria, acute, Chester type
Megaloblastic anemia syndrome
Friend leukemia virus integration
Ewing sarcoma
Histiocytosis with joint contractures and deafness
Opioid-binding protein/cell adhesion molecule
Bartter syndrome, type 2

12

143 million bases

Lupus erythematosus
Hypophosphatemic rickets, autosomal dominant
Coagulation factor VIII (von Willebrand factor)
Tumor necrosis factor receptor superfamily
Periodic fever, familial
Keutel syndrome
Periodic fever, familial (Hibernian fever)
Episodic ataxia/myokymia syndrome
Pseudohypoaldosteronism, type I
Hemolytic anemia
Diabetes-associated peptide (amylin)
Lactate dehydrogenase-B deficiency
Colorectal cancer
Fibrosis of extraocular muscles, autosomal dominant
Adrenoleukodystrophy
Palmoplantar keratoderma, Bothnia type
Melanoma
Rickets, vitamin D-resistant
Anti-Mullerian hormone receptor, type II
Persistent Mullerian duct syndrome, type II
Activating transcription factor 1
Soft tissue clear cell sarcoma
Myopathy, congenital
Meesmann corneal dystrophy
Epidermolysis bullosa simplex
Cataract, polymorphic and lamellar
Sarcoma amplified sequence
Enuresis, nocturnal
Achondrogenesis-hypochondrogenesis, type II
Osteoarthrosis, precocious
Wagner syndrome, type II
SMED, Strudwick type
Scapuloperoneal syndrome
Sanfilippo syndrome, type D
Lipoma
Salivary adenoma
Uterine leiomyoma
Myopia, high grade, autosomal dominant
Darier disease
Spinocerebellar ataxia
Mevalonicaciduria
Hyperimmunoglobulinemia D and periodic fever
Spinal muscular atrophy
Phenylketonuria
Ulnar-mammary syndrome
Diabetes mellitus
Maturity-Onset Diabetes of the Young
Oral cancer

Dentatorubro-pallidoluysian atrophy
Emphysema
Alzheimer disease, susceptibility to
Inflammatory bowel disease
Leukemia, acute lymphoblastic
Hypertension, essential, susceptibility to
Leukemia factor, myeloid
Spastic paraplegia, autosomal dominant
Taste receptors
Glycogen storage disease, type 0
Hypertension with brachydactyly
Alzheimer disease, familial
Retinoblastoma-binding protein
Ichthyosis bullosa of Siemens
Telangiectasia, hereditary hemorrhagic
Leukemia: myeloid, lymphoid, or mixed-lineage
Allgrove syndrome
Diabetes insipidus, nephrogenic, dominant and recessive
Human papillomavirus type 18 integration site
Epidermolytic hyperkeratosis
Keratoderma, palmoplantar, nonepidermolytic
Cyclic ichthyosis with epidermolytic hyperkeratosis
White sponge nevus
Pachyonychia congenita
Fundus albipunctatus
Glioma
Myxoid liposarcoma
Stickler syndrome, type I
SED congenita
Kniest dysplasia
Glycogen storage disease
Rickets, pseudovitamin D deficiency
Interferon, immune, deficiency
Cornea plana congenita, recessive
Growth retardation with deafness and mental retardation
Spinal muscular atrophy, congenital nonprogressive
Cardiomyopathy, hypertrophic
Brachydactyly, type C
Noonan syndrome
Cardiofaciocutaneous syndrome
Tyrosinemia, type III
Lymphoma, B-cell non-Hodgkin, high-grade
Holt-Oram syndrome
Alcohol intolerance, acute
Tumor rejection antigen
Human immunodeficiency virus-1 expression
Amyloidosis, renal

13

114 million bases

Cholesterol-lowering factor
Deafness, autosomal dominant and recessive
Vohwinkel syndrome
Ectodermal dysplasia
Muscular dystrophy, limb-girdle, type 2C
Breast cancer, early onset
Pancreatic cancer
Disrupted in B-cell neoplasia
Leukemia, chronic lymphocytic, B-cell
MHC class II deficiency, group B
Hyperornithinemia, hyperammonemia, homocitrullinemia
Serotonin receptor
Retinoblastoma
Osteosarcoma
Bladder cancer
Pinealoma with bilateral retinoblastoma
Wilson disease
Postaxial polydactyly, type A2
Hirschsprung disease
Propionicacidemia, types I or pccA
Holoprosencephaly
Bile acid malabsorption, primary

Cataract, zonular pulverulent
Stem-cell leukemia/lymphoma syndrome
Spastic ataxia, Charlevoix-Saguenay type
Pancreatic agenesis
Maturity Onset Diabetes of the Young, type IV
Enuresis, nocturnal
Dementia, familial British
Rieger syndrome, type 2
X-ray sensitivity
Rhabdomyosarcoma, alveolar
Lung cancer, non small-cell
Spinocerebellar ataxia
Ceroid-lipofuscinosis, neuronal
Microcoria, congenital
Schizophrenia susceptibility
Xeroderma pigmentosum, group G
Coagulation Factor VII deficiency
Oguchi disease
Stargardt disease, autosomal dominant
Coagulation Factor X deficiency
SRY (sex determining region Y)
Breast cancer, ductal

14

109 million bases

Chorea, hereditary benign
Meningioma-expressed antigen
Myopathy, distal
Defender against cell death
Temperature-sensitive apoptosis
Lysinuric protein intolerance
Ichthyosis, lamellar, autosomal recessive
Ichthyosiform erythroderma, congenital
Spastic paraplegia
Deafness, autosomal recessive
Deafness, autosomal dominant
Meniere disease
Arrhythmogenic right ventricular dysplasia
Immunodeficiency
Glycogen storage disease
Phenylketonuria, atypical
Dystonia, DOPA-responsive
Leber congenital amaurosis, type III
Tyrosinemia, type Ib
Alzheimer disease
Machado-Joseph disease
Ovarian cancer
Microphthalmia, autosomal recessive
Cerebrovascular disease, occlusive
Leukemia/lymphoma, T-cell
Agammaglobulinemia
Achromatopsia

Basal ganglia calcification (Fahr disease)
Multinodular goiter
Retinitis pigmentosa, autosomal dominant
Leukemia/lymphoma, T-cell
Oculopharyngeal muscular dystrophy, autosomal recessive
APEX nuclease (multifunctional DNA repair enzyme)
Cardiomyopathy, familial hypertrophic
Oligodontia
Goiter, familial
Carbohydrate-deficient glycoprotein syndrome, type II
Elliptocytosis
Spherocytosis
Anemia, neonatal hemolytic, fatal and near-fatal
Arrhythmogenic right ventricular dysplasia
Marfan syndrome, atypical
DNA mismatch repair gene MLH3
Diabetes mellitus, insulin-dependent
Krabbe disease
Hypothyroidism, congenital
Thyroid adenoma, hyperfunctioning
Graves disease
Hyperthroidism, congenital
Usher syndrome, autosomal recessive
Emphysema-cirrhosis
Hemorrhagic diathesis
X-ray repair

15

106 million bases

Hypertension, essential, susceptibility to
CLL/lymphoma, B-cell
Lymphoma, diffuse large cell
Necdin
Prader-Willi syndrome
Angelman syndrome
Hair color, brown
Spastic paraplegia
Limb deformity
Schizophrenia, neurophysiologic defect in
Isovalericacidemia
Spherocytosis, hereditary, Japanese type
Bartter syndrome
Amytrophic lateral sclerosis, juvenile recessive
Dyserythropoietic anemia, congenital, type III
Griscelli syndrome
Deafness, autosomal recessive
Hepatic lipase deficiency
Marfan syndrome
Shprintzen-Goldberg syndrome
Ectopia lentis, familial
Leukemia, acute promyelocytic, PML/RARA type
Cardiomyopathy, familial hypertrophic
Enhanced S-cone syndrome
Glutaricaciduria, type IIA
Epilepsy, nocturnal frontal lobe, type 2
PAPA syndrome
Diabetes mellitus, insulin-dependent

Prader-Willi/Angelman syndrome (paternally imprinted)
Eye color, brown
Human coronavirus sensitivity
Albinism, oculocutaneous, type II and ocular
Andermann syndrome
Cardiomyopathy, dilated and familial hypertrophic
Epilepsy, juvenile myoclonic
Spinocerebellar ataxia
Microcephaly, primary autosomal recessive
Dyserythropoietic anemia, congenital, type I
Muscular dystrophy, limb-girdle, type 2A
Dyslexia
Amyloidosis, hemodialysis-related
Ceroid-lipofuscinosis, neuronal, late infantile
Gynecomastia, familial
Virilization, maternal and fetal
Colorectal cancer
Carbohydrate-deficient glycoprotein syndrome, type Ib
Bardet-Biedl syndrome
Tay-Sachs disease
GM2-gangliosidosis
Tyrosinemia, type I
Mental retardation, severe
Hypercholesterolemia, familial, autosomal recessive
Retinitis pigmentosa, autosomal recessive
Otosclerosis
Bloom syndrome

16

98 million bases

Methemoglobinemias, alpha
Erythremias, alpha
Heinz body anemias, alpha
Alpha-thalassemia/mental retardation
Axis inhibitor
Hepatocellular carcinoma
Rubenstein-Taybi syndrome
Tuberous sclerosis
Polycystic kidney disease, adult type I
Leukemia, acute myelomonocytic
Pseudoxanthoma elasticum
Epilepsy, myoclonic, infantile
MHC class II deficiency
Retinitis pigmentosa
Atopy, susceptibility to
Glycogenosis, hepatic, autosomal
Medullary cystic kidney disease, autosomal dominant
Convulsions, infantile and paroxysmal choreoathetosis
Arthrocutaneouveal granulomatosis (Blau syndrome)
Paroxysmal kinesigenic choreoathetosis
Wilms tumor
Hypodontia, autosomal recessive
Cocaine- and antidepressant-sensitive
Orthostatic intolerance
Leukemia, acute myelogenous
Macular dystrophy, corneal
Cataract, Marner type
Norum disease
Fish-eye disease
Tyrosinemia, type II
Breast cancer antiestrogen resistance
Fibrosis of extraocular muscles, congenital
Fanconi anemia, complementation group A
Lymphedema with distichiasis
Spastic paraplegia
Chronic granulomatous disease, autosomal
Giant axonal neuropathy
Urolithiasis, 2,8-dihydroxyadenine
Mucopolysaccharidosis
UV-induced skin damage, vulnerability to

Thalassemia, alpha
Erythrocytosis
Heinz body anemia
Hemoglobin H disease
Hypochromic microcytic anemia
GABA-transaminase deficiency
Cataract, congenital, with microphthalmia
Polycystic kidney disease, infantile severe
Ubiquitin-specific protease, herpes virus-associated
Xeroderma pigmentosum, group F
Microhydranencephaly
Tamm-Horsfall glycoprotein
Cerebellar degeneration-related antigen
Familial Mediterranean fever
Liddle syndrome
Pseudohypoaldosteronism, type I
Batten disease
Mitral valve prolapse, familial
Brody myopathy
Retinoblastoma-binding protein
Inflammatory bowel disease (Crohn disease)
Myxoid liposarcoma, fusion gene in
Cylindromatosis, familial
Spiegler-Brooke syndrome
Townes-Brocks syndrome
Retinoblastoma
Gitelman syndrome
Bardet-Biedl syndrome
Leukemia, acute myeloid, M4Eo subtype
Ras-related gene associated with diabetes
Endometrial carcinoma
Ovarian carcinoma
Breast cancer, lobular
Gastric cancer, familial
Benzene toxicity, susceptibility to
Leukemia, postchemotherapy, susceptibility to
Spinocerebellar ataxia
Stomatocytosis, dehydrated hereditary
Pseudohyperkalemia, familial

92 million bases

Canavan disease
Ovarian cancer
Miller-Dieker syndrome
Retinitis pigmentosa
Tumor protein p53
Colorectal cancer
Li-Fraumeni syndrome
Cystinosis, nephropathic
Diabetes mellitus, noninsulin-dependent
Cone dystrophy
Myasthenic syndrome
Deafness, autosomal recessive
Smith-Magenis syndrome
VLCAD deficiency
Maturity Onset Diabetes of the Young, type V
Hypertension, essential, susceptibility to
T-cell immunodeficiency, alopecia, and nail dystrophy
Chondrosarcoma, extraskeletal myxoid
Neurotransmitter transporter, serotonin (anxiety-related)
Neurofibromatosis, type 1
Watson syndrome
Leukemia, juvenile myelomonocytic
HIV-1 disease, delayed progression of
Meesmann corneal dystrophy
Muscular dystrophy, limb-girdle
Epidermolysis bullosa simplex, recessive
Pachyonychia congenita, Jackson-Lawler type
Steatocystoma multiplex
Wilms tumor, type 4
Glycogen storage disease (von Gierke disease)
Parkinsonism-dementia
Epidermolytic hyperkeratosis
Patella aplasia or hypoplasia
Osteogenesis imperfecta
Ehlers-Danlos syndrome, types I and VIIA
Osteoporosis, idiopathic
Ovarian carcinoma antigen
Neuroblastoma
Glanzmann thrombasthenia, type A
Thrombocytopenia, neonatal alloimmune
CLL/lymphoma, B-cell
Retinitis pigmentosa
Pituitary tumor, invasive
Myocardial infarction, susceptibility to
Alzheimer disease, susceptibility to
Myotonia congenita, atypical
Cramps, familial
Fetal Alzheimer antigen
Lung cancer, small-cell
SRY (sex-determining region Y)
Campomelic dysplasia with autosomal sex reversal
Apoptosis inhibitor
Diabetes mellitus, type II
Radical Fringe

Bernard-Soulier syndrome
Breast cancer-related regulator of TP53
Hypermethylated in cancer
Lissencephaly
Subcortical laminar heterotopia
Leber congenital amaurosis, type I
Medulloblastoma
Cataract, anterior polar
Myasthenia gravis, familial infantile
Bruck syndrome
Sjogren-Larsson syndrome
Charcot-Marie-Tooth neuropathy
Dejerine-Sottas disease
Van der Woude syndrome modifier
Choroidal dystrophy, central areolar
Huntingtin-associated protein
Psoriasis susceptibility
Epidermolysis bullosa
Alzheimer disease, susceptibility to
Van Buchem disease
Malignant hyperthermia susceptibility
Leukemia, acute promyelocytic
Epidermolytic palmoplantar keratoderma
Pachyonychia congenita, Jadassohn-Lewandowsky type
Keratoderma, nonepidermolytic palmoplantar
Sclerosteosis
Muscular dystrophy, Duchenne-like, type 2
Adhalinopathy, primary
Breast cancer, early onset
Ovarian cancer
Leukemia, myeloid/lymphoid or mixed-lineage
Breast cancer, sporadic
Gliosis, familial progressive subcortical
Pseudohypoaldosteronism type II
Spherocytosis, hereditary
Hemolytic anemia
Renal tubular acidosis, distal
T-cell leukemia virus (I and II) receptor
Dementia, frontotemporal, with Parkinsonism
Trichodontoosseous syndrome
Glanzmann thrombasthenia, type B
Symphalangism, proximal
Synostoses syndrome, multiple
Mulibrey nanism
Growth hormone deficiency
Myeloperoxidase deficiency
Cataracts
Tylosis with esophageal cancer
Adrenoleukodystrophy, pseudoneonatal
Deafness, autosomal dominant
Leukemia, acute myeloid, therapy-related
Myasthenic syndrome, slow-channel congenital
Sanfilippo syndrome, types A and B

18

85 million bases

Myopia, high grade, autosomal dominant
Holoprosencephaly
Torsion dystonia, adult-onset, focal
Orthostatic hypotensive disorder of Streeten
Hepatitis B virus integration site
Retinoblastoma-binding protein
Amyloid neuropathy, familial
Amyloidosis, senile systemic
Carpal tunnel syndrome, familial
Pemphigus vulgaris antigen
Diabetes mellitus, insulin-dependent
Pancreatic cancer
Polyposis, juvenile intestinal
Leukemia/lymphoma, B-cell
Colorectal cancer
Lymphoma/leukemia, B-cell, variant
Combined factor V and VIII deficiency
Tumor necrosis factor receptor superfamily

Parkinson disease, susceptibility to
Glucocorticoid deficiency
Schizophrenia
Niemann-Pick disease, types C1 and D
Epidermolysis bullosa
Synovial sarcoma
Keratosis palmoplantaris striata
Cholestasis
Osteosarcoma
Cone dystrophy
Carnosinemia
Protoporphyria, erythropoietic
Squamous cell carcinoma
Osteolysis, familial expansile
Obesity, autosomal dominant
Paget disease of bone
Methemoglobinemia

19

67 million bases

Coxsackie virus sensitivity
Cyclic hematopoiesis
Fucosyltransferase-6 deficiency
Hypocalciuric hypercalcemia, type II
Leukemia, myeloid/lymphoid or mixed-lineage
Wegener granulomatosis autoantigen
Bleeding disorder
Persistent Mullerian duct syndrome, type I
Mucolipidosis
Glutaricaciduria, type I
Leprechaunism
Rabson-Mendenhall syndrome
Diabetes mellitus, insulin-resistant
Ichthyosis
Leukemia, T-cell acute lymphoblastoid
Liposarcoma
Mycobacterial and salmonella infections, susceptibility to
Eye color, green/blue
Hemiplegic migraine, familial
Episodic ataxia, type 2
Ataxia, spinocerebellar and cerebellar
Leukemia, acute myeloid
Mannosidosis, alpha, types I and II
Alzheimer disease, late onset
Glomerulosclerosis, focal segmental
Deafness, autosomal dominant
Hypercalcemia, familial benign, Oklahoma type, type III
Orofacial cleft
Charcot-Leyden crystal protein
Hemolytic anemia
Hydrops fetalis
Malignant hyperthermia susceptibility
Central core disease
Osteodysplasia, polycystic lipomembranous
Maple syrup urine disease, type Ia
Camurati-Engelmann disease
Myotonic dystrophy
Heart block, progressive familial, type I
Optic atrophy
3-methylglutaconicaciduria, type III
Cystic fibrosis modifier
Meconium ileus in cystic fibrosis, susceptibility to
Cone dystrophy
Leber congenital amaurosis
Retinitis pigmentosa, late-onset dominant
Diabetes mellitus, noninsulin-dependent
Hyperferritinemia-cataract syndrome
Hypogonadism, hypergonadotropic
Retinitis pigmentosa, autosomal dominant
Ectrodactyly, ectodermal dysplasia, cleft lip/palate

Ataxia, cerebellar, Cayman type
Convulsions, familial febrile
Guanidinoacetate methyltransferase deficiency
Muscular dystrophy
Hirschsprung disease
Peutz-Jeghers syndrome
Leukemia, acute lymphoblastic
Atherosclerosis, susceptibility to
Malaria, cerebral, susceptibility to
Sicca syndrome
Glioblastoma
Thyroid carcinoma, nonmedullary
Low density lipoprotein receptor
Hypercholesterolemia, familial
Arteriopathy, cerebral
Pseudoachondroplasia
Epiphyseal dysplasia, multiple
Severe combined immunodeficiency disease
Hair color, brown
Leigh syndrome
MHC class II deficiency
Exostoses, multiple, type 3
Benign familial infantile convulsions
Leukemia/lymphoma, B-cell
Spondylocostal dysostosis, autosomal recessive
Prostate-specific antigen
Spastic paraplegia , autosomal dominant
Cystinuria, types II and III
Nephrosis, congenital, Finnish type
Generalized epilepsy with febrile seizures plus
Ovarian carcinoma
Microcephaly, autosomal recessive
Hyperlipoproteinemia, types Ib and III
Myocardial infarction susceptibility
Cytochrome P450 (coumarin resistance)
Nicotine addiction, protection from
X-ray repair
Excision repair
Xeroderma pigmentosum, group D
Trichothiodystrophy
DNA ligase I deficiency
Polio virus receptor
Herpes virus entry mediator B
Glutaricaciduria, type IIB
Colorectal cancer
Leukemia, T-cell acute lymphoblastic
Shaw-related subfamily genes
Melanoma inhibitory activity
Cardiomyopathy, familial hypertrophic

72 million bases

Creutzfeldt-Jakob disease
Gerstmann-Straussler disease
Insomnia, fatal familial
Hallervorden-Spatz syndrome
Alagille syndrome
Corneal dystrophy
Inhibitor of DNA binding, dominant negative
Facial anomalies syndrome
Gigantism
Retinoblastoma
Rous sarcoma
Colon cancer
Galactosialidosis
Severe combined immunodeficiency
Hemolytic anemia
Obesity/hyperinsulinism
Pseudohypoparathyroidism, type Ia
McCune-Albright polyostotic fibrous dysplasia
Somatotrophinoma
Pituitary ACTH secreting adenoma
Shah-Waardenburg syndrome

Diabetes insipidus, neurohypophyseal
SRY (sex-determining region Y)
McKusick-Kaufman syndrome
Cerebral amyloid angiopathy
Thrombophilia
Myocardial infarction, susceptibility to
Huntington-like neurodegenerative disorder
Anemia, congenital dyserythropoietic
Acromesomelic dysplasia, Hunter-Thompson type
Brachydactyly, type C
Chondrodysplasia, Grebe type
Hemolytic anemia
Myeloid tumor suppressor
Breast cancer
Maturity Onset Diabetes of the Young, type 1
Diabetes mellitus, noninsulin-dependent
Graves disease, susceptibility to
Epilepsy, nocturnal frontal lobe and benign neonatal, type 1
Epiphyseal dysplasia, multiple
Electro-encephalographic variant pattern
Pseudohypoparathyroidism, type IB

50 million bases

Coxsackie and adenovirus receptor
Amyloidosis, cerebroarterial, Dutch type
Alzheimer disease, APP-related
Schizophrenia, chronic
Usher syndrome, autosomal recessive
Amytrophic lateral sclerosis
Oligomycin sensitivity
Jervell and Lange-Nielsen syndrome
Long QT syndrome
Down syndrome cell adhesion molecule
Homocystinuria
Cataract, congenital, autosomal dominant
Deafness, autosomal recessive
Myxovirus (influenza) resistance
Leukemia, acute myeloid

Myeloproliferative syndrome, transient
Leukemia, transient, of Down syndrome
Enterokinase deficiency
Multiple carboxylase deficiency
T-cell lymphoma invasion and metastasis
Mycobacterial infection, atypical
Down syndrome (critical region)
Autoimmune polyglandular disease, type I
Bethlem myopathy
Epilepsy, progressive myoclonic
Holoprosencephaly, alobar
Knobloch syndrome
Hemolytic anemia
Breast cancer
Platelet disorder, with myeloid malignancy

22

56 million bases

Cat eye syndrome
Thrombophilia
Rhabdoid predisposition syndrome, familial
Schizophrenia susceptibility locus
Bernard-Soulier syndrome, type B
Giant platelet disorder, isolated
Hyperprolinemia, type I
Cataract, cerulean, type 2
Leukemia, chronic myeloid
Ewing sarcoma
Neuroepithelioma
Li-Fraumeni syndrome
Fechtner syndrome
Amyotrophic lateral sclerosis
Pulmonary alveolar proteinosis
Meningioma, SIS-related
Dermatofibrosarcoma protuberans
Giant-cell fibroblastoma
Spinocerebellar ataxia
SRY (sex-determining region Y)
Waardenburg-Shah syndrome
Yemenite deaf-blind hypopigmentation syndrome
Debrisoquine sensitivity
Polycystic kidney disease
Leukodystrophy, metachromatic
Myoneurogastrointestinal encephalomyopathy
Leukoencephalopathy

DiGeorge syndrome
Velocardiofacial syndrome
Schindler disease
Kanzaki disease
NAGA deficiency, mild
Epilepsy, partial
Glutathioninuria
Opitz G syndrome, type II
Ubiquitin fusion degradation
Transcobalamin deficiency
Heme oxygenase deficiency
Manic Fringe
Leukemia inhibitory factor
Sorsby fundus dystrophy
Neurofibromatosis, type 2
Meningioma, NF2-related, sporadic
Schwannoma, sporadic
Neurolemmomatosis
Malignant mesothelioma, sporadic
Deafness, autosomal dominant
Colorectal cancer
Cardioencephalomyopathy, fatal infantile
Adenylosuccinase deficiency
Autism, succinylpurinemic
Glucose/galactose malabsorption
Benzodiazepine receptor, peripheral type
Methemoglobinemia, types I and II

164 million bases

Short stature, idiopathic familial
Leri-Weill dyschondrosteosis
Langer mesomelic dysplasia
Leukemia, acute myeloid, M2 type
Chondrodysplasia punctata
Kallmann syndrome
Ocular albinism, Nettleship-Falls type
Oral-facial-digital syndrome
Nance-Horan cataract-dental syndrome
Heterocellular hereditary persistence of fetal hemoglobin
Pyruvate dehydrogenase deficiency
Glycogen storage disease
Coffin-Lowry syndrome
Mental retardation
Spondyloepiphyseal dysplasia tarda
Paroxysmal nocturnal hemoglobinuria
Infantile spasm syndrome
Aicardi syndrome
Deafness, sensorineural
Simpson-Golabi-Behmel syndrome, type 2
Adrenal hypoplasia, congenital
Dosage-sensitive sex reversal
Deafness, congenital sensorineural
Retinitis pigmentosa
Wilson-Turner syndrome
Cone dystrophy
Aland island eye disease (ocular albinism)
Optic atrophy
Night blindness, congenital stationary, type 1
Erythroid-potentiating activity
Arthrogryposis multiplex congenita
Night blindness, congenital stationary, type 2
Brunner syndrome
Wiskott-Aldrich syndrome
Thrombocytopenia
Dent disease
Nephrolithiasis, type I
Hypophosphatemia, type III
Proteinuria
Anemia, sideroblastic/hypochromic
Cerebellar ataxia
Renal cell carcinoma, papillary
Diabetes mellitus, insulin-dependent
Sutherland-Haan syndrome
Cognitive function, social
Mental retardation, nonspecific
Menkes disease
Occipital horn syndrome
Cutis laxa, neonatal
FG syndrome
Immunodeficiency, moderate and severe
Miles-Carpenter syndrome
Charcot-Marie-Tooth neuropathy, dominant
Mental retardation
X-inactivation center
Premature ovarian failure
Arts syndrome
Cleft palate and/or ankyloglossia
Megalocornea
Epilepsy (Juberg-Hellman syndrome)
Pelizaeus-Merzbacher disease
Spastic paraplegia
Alport syndrome
Cowchock syndrome
Hypertrichosis, congenital generalized
Ptosis, hereditary congenital
Apoptosis inhibitor
Panhypopituitarism
Thoracoabdominal syndrome
Simpson-Golabi-Behmel syndrome, type 1
Split hand/foot malformation, type 2
Hypoparathyroidism
Mental retardation, Shashi type
Lesch-Nyhan syndrome
HPRT-related gout
Lowe syndrome
Borjeson-Forssman-Lehmann syndrome
Testicular germ cell tumor
Hemophilia B
Warfarin sensitivity
Osseous dysplasia (male lethal), digital
Adrenoleukodystrophy
Adrenomyeloneuropathy
Colorblindness, blue monochromatic
Cardiac valvular dysplasia
Emery-Dreifuss muscular dystrophy
Heterotopia, periventricular
Favism
Hemolytic anemia
Colorblindness, green cone pigment
Incontinentia pigmenti, type II
Hydrocephalus
MASA syndrome
Spastic paraplegia
Rett syndrome
Mature T-cell proliferation
Myopia (Bornholm eye disease)
Mental retardation with psychosis
Endocardial fibroelastosis

Hodgkin disease susceptibility, pseudoautosomal
Ichthyosis
Microphthalmia, dermal aplasia, and sclerocornea
Episodic muscle weakness
Mental retardation
Ocular albinism and sensorineural deafness
Amelogenesis imperfecta
Charcot-Marie-Tooth disease, recessive
Keratosis follicularis spinulosa decalvans
Hypophosphatemia, hereditary
Partington syndrome
Retinoschisis
Gonadal dysgenesis, XY female type
Mental retardation, non-dysmorphic
Agammaglobulinemia, type 2
Craniofrontonasal dysplasia
Opitz G syndrome, type I
Pigment disorder, reticulate
Melanoma
Duchenne muscular dystrophy
Becker muscular dystrophy
Cardiomyopathy, dilated
Chronic granulomatous disease
Snyder-Robinson mental retardation
Norrie disease
Exudative vitreoretinopathy
Coats disease
Renpenning syndrome
Retinitis pigmentosa, recessive
Mental retardation, nonspecific and syndromic
Dyserythropoietic anemia with thrombocytopenia
Chondrodysplasia punctata, dominant
Autoimmunity-immunodeficiency syndrome
Renal cell carcinoma, papillary
Faciogenital dysplasia (Aarskog-Scott syndrome)
Choroideremia with mental retardation
Sarcoma, synovial
Prieto syndrome
Spinal muscular atrophy, lethal infantile
Migraine, familial typical
Androgen insensitivity
Spinal and bulbar muscular atrophy
Prostate cancer
Perineal hypospadias
Breast cancer, male, with Reifenstein syndrome
Ectodermal dysplasia, anhidrotic
Alpha-thalassemia/mental retardation
Juberg-Marsidi syndrome
Sutherland-Haan syndrome
Smith-Fineman-Myers syndrome
Hemolytic anemia
Myoglobinuria/hemolysis
Wieacker-Wolff syndrome
Torsion dystonia-parkinsonism, Filipino type
Leukemia, myeloid/lymphoid or mixed-lineage
Anemia, sideroblastic, with ataxia
Allan-Herndon syndrome
Deafness
Choroideremia
Agammaglobulinemia
Fabry disease
Mohr-Tranebjaerg syndrom
Jensen syndrome
Lissencephaly
Bazex syndrome
Mental retardation with growth hormone deficiency
Mental retardation, South African type
Lymphoproliferative syndrome
X inactivation, familial skewed
Pettigrew syndrome
Gustavson mental retardation syndrome
Immunodeficiency, with hyper-IgM
Retinitis pigmentosa
SRY (sex determining region Y)
Wood neuroimmunologic syndrome
Heterotaxy, visceral
Albinism-deafness syndrome
Cone dystrophy, progressive
Prostate cancer susceptibility
Fragile X mental retardation
Epidermolysis bullosa, macular type
Diabetes insipidus, nephrogenic
Cancer/testis antigen
Dyskeratosis
Hemophilia A
Hunter syndrome
Mucopolysaccharidosis
Intestinal pseudoobstruction, neuronal
Melanoma antigens
Mental retardation-skeletal dysplasia
Myotubular myopathy
Otopalatodigital syndrome, type I
Colorblindness, red cone pigment
Goeminne TKCR syndrome
Waisman parkinsonism-mental retardation
Barth syndrome
Cardiomyopathy, dilated
Noncompaction of left ventricular myocardium
Von Hippel-Lindau binding protein

59 million bases

Sex-determining region Y (testis determining factor)
Gonadal dysgenesis, XY type
Azoospermia factors

Comparison of DNA from Sample 1 and Sample 2 (Please don't write on this page)

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Sample 1        GATACCCCACTATGCTTAGCCCTAAACCTCAACAGTTAAATCAACAAAACTGCTCGCCAG 1070
Sample 2        GATACCCCACTATGCTTAGCCCTAAACCTCAACAGTTAAATCAACAAAACTGCTCGCCAG
                ************************************************************

Sample 1        AACACTACGAGCCACAGCTTAAAACTCAAAGGACCTGGCGGTGCTTCATATCCCTCTAGA 1130
Sample 2        AACACTACGAGCCACAGCTTAAAACTCAAAGGACCTGGCGGTGCTTCATATCCCTCTAGA
                ************************************************************

Sample 1        GGAGCCTGTTCTGTAATCGATAAACCCCGATCAACCTCACCACCTCTTGCTCAGCCTATA 1190
Sample 2        GGAGCCTGTTCTGTAATCGATAAACCCCGATCAACCTCACCACCTCTTGCTCAGCCTATA
                ************************************************************

Sample 1        TACCGCCATCTTCAGCAAACCCTGATGAAGGCTACAAAGTAAGCGCAAGTACCCACGTAA 1250
Sample 2        TACCGCCATCTTCAGCAAACCCTGATGAAGGCTACAAAGTAAGCGCAAGTACCCACGTAA
                ************************************************************

Sample 1        AGACGTTAGGTCAAGGTGTAGCCCATGAGGTGGCAAGAAATGGGCTACATTTTCTACCCC 1310
Sample 2        AGACGTTAGGTCAAGGTGTAGCCCATGAGGTGGCAAGAAATGGGCTACATTTTCTACCCC
                ************************************************************

Sample 1        AGAAAACTACGATAGCCCTTATGAAACTTAAGGGTCGAAGGTGGATTTAGCAGTAAACTG 1370
Sample 2        AGAAAACTACGATAGCCCTTATGAAACTTAAGGGTCGAAGGTGGATTTAGCAGTAAACTG
                ************************************************************

Sample 1        AGAGTAGAGTGCTTAGTTGAACAGGGCCCTGAAGCGCGTACACACCGCCCGTCACCCTCC 1430
Sample 2        AGAGTAGAGTGCTTAGTTGAACAGGGCCCTGAAGCGCGTACACACCGCCCGTCACCCTCC
                ************************************************************

Sample 1        TCAAGTATACTTCAAAGGACATTTAACTAAAACCCCTACGCATTTATATAGAGGAGACAA 1490
Sample 2        TCAAGTATACTTCAAAGGACATTTAACTAAAACCCCTACGCATTTATATAGAGGAGACAA
                ************************************************************

Sample 1        GTCGTAACATGGTAAGTGTACTGGAAAGTGCACTTGGACGAACCAGAGTGTAGCTTAACA 1550
Sample 2        GTCGTAACATGGTAAGTGTACTGGAAAGTGCACTTGGACGAACCAGAGTGTAGCTTAACA
                ************************************************************

Sample 1        CAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTGAGCTAAACC 1610
Sample 2        CAAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTGAGCTAAACC
                ************************************************************

Sample 1        TAGCCCCAAACCCACTCCACCTTACTACCAGACAACCTTAGCCAAACCATTTACCCAAAT 1670
Sample 2        TAGCCCCAAACCCACTCCACCTTACTACCAGACAACCTTAGCCAAACCATTTACCCAAAT
                ************************************************************

Sample 1        AAAGTATAGGCGATAGAAATTGAAACCTGGCGCAATAGATATAGTACCGCAAGGGAAAGA 1730
Sample 2        AAAGTATAGGCGATAGAAATTGAAACCTGGCGCAATAGATATAGTACCGCAAGGGAAAGA
                ************************************************************

Sample 1        TGAAAAATTATAACCAAGCATAATATAGCAAGGACTAACCCCTATACCTTCTGCATAATG 1790
Sample 2        TGAAAAATTATAACCAAGCATAATATAGCAAGGACTAACCCCTATACCTTCTGCATAATG
                ************************************************************

Sample 1        AATTAACTAGAAATAACTTTGCAAGGAGAGCCAAAGCTAAGACCCCCGAAACCAGACGAG 1850
Sample 2        AATTAACTAGAAATAACTTTGCAAGGAGAGCCAAAGCTAAGACCCCCGAAACCAGACGAG
                ************************************************************

Sample 1        CTACCTAAGAACAGCTAAAAGAGCACACCCGTCTATGTAGCAAAATAGTGGGAAGATTTA 1910
Sample 2        CTACCTAAGAACAGCTAAAAGAGCACACCCGTCTATGTAGCAAAATAGTGGGAAGATTTA
                ************************************************************

Sample 1        TAGGTAGAGGCGACAAACCTACCGAGCCTGGTGATAGCTGGTTGTCCAAGATAGAATCTT 1970
Sample 2        TAGGTAGAGGCGACAAACCTACCGAGCCTGGTGATAGCTGGTTGTCCAAGATAGAATCTT
                ************************************************************

Sample 1        AGTTCAACTTTAAATTTGCCCACAGAACCCTCTAAATCCCCTTGTAAATTTAACTGTTAG 2030
Sample 2        AGTTCAACTTTAAATTTGCCCACAGAACCCTCTAAATCCCCTTGTAAATTTAACTGTTAG
                ************************************************************

Sample 1        TCCAAAGAGGAACAGCTCTTTGGACACTAGGAAAAAACCTTGTAGAGAGAGTAAAAAATT 2090
Sample 2        TCCAAAGAGGAACAGCTCTTTGGACACTAGGAAAAAACCTTGTAGAGAGAGTAAAAAATT
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Sample 1        TAACACCCATAGTAGGCCTAAAAGCAGCCACCAATTAAGAAAGCGTTCAAGCTCAACACC 2150
Sample 2        TAACACCCATAGTAGGCCTAAAAGCAGCCACCAATTAAGAAAGCGTTCAAGCTCAACACC
                ************************************************************

Sample 1        CACTACCTAAAAAATCCCAAACATATAACTGAACTCCTCACACCCAATTGGACCAATCTA 2210
Sample 2        CACTACCTAAAAAATCCCAAACATATCACTGAACTCCTCACACCCAATTGGACCAATCTA
                ************************* ******************************

Sample 1        TCACCCTATAGAAGAACTAATGTTAGTATAAGTAACATGAAAACATTCTCCTCCGCATAA 2270
Sample 2        TCACCCTATAGAAGAACTAATGTTAGTATAAGTAACATGAAAACATTCTCCTCCGCATAA
                ************************************************************

Sample 1        GCCTGCGTCAGATTAAAACACTGAACTGACAATTAACAGCCCAATATCTACAATCAACCA 2330
Sample 2        GCCTGCGTCAGATTAAAACACTGAACTGACAATTAACAGCCCAATATCTACAATCAACCA
                ************************************************************

Sample 1        ACAAGTCATTATTACCCTCACTGTCAACCCAACACAGGCATGCTCATAAGGAAAGGTTAA 2390
Sample 2        ACAAGTCATTATTACCCTCACTGTCAACCCAACACAGGCATGCTCATAAGGAAAGGTTAA
                ************************************************************

Sample 1        AAAAAGTAAAAGGAACTCGGCAAATCTTACCCCGCCTGTTTACCAAAAACATCACCTCTA 2450
Sample 2        AAAAAGTAAAAGGAACTCGGCAAATCTTACCCCGCCTGTTTACCAAAAACATCACCTCTA
                ************************************************************

Sample 1        GCATCACCAGTATTAGAGGCACCGCCTGCCCAGTGACACATGTTTAACGGCCGCGGTACC 2510
Sample 2        GCATCACCAGTATTAGAGGCACCGCCTGCCCAGTGACACATGTTTAACGGCCGCGGTACC
                ************************************************************

Sample 1        CTAACCGTGCAAAGGTAGCATAATCACTTGTTCCTTAAATAGGGACCTGTATGAATGGCT 2570
Sample 2        CTAACCGTGCAAAGGTAGCATAATCACTTGTTCCTTAAATAGGGACCTGTATGAATGGCT
                ************************************************************

Sample 1        CCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAGTGAAATTGACCTGCCCGTGAAGAGG 2630
Sample 2        CCACGAGGGTTCAGCTGTCTCTTACTTTTAACCAGTGAAATTGACCTGCCCGTGAAGAGG
                ************************************************************

Sample 1        CGGGCATGACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTATTAATGCAAACAG 2690
Sample 2        CGGGCATGACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTATTAATGCAAACAA
                ************************************************************

Sample 1        TACCTAACAAACCCACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTCGGTTGGGGC 2750
Sample 2        TACCTAACAAACCCACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTCGGTTGGGGC
                ************************************************************

Sample 1        GACCTCGGAGCAGAACCCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCG 2810
Sample 2        GACCTCGGAGCAGAACCCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCG
                ************************************************************

Sample 1        AACTACTATACTCAATTGATCCAATAACTTGACCAACGGAACAAGTTACCCTAGGGATAA 2870
Sample 2        AACTACCATACTCAATTGATCCAATAACTTGACCAACGGAACAAGTTACCCTAGGGATAA
                ****** **************************************************

Sample 1        CAGCGCAATCCTATTCTAGAGTCCATATCAACAATAGGGTTTACGACCTCGATGTTGGAT 2930
Sample 2        CAGCGCAATCCTATTCTAGAGTCCATATCAACAATAGGGTTTACGACCTCGATGTTGGAT
                ************************************************************

Sample 1        CAGGACATCCCGATGGTGCAGCCGCTATTAAAGGTTCGTTTGTTCAACGATTAAAGTCCT 2990
Sample 2        CAGGACATCCCGATGGTGCAGCCGCTATTAAAGGTTCGTTTGTTCAACGATTAAAGTCCT
                ************************************************************

Sample 1        ACGTGATCTGAGTTCAGACCGGAGTAATCCAGGTCGGTTTCTATCTACTTCAAATTCCTC 3050
Sample 2        ACGTGATCTGAGTTCAGACCGGAGTAATCCAGGTCGGTTTCTATCTACTTCAAATTCCTC
                ************************************************************

Sample 1        CCTGTACGAAAGGACAAGAGAAATAAGGCCTACTTCACAAAGCGCCTTCCCCCGTAAATG 3110
Sample 2        CCTGTACGAAAGGACAAGAGAAATAAGGCCTACTTCACAAAGCGCCTTCCCCCGTAAATG
                ************************************************************

Sample 1        ATATCATCTCAACTTAGTATTATACCCACACCCACCCAAGAACAGGGTTTGTTAAGATGG 3170
Sample 2        ATATCATCTCAACTTAGTATTATACCCACACCCACCCAAGAACAGGGTTTGTTAAGATGG
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Sample 1        CAGAGCCCGGTAATCGCATAAAACTTAAAACTTTACAGTCAGAGGTTCAATTCCTCTTCT 3230
Sample 2        CAGAGCCCGGTAATCGCATAAAACTTAAAACTTTACAGTCAGAGGTTCAATTCCTCTTCT
                ************************************************************

Sample 1        TAACAACATACCCATGGCCAACCTCCTACTCCTCATTGTACCCATTCTAATCGCAATGGC 3290
Sample 2        TAACAACATACCCATGGCCAACCTCCTACTCCTCATTGTACCCATTCTAATCGCAATGGC
                ************************************************************

Sample 1        ATTCCTAATGCTTACCGAACGAAAAATTCTAGGCTATATACAACTACGCAAAGGCCCCAA 3350
Sample 2        ATTCCTAATGCTTACCGAACGAAAAATTCTAGGCTATATACAACTACGCAAAGGCCCCAA
                ************************************************************

Sample 1        CGTTGTAGGCCCCTACGGGCTACTACAACCCTTCGCTGACGCCATAAAACTCTTCACCAA 3410
Sample 2        CGTTGTAGGCCCCTACGGGCTACTACAACCCTTCGCTGACGCCATAAAACTCTTCACCAA
                ************************************************************

Sample 1        AGAGCCCCTAAAACCCGCCACATCTACCATCACCCTCTACATCACCGCCCCGACCTTAGC 3470
Sample 2        AGAGCCCCTAAAACCCGCCACATCTACCATCACCCTATACATCACCGCCCCGACCTTAGC
                ********************************** ***********************

Sample 1        TCTCACCATCGCTCTTCTACTATGAACCCCCCTCCCCATACCCAACCCCCTGGTCAACCT 3530
Sample 2        TCTCACCATCGCTCTTCTACTATGAACCCCCCTCCCCATACCCAACCCCCTGGTTAACCT
                ************************************************** *****

Sample 1        CAACCTAGGCCTCCTATTTATTCTAGCCACCTCTAGCCTAGCCGTTTACTCAATCCTCTG 3590
Sample 2        CAACCTAGGCCTCCTATTTATTCTAGCCACCTCTAGCCTAGCCGTTTACTCAATCCTCTG
                ************************************************************

Sample 1        ATCAGGGTGAGCATCAAACTCAAACTACGCCCTGATCGGCGCACTGCGAGCAGTAGCCCA 3650
Sample 2        ATCAGGGTGAGCATCAAACTCAAACTACGCCCTGATCGGCGCACTGCGAGCAGTAGCCCA
                ************************************************************

Sample 1        AACAATCTCATATGAAGTCACCCTAGCCATCATTCTACTATCAACATTACTAATAAGTGG 3710
Sample 2        AACAATCTCATATGAAGTCACCCTAGCCATCATTCTACTATCAACATTACTAATAAGTGG
                ************************************************************

Sample 1        CTCCTTTAACCTCTCCACCCTTATCACAACACAAGAACACCTCTGATTACTCCTGCCATC 3770
Sample 2        CTCCTTTAACCTCTCCACCCTTATCACAACACAAGAACACCTCTGATTACTCCTGCCATC
                ************************************************************

Sample 1        ATGACCCTTGGCCATAATATGATTTATCTCCACACTAGCAGAGACCAACCGAACCCCCTT 3830
Sample 2        ATGACCCTTGGCCATAATATGATTTACCTCCACACTAGCAGAGACCAACCGAACCCCCTT
                ************************* *********************************

Sample 1        CGACCTTGCCGAAGGGGAGTCCGAACTAGTCTCAGGCTTCAACATCGAATACGCCGCAGG 3890
Sample 2        CGACCTTGCCGAAGGGGAGTCCGAACTAGTCTCAGGCTTCAACATCGAATACGCCGCAGG
                ************************************************************

Sample 1        CCCCTTCGCCCTATTCTTCATAGCCGAATACACAAACATTATTATAATAAACACCCTCAC 3950
Sample 2        CCCCTTCGCCCTATTCTTCATAGCCGAATACACAAACATTATTATAATAAACACCCTCAC
                ************************************************************

Sample 1        CACTACAATCTTCCTAGGAACAACATATGACGCACTCTCCCCTGAACTCTACACAACATA 4010
Sample 2        CACTACAATCTTCCTAGGAACAACATATGACGCACTCTCCCCTGAACTCTACACAACATA
                ************************************************************

Sample 1        TTTTGTCACCAAGACCCTACTTCTAACCTCCCTGTTCTTATGAATTCGAACAGCATACCC 4070
Sample 2        TTTTGTCACCAAGACCCTACTTCTGACCTCCCTGTTCTTATGAATTCGAACAGCATACCC
                ********************** ***********************************

Sample 1        CCGATTCCGCTACGACCAACTCATACACCTCCTATGAAAAAACTTCCTACCACTCACCCT 4130
Sample 2        CCGATTCCGCTACGACCAACTCATACACCTCCTATGAAAAAACTTCCTACCACTCACCCT
                ************************************************************

Sample 1        AGCATTACTTATATGATATGTCTCCATACCCATTACAATCTCCAGCATTCCCCCTCAAAC 4190
Sample 2        AGCATTACTTATATGATATGTCTCCATACCCATTACAATCTCCAGCATTCCCCCTCAAAC
                ************************************************************

Sample 1        CTAAGAAATATGTCTGATAAAAGAGTTACTTTGATAGAGTAAATAATAGGAGCTTAAACC 4250
Sample 2        CTAAGAAATATGTCTGATAAAAGAGTTACTTTGATAGAGTAAATAATAGGAGTTTAAACC
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Sample 1        CCCTTATTTCTAGGACTATGAGAATCGAACCCATCCCTGAGAATCCAAAATTCTCCGTGC 4310
Sample 2        CCCTTATTTCTAGGACTATGAGAATCGAACCCATCCCTGAGAATCCAAAATTCTCCGTGC
                ************************************************************

Sample 1        CACCTATCACACCCCATCCTAAAGTAAGGTCAGCTAAATAAGCTATCGGGCCCATACCCC 4370
Sample 2        CACCTATCACACCCCATCCTAAAGTAAGGTCAGCTAAATAAGCTATCGGGCCCATACCCC
                ************************************************************

Sample 1        GAAAATGTTGGTTATACCCTTCCCGTACTAATTAATCCCCTGGCCCAACCCGTCATCTAC 4430
Sample 2        GAAAATGTTGGTTATACCCTTCCCGTACTAATTAATCCCCTGGCCCAACCCGTCATCTAC
                ************************************************************

Sample 1        TCTACCATCTTTGCAGGCACACTCATCACAGCGCTAAGCTCGCACTGATTTTTTACCTGA 4490
Sample 2        TCTACCATCTTTGCAGGCACACTCATCACAGCGCTAAGCTCGCACTGATTTTTTACCTGA
                ************************************************************

Sample 1        GTAGGCCTAGAAATAAACATACTAGCTTTTATTCCAGTTCTAACCAAAAAAATAAACCCT 4550
Sample 2        GTAGGCCTAGAAATAAACATGCTAGCCTTTATTCCAGTTCTAACCAAAAAAATAAACCCT
                ******************* ***** ********************************

Sample 1        CGTTCCACAGAAGCTGCCATCAAGTATTTCCTCACGCAAGCAACCGCATCCATAATCCTT 4610
Sample 2        CGTTCCACAGAAGCTGCCATCAAGTATTTCCTCACGCAAGCAACCGCATCCATAATCCTT
                ************************************************************

Sample 1        CTAATAGCTATCCTCTTCAACAATATACTCTCCGGACAATGAACCATAACCAATACTACC 4670
Sample 2        CTAATAGCTATCCTCTTCAACAATATACTCTCCGGACAATGAACCATAACCAATACTACC
                ************************************************************

Sample 1        AATCAATACTCATCATTAATAATCATAATGGCTATAGCAATAAAACTAGGAATAGCCCCC 4730
Sample 2        AATCAATACTCATCATTAATAATCATAATGGCTATAGCAATAAAACTAGGAATAGCCCCC
                ************************************************************

Sample 1        TTTCACTTCTGAGTCCCAGAGGTTACCCAAGGCACCCCTCTGACATCCGGCCTGCTTCTT 4790
Sample 2        TTTCACTTCTGAGTCCCAGAGGTTACCCAAGGCACCCCTCTGACATCCGGCCTGCTTCTT
                ************************************************************

Sample 1        CTCACATGACAAAAACTAGCCCCCATCTCAATCATATACCAAATCTCTCCCTCACTAAAC 4850
Sample 2        CTCACATGACAAAAACTAGCCCCCATCTCAATCATATACCAAATCTCTCCCTCACTAAAC
                ************************************************************

Sample 1        GTAAGCCTTCTCCTCACTCTCTCAATCTTATCCATCATAGCAGGCAGTTGAGGTGGATTA 4910
Sample 2        GTAAGCCTTCTCCTCACTCTCTCAATCTTATCCATCATAGCAGGCAGTTGAGGTGGATTA
                ************************************************************

Sample 1        AACCAAACCCAGCTACGCAAAATCTTAGCATACTCCTCAATTACCCACATAGGATGAATA 4970
Sample 2        AACCAAACCCAGCTACGCAAAATCTTAGCATACTCCTCAATTACCCACATAGGATGAATA
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Sample 1        ATAGCAGTTCTACCGTACAACCCTAACATAACCATTCTTAATTTAACTATTTATATTATC 5030
Sample 2        ATAGCAGTTCTACCGTACAACCCTAACATAACCATTCTTAATTTAACTATTTATATCATC
                ************************************************************ ***

Sample 1        CTAACTACTACCGCATTCCTACTACTCAACTTAAACTCCAGCACCACGACCCTACTACTA 5090
Sample 2        CTAACTACTACCGCATTCCTACTACTCAACTTAAACTCCAGCACCACGACCCTACTACTA
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Sample 1        TCTCGCACCTGAAACAAGCTAACATGACTAACACCCTTAATTCCATCCACCCTCCTCTCC 5150
Sample 2        TCTCGCACCTGAAACAAGCTAACATGACTAACACCCTTAATTCCATCCACCCTCCTCTCC
                ************************************************************

Sample 1        CTAGGAGGCCTGCCCCCGCTAACCGGCTTTTTGCCCAAATGGGCCATTATCGAAGAATTC 5210
Sample 2        CTAGGAGGCCTACCCCCGCTAACCGGCTTTTTGCCCAAATGGGCCATTATCGAAGAATTC
                ********** ***************************************************

Sample 1        ACAAAAAACAATAGCCTCATCATCCCCACCATCATAGCCACCATCACCCTCCTTAACCTC 5270
Sample 2        ACAAAAAACAATAGCCTCATCATCCCCACCATCATAGCCACCATCACCCTCCTTAACCTC
                ************************************************************

Sample 1        TACTTCTACCTACGCCTAATCTACTCCACCTCAATCACACTACTCCCCATATCTAACAAC 5330
Sample 2        TACTTCTACCTACGCCTAATCTACTCCACCTCAATCACACTACTCCCCATATCTAACAAC
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Sample 1        GTAAAAATAAAATGACAGTTTGAACATACAAAACCCACCCCATTCCTCCCCACACTCATC 5390
Sample 2        GTAAAAATAAAATGACAGTTTGAACATACAAAACCCACCCCACTCCTCCCCACACTCATC
                **************************************** **********

Sample 1        GCCCTTACCACGCTACTCCTACCTATCTCCCCTTTTATACTAATAATCTTATAGAAATTT 5450
Sample 2        ACCCTTACCACGCTACTCCTACCTATCTCCCCTTTTATACTAATAATCTTATAGAAATTT
                 ************************************************************

Sample 1        AGGTTAAATACAGACCAAGAGCCTTCAAAGCCCTCAGTAAGTTGCAATACTTAATTTCTG 5510
Sample 2        AGGTTAAATACAGACCAAGAGCCTTCAAAGCCCTCAGTAAGTTGCAATACTTAATTTCTG
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Sample 1        TAACAGCTAAGGACTGCAAAACCCCACTCTGCATCAACTGAACGCAAATCAGCCACTTTA 5570
Sample 2        TAACAGCTAAGGACTGCAAAACCTCACTCTGCATCAACTGAACGCAAATCAGCCACTTTA
                ********************** ***********************************

Sample 1        ATTAAGCTAAGCCCTTACTAGACCAATGGGACTTAAACCCACAAACACTTAGTTAACAGC 5630
Sample 2        ATTAAGCTAAGCCCTTACTAGACCAATGGGACTTAAACCCACAAACACTTAGTTAACAGC
                ************************************************************

Sample 1        TAAGCACCCTAATCAACTGGCTTCAATCTACTTCTCCCGCCGCCGGGAAAAAAGGCGGGA 5690
Sample 2        TAAGCACCCTAATCAACTGGCTTCAATCTACTTCTCCCGCCGCCGGGAAAAAAGGCGGGA
                ************************************************************

Sample 1        GAAGCCCCGGCAGGTTTGAAGCTGCTTCTTCGAATTTGCAATTCAATATGAAAATCACCT 5750
Sample 2        GAAGCCCCGGCAGGTTTGAAGCTGCTTCTTCGAATTTGCAATTCAATATGAAAATCACCT
                ************************************************************

Sample 1        CGGAGCTGGTAAAAAGAGGCCTAACCCCTGTCTTTAGATTTACAGTCCAATGCTTCACTC 5810
Sample 2        CGGAGCTGGTAAAAAGAGGCCTAACCCCTGTCTTTAGATTTACAGTCCAATGCTTCACTC
                ************************************************************

Sample 1        AGCCATTTTACCTCACCCCCACTGATGTTCGCCGACCGTTGACTATTCTCTACAAACCAC 5870
Sample 2        AGCCATTTTACCTCACCCCCACTGATGTTCGCCGACCGTTGACTATTCTCTACAAACCAC
                ************************************************************

Sample 1        AAAGACATTGGAACACTATACCTATTATTCGGCGCATGAGCTGGAGTCCTAGGCACAGCT 5930
Sample 2        AAAGACATTGGAACACTATACCTATTATTCGGCGCATGAGCTGGAGTCCTAGGCACAGCT
                ************************************************************

Sample 1        CTAAGCCTCCTTATTCGAGCCGAGCTGGGCCAGCCAGGCAACCTTCTAGGTAACGACCAC 5990
Sample 2        CTAAGCCTCCTTATTCGAGCCGAGCTGGGCCAGCCAGGCAACCTTCTAGGTAACGACCAC
                ************************************************************

Sample 1        ATCTACAACGTTATCGTCACAGCCCATGCATTTGTAATAATCTTCTTCATAGTAATACCC 6050
Sample 2        ATCTACAACGTTATCGTCACAGCCCATGCATTTGTAATAATCTTCTTCATAGTAATACCC
                ************************************************************

Sample 1        ATCATAATCGGAGGCTTTGGCAACTGACTAGTTCCCCTAATAATCGGTGCCCCCGATATG 6110
Sample 2        ATCATAATCGGAGGCTTTGGCAACTGACTAGTTCCCCTAATAATCGGTGCCCCCGATATG
                ************************************************************

Sample 1        GCGTTTCCCCGCATAAACAACATAAGCTTCTGACTCTTACCTCCCTCTCTCCTACTCCTG 6170
Sample 2        GCGTTCCCCCGCATAAACAACATAAGCTTCTGACTCTTACCTCCCTCTCTCCTACTCCTG
                ***** ********************************************************

Sample 1        CTCGCATCTGCTATAGTGGAGGCCGGAGCAGGAACAGGTTGAACAGTCTACCCTCCCTTA 6230
Sample 2        CTCGCATCTGCTATAGTGGAGGCCGGAGCAGGAACAGGTTGAACAGTCTACCCTCCCTTA
                ************************************************************

Sample 1        GCAGGGAACTACTCCCACCCTGGAGCCTCCGTAGACCTAACCATCTTCTCCTTACACCTA 6290
Sample 2        GCAGGGAACTACTCCCACCCTGGAGCCTCCGTAGACCTAACCATCTTCTCCTTACACCTA
                ************************************************************

Sample 1        GCAGGTGTCTCCTCTATCTTAGGGGCCATCAATTTCATCACAACAATTATCAATATAAAA 6350
Sample 2        GCAGGTGTCTCCTCTATCTTAGGGGCCATCAATTTCATCACAACAATTATCAATATAAAA
                ************************************************************

Sample 1        CCCCCTGCCATAACCCAATACCAAACGCCCCTCTTCGTCTGATCCGTCCTAATCACAGCA 6410
Sample 2        CCCCCTGCCATAACCCAATACCAAACGCCCCTCTTCGTCTGATCCGTCCTAATCACAGCA
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Sample 1        GTCCTACTTCTCCTATCTCTCCCAGTCCTAGCTGCTGGCATCACTATACTACTAACAGAC 6470
Sample 2        GTCCTACTTCTCCTATCTCTCCCAGTCCTAGCTGCTGGCATCACTATACTACTAACAGAC
                ************************************************************

Sample 1        CGCAACCTCAACACCACCTTCTTCGACCCCGCCGGAGGAGGAGACCCCATTCTATACCAA 6530
Sample 2        CGCAACCTCAACACCACCTTCTTCGACCCCGCCGGAGGAGGAGACCCCATTCTATACCAA
                ************************************************************

Sample 1        CACCTATTCTGATTTTTCGGTCACCCTGAAGTTTATATTCTTATCCTACCAGGCTTCGGA 6590
Sample 2        CACCTATTCTGATTTTTCGGTCACCCTGAAGTTTATATTCTTATCCTACCAGGCTTCGGA
                ************************************************************

Sample 1        ATAATCTCCCATATTGTAACTTACTACTCCGGAAAAAAAGAACCATTTGGATACATAGGT 6650
Sample 2        ATAATCTCCCATATTGTAACTTACTACTCCGGAAAAAAAGAACCATTTGGATACATAGGT
                ************************************************************

Sample 1        ATGGTCTGAGCTATGATATCAATTGGCTTCCTAGGGTTTATCGTGTGAGCACACCATATA 6710
Sample 2        ATGGTCTGAGCTATGATATCAATTGGCTTCCTAGGGTTTATCGTGTGAGCACACCATATA
                ************************************************************

Sample 1        TTTACAGTAGGAATAGACGTAGACACACGAGCATATTTCACCTCCGCTACCATAATCATC 6770
Sample 2        TTTACAGTAGGAATAGACGTAGACACACGAGCATATTTCACCTCCGCTACCATAATCATC
                ************************************************************

Sample 1        GCTATCCCCACCGGCGTCAAAGTATTTAGCTGACTCGCCACACTCCACGGAAGCAATATG 6830
Sample 2        GCTATCCCCACCGGCGTCAAAGTATTTAGCTGACTCGCCACACTCCACGGAAGCAATATG
                ************************************************************

Sample 1        AAATGATCTGCTGCAGTGCTCTGAGCCCTAGGATTCATCTTTCTTTTCACCGTAGGTGGC 6890
Sample 2        AAATGATCTGCTGCAGTGCTCTGAGCCCTAGGATTCATCTTTCTTTTCACCGTAGGTGGC
                ************************************************************

Sample 1        CTGACTGGCATTGTATTAGCAAACTCATCACTAGACATCGTACTACACGACACGTACTAC 6950
Sample 2        CTGACTGGCATTGTATTAGCAAACTCATCACTAGACATCGTACTACACGACACGTACTAC
                ************************************************************

Sample 1        GTTGTAGCTCACTTCCACTATGTCCTATCAATAGGAGCTGTATTTGCCATCATAGGAGGC 7010
Sample 2        GTTGTAGCTCACTTCCACTATGTCCTATCAATAGGAGCTGTATTTGCCATCATAGGAGGC
                ************************************************************

Sample 1        TTCATTCACTGATTTCCCCTATTCTCAGGCTACACCCTAGACCAAACCTACGCCAAAATC 7070
Sample 2        TTCATTCACTGATTTCCCCTATTCTCAGGCTACACCCTAGACCAAACCTACGCCAAAATC
                ************************************************************

Sample 1        CATTTCACTATCATATTCATCGGCGTAAATCTAACTTTCTTCCCACAACACTTTCTCGGC 7130
Sample 2        CATTTCGCTATCATATTCATCGGCGTAAATCTAACTTTCTTCCCACAACACTTTCTCGGC
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Sample 1        CTATCCGGAATGCCCCGACGTTACTCGGACTACCCCGATGCATACACCACATGAAACATC 7190
Sample 2        CTATCCGGAATGCCCCGACGTTACTCGGACTACCCCGATGCATACACCACATGAAATATC
                ************************************************************ ***

Sample 1        CTATCATCTGTAGGCTCATTCATTTCTCTAACAGCAGTAATATTAATAATTTTCATGATT 7250
Sample 2        CTATCATCTGTAGGCTCATTCATTTCTCTAACAGCAGTAATATTAATAATTTTCATGATT
                ************************************************************

Sample 1        TGAGAAGCCTTCGCTTCGAAGCGAAAAGTCCTAATAGTAGAAGAACCCTCCATAAACCTG 7310
Sample 2        TGAGAAGCCTTCGCTTCGAAGCGAAAAGTCCTAATAGTAGAAGAACCCTCCATAAACCTG
                ************************************************************

Sample 1        GAGTGACTATATGGATGCCCCCCACCCTACCACACATTCGAAGAACCCGTATACATAAAA 7370
Sample 2        GAGTGACTATATGGATGCCCCCCACCCTACCACACATTCGAAGAACCCGTATACATAAAA
                ************************************************************

Sample 1        TCTAGACAAAAAAGGAAGGAATCGAACCCCCCAAAGCTGGTTTCAAGCCAACCCCATGGC 7430
Sample 2        TCTAGACAAAAAAGGAAGGAATCGAACCCCCCAAAGCTGGTTTCAAGCCAACCCCATGGC
                ************************************************************

Sample 1        CTCCATGACTTTTTCAAAAAGGTATTAGAAAAACCATTTCATAACTTTGTCAAAGTTAAA 7490
Sample 2        CTCCATGACTTTTTCAAAAAGATATTAGAAAAACCATTTCATAACTTTGTCAAAGTTAAA
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Sample 1        TTATAGGCTAAATCCTATATATCTTAATGGCACATGCAGCGCAAGTAGGTCTACAAGACG 7550
Sample 2        TTATAGGCTAAATCCTATATATCTTAATGGCACATGCAGCGCAAGTAGGTCTACAAGACG
                ************************************************************

Sample 1        CTACTTCCCCTATCATAGAAGAGCTTATCACCTTTCATGATCACGCCCTCATAATCATTT 7610
Sample 2        CTACTTCCCCTATCATAGAAGAGCTTATCACCTTTCATGATCACGCCCTCATAATCATTT
                ************************************************************

Sample 1        TCCTTATCTGCTTCCTAGTCCTGTATGCCCTTTTCCTAACACTCACAACAAAACTAACTA 7670
Sample 2        TCCTTATCTGCTTCCTAGTCCTGTATGCCCTTTTCCTAACACTCACAACAAAACTAACTA
                ************************************************************

Sample 1        ATACTAACATCTCAGACGCTCAGGAAATAGAAACCGTCTGAACTATCCTGCCCGCCATCA 7730
Sample 2        ATACTAACATCTCAGACGCTCAGGAAATAGAAACCGTCTGAACTATCCTGCCCGCCATCA
                ************************************************************

Sample 1        TCCTAGTCCTCATCGCCCTCCCATCCCTACGCATCCTTTACATAACAGACGAGGTCAACG 7790
Sample 2        TCCTAGTCCTCATCGCCCTCCCATCCCTACGCATCCTTTACATAACAGACGAGGTCAACG
                ************************************************************

Sample 1        ATCCCTCCCTTACCATCAAATCAATTGGCCACCAATGGTACTGAACCTACGAGTACACCG 7850
Sample 2        ATCCCTCCCTTACCATCAAATCAATTGGCCACCAATGGTACTGAACCTACGAGTACACCG
                ************************************************************

Sample 1        ACTACGGCGGACTAATCTTCAACTCCTACATACTTCCCCCATTATTCCTAGAACCAGGCG 7910
Sample 2        ACTACGGCGGACTAATCTTCAACTCCTACATACTTCCCCCATTATTCCTAGAACCAGGCG
                ************************************************************

Sample 1        ACCTGCGACTCCTTGACGTTGACAATCGAGTAGTACTCCCGATTGAAGCCCCCATTCGTA 7970
Sample 2        ACCTGCGACTCCTTGACGTTGACAATCGAGTAGTACTCCCGATTGAAGCCCCCATTCGTA
                ************************************************************

Sample 1        TAATAATTACATCACAAGACGTCTTGCACTCATGAGCTGTCCCCACATTAGGCTTAAAAA 8030
Sample 2        TAATAATTACATCACAAGACGTCTTGCACTCATGAGCTGTCCCCACATTAGGCTTAAAAA
                ************************************************************

Sample 1        CAGATGCAATTCCCGGACGTCTAAACCAAACCACTTTCACCGCTACACGACCGGGGGTAT 8090
Sample 2        CAGATGCAATTCCCGGACGTCTAAACCAAACCACTTTCACCGCTACACGACCGGGGGTAT
                ************************************************************

Sample 1        ACTACGGTCAATGCTCTGAAATCTGTGGAGCAAACCACAGTTTCATGCCCATCGTCCTAG 8150
Sample 2        ACTACGGTCAATGCTCTGAAATCTGCGGAGCAAACCACAGTTTCATGCCCATCGTCCTAG
                ************************* **********************************

Sample 1        AATTAATTCCCCTAAAAATCTTTGAAATAGGGCCCGTATTTACCCTATAGCACCCCCTCT 8210
Sample 2        AATTAATTCCCCTAAAAATCTTTGAAATAGGGCCCGTATTTACCCTATAGCACCCCCTCT
                ************************************************************

Sample 1        ACCCCCTCTAGAGCCCACTGTAAAGCTAACTTAGCATTAACCTTTTAAGTTAAAGATTAA 8270
Sample 2        ACCCCCTCTAGAGCCCACTGTAAAGCTAACTTAGCATTAACCTTTTAAGTTAAAGATTAA
                ************************************************************

Sample 1        GAGAGCCAACACCTCTTTACAGTGAAATGCCCCAACTAAATACTACCGTATGGCCCACCA 8330
Sample 2        GAGAACCAACACCTCTTTACAGTGAAATGCCCCAACTAAATACTACCGTATGGCCCACCA
                **** ********************************************************

Sample 1        TAATTACCCCCATACTCCTTACACTATTCCTCATCACCCAACTAAAAATATTAAACACAA 8390
Sample 2        TAATTACCCCCATACTCCTTACACTATTTCTCATCACCCAACTAAAAATATTAAACACAA
                ************************** ***************************************

Sample 1        ACTACCACCTACCTCCCTCACCAAAGCCCATAAAAATAAAAAATTATAACAAACCCTGAG 8450
Sample 2        ACTACCACTTACCTCCCTCACCAAAGCCCATAAAAATAAAAAATTATAACAAACCCTGAG
                ******** ****************************************************

Sample 1        AACCAAAATGAACGAAAATCTGTTCGCTTCATTCATTGCCCCCACAATCCTAGGCCTACC 8510
Sample 2        AACCAAAATGAACGAAAATCTGTTCGCTTCATTCATTGCCCCCACAGTCCTAGGCCTACC
                ******************************************** *************

Sample 1        CGCCGCAGTACTGATCATTCTATTTCCCCCTCTATTGATCCCCACCTCCAAATATCTCAT 8570
Sample 2        CGCCGCAGTACTGATCATTCTATTTCCCCCTCTATTGATCCCCACCTCCAAATATCTCAT
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Sample 1        CAACAACCGACTAATCACCACCCAACAATGACTAATCAAACTAACCTCAAAACAAATGAT 8630
Sample 2        CAACAACCGACTAATTACCACCCAACAATGACTAATCAAACTAACCTCAAAACAAATGAT
                ************** ******************************************

Sample 1        AACCATACACAACACTAAAGGACGAACCTGATCTCTTATACTAGTATCCTTAATCATTTT 8690
Sample 2        AGCCATACACAACACTAAAGGACGAACCTGATCTCTTATACTAGTATCCTTAATCATTTT
                * ************************************************************

Sample 1        TATTGCCACAACTAACCTCCTCGGACTCCTGCCTCACTCATTTACACCAACCACCCAACT 8750
Sample 2        TATTGCCACAACTAACCTCCTCGGACTCCTGCCTCACTCATTTACACCAACCACCCAACT
                ************************************************************

Sample 1        ATCTATAAACCTAGCCATGGCCATCCCCTTATGAGCGGGCGCAGTGATTATAGGCTTTCG 8810
Sample 2        ATCTATAAACCTAGCCATGGCCATCCCCTTATGAGCGGGCGCAGTGATTATAGGCTTTCG
                ************************************************************

Sample 1        CTCTAAGATTAAAAATGCCCTAGCCCACTTCTTACCACAAGGCACACCTACACCCCTTAT 8870
Sample 2        CTCTAAGATTAAAAATGCCCTAGCCCACTTCTTACCACAAGGCACACCTACACCCCTTAT
                ************************************************************

Sample 1        CCCCATACTAGTTATTATCGAAACCATCAGCCTACTCATTCAACCAATAGCCCTGGCCGT 8930
Sample 2        CCCCATACTAGTTATTATCGAAACCATCAGCCTACTCATTCAACCAATAGCCCTGGCCGT
                ************************************************************

Sample 1        ACGCCTAACCGCTAACATTACTGCAGGCCACCTACTCATGCACCTAATTGGAAGCGCCAC 8990
Sample 2        ACGCCTAACCGCTAACATTACTGCAGGCCACCTACTCATGCATCTAATTGGAAGCGCCAC
                ************************************** *****************

Sample 1        CCTAGCAATATCAACCATTAACCTTCCCTCTACACTTATCATCTTCACAATTCTAATTCT 9050
Sample 2        CCTAGCAATATCAACCATTAACCTTCCCTCTACACTTATCATCTTCACAATTCTAATTCT
                ************************************************************

Sample 1        ACTGACTATCCTAGAAATCGCTGTCGCCTTAATCCAAGCCTACGTTTTCACACTTCTAGT 9110
Sample 2        ACTGACTATCCTAGAAATCGCTGTCGCCTTAATCCAAGCCTACGTTTTCACACTTCTAGT
                ************************************************************

Sample 1        AAGCCTCTACCTGCACGACAACACATAATGACCCACCAATCACATGCCTATCATATAGTA 9170
Sample 2        AAGCCTCTACCTGCACGACAACACATAATGACCCACCAATCACATGCCTATCATATAGTA
                ************************************************************

Sample 1        AAACCCAGCCCATGACCCCTAACAGGGGCCCTCTCAGCCCTCCTAATGACCTCCGGCCTA 9230
Sample 2        AAACCCAGCCCATGACCCCTAACAGGGGCCCTCTCAGCCCTCCTAATGACCTCCGGCCTA
                ************************************************************

Sample 1        GCCATGTGATTTCACTTCCACTCCATAACGCTCCTCATACTAGGCCTACTAACCAACACA 9290
Sample 2        GCCATGTGATTTCACTTCCACTCCATAACGCTCCTCATACTAGGCCTGCTAACCAACACA
                ********************************************** ************

Sample 1        CTAACCATATACCAATGATGGCGCGATGTAACACGAGAAAGCACATACCAAGGCCACCAC 9350
Sample 2        CTAACCATATACCAATGATGGCGCGATGTAACACGAGAAAGCACATACCAAGGCCACCAC
                ************************************************************

Sample 1        ACACCACCTGTCCAAAAAGGCCTTCGATACGGGATAATCCTATTTATTACCTCAGAAGTT 9410
Sample 2        ACACCACCTGTCCAAAAAGGCCTTCGATACGGGATAATCCTATTTATTACCTCAGAAGTT
                ************************************************************

Sample 1        TTTTTCTTCGCAGGATTTTTCTGAGCCTTTTACCACTCCAGCCTAGCCCCTACCCCCCAA 9470
Sample 2        TTTTTCTTCGCAGGATTTTTCTGAGCCTTTTACCACTCCAGCCTAGCCCCTACCCCCCAA
                ************************************************************

Sample 1        TTAGGAGGGCACTGGCCCCCAACAGGCATCACCCCGCTAAATCCCCTAGAAGTCCCACTC 9530
Sample 2        CTAGGAGGGCACTGGCCCCCAACAGGCATCACCCCGCTAAATCCCCTAGAAGTCCCACTC
                 ************************************************************

Sample 1        CTAAACACATCCGTATTACTCGCATCAGGAGTATCAATCACCTGAGCTCACCATAGTCTA 9590
Sample 2        CTAAACACATCCGTATTACTCGCATCAGGAGTATCAATCACCTGAGCTCACCATAGTCTA
                ************************************************************

Sample 1        ATAGAAAACAACCGAAACCAAATAATTCAAGCACTGCTTATTACAATTTTACTGGGTCTC 9650
Sample 2        ATAGAAAACAACCGAAACCAAATAATTCAAGCACTGCTTATTACAATTTTACTGGGTCTC
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Sample 1        TATTTTACCCTCCTACAAGCCTCAGAGTACTTCGAGTCTCCCTTCACCATTTCCGACGGC 9710
Sample 2        TATTTTACCCTCCTACAAGCCTCAGAGTACTTCGAATCTCCCTTCACCATTTCCGACGGC
                ********************************** **********************

Sample 1        ATCTACGGCTCAACATTTTTTGTAGCCACAGGCTTCCACGGACTTCACGTCATTATTGGC 9770
Sample 2        ATCTACGGCTCAACATTTTTTGTAGCCACAGGCTTCCATGGACTTCACGTCATTATTGGC
                ************************************ ********************

Sample 1        TCAACTTTCCTCACTATCTGCTTCATCCGCCAACTAATATTTCACTTTACATCCAAACAT 9830
Sample 2        TCAACTTTCCTCACTATCTGCTTCATCCGCCAACTAATATTTCACTTTACATCCAAACAT
                ************************************************************

Sample 1        CACTTTGGCTTCGAAGCCGCCGCCTGATACTGGCATTTTGTAGATGTGGTTTGACTATTT 9890
Sample 2        CACTTTGGCTTCGAAGCCGCCGCCTGATACTGGCATTTTGTAGATGTGGTTTGACTATTT
                ************************************************************

Sample 1        CTGTATGTCTCCATCTATTGATGAGGGTCTTACTCTTTTAGTATAAATAGTACCGTTAAC 9950
Sample 2        CTGTATGTCTCCATCTATTGATGAGGGTCTTACTCTTTTAGTATAAATAGTACCGTTAAC
                ************************************************************

Sample 1        TTCCAATTAACTAGTTTTGACAACATTCAAAAAAGAGTAATAAACTTCGCCTTAATTTTA 10010
Sample 2        TTCCAATTAACTAGTTTTGACAACATTCAAAAAAGAGTAATAAACTTCGCCTTAATTTTA
                ************************************************************

Sample 1        ATAATCAACACCCTCCTAGCCTTACTACTAATAATTATTACATTTTGACTACCACAACTC 10070
Sample 2        ATAATCAACACCCTCCTAGCCTTACTACTAATAATTATTACATTTTGACTACCACAACTC
                ************************************************************

Sample 1        AACGGCTACATAGAAAAATCCACCCCTTACGAGTGCGGCTTCGACCCTATATCCCCCGCC 10130
Sample 2        AACGGCTACATAGAAAAATCCACCCCTTACGAGTGCGGCTTCGACCCTATATCCCCCGCC
                ************************************************************

Sample 1        CGCGTCCCTTTCTCCATAAAATTCTTCTTAGTAGCTATTACCTTCTTATTATTTGATCTA 10190
Sample 2        CGCGTCCCTTTCTCCATAAAATTCTTCTTAGTAGCTATTACCTTCTTATTATTTGATCTA
                ************************************************************

Sample 1        GAAATTGCCCTCCTTTTACCCCTACCATGAGCCCTACAAACAACTAACCTGCCACTAATA 10250
Sample 2        GAAATTGCCCTCCTTTTACCCCTACCATGAGCCCTACAAACAACTAACCTGCCACTAATA
                ************************************************************

Sample 1        GTTATGTCATCCCTCTTATTAATCATCATCCTAGCCCTAAGTCTGGCCTATGAGTGACTA 10310
Sample 2        GTTATGTCATCCCTCTTATTAATCATCATCCTAGCCCTAAGTCTGGCCTATGAGTGACTA
                ************************************************************

Sample 1        CAAAAAGGATTAGACTGAACCGAATTGGTATATAGTTTAAACAAAACGAATGATTTCGAC 10370
Sample 2        CAAAAAGGATTAGACTGAGCCGAATTGGTATATAGTTTAAACAAAACGAATGATTTCGAC
                ****************** ****************************************

Sample 1        TCATTAAATTATGATAATCATATTTACCAAATGCCCCTCATTTACATAAATATTATACTA 10430
Sample 2        TCATTAAATTATGATAATCATATTTACCAAATGCCCCTCATTTACATAAATATTATACTA
                ************************************************************

Sample 1        GCATTTACCATCTCACTTCTAGGAATACTAGTATATCGCTCACACCTCATATCCTCCCTA 10490
Sample 2        GCATTTACCATCTCACTTCTAGGAATACTAGTATATCGCTCACACCTCATATCCTCCCTA
                ************************************************************

Sample 1        CTATGCCTAGAAGGAATAATACTATCGCTGTTCATTATAGCTACTCTCATAACCCTCAAC 10550
Sample 2        CTATGCCTAGAAGGAATAATACTATCGCTATTCATTATAGCTACTCTCATAACCCTCAAC
                ***************************** ******************************

Sample 1        ACCCACTCCCTCTTAGCCAATATTGTGCCTATTGCCATACTAGTCTTTGCCGCCTGCGAA 10610
Sample 2        ACCCACTCCCTCTTAGCCAATATTGTGCCTATTGCCATACTAGTTTTTGCCGCCTGCGAA
                ****************************************** ***************

Sample 1        GCAGCGGTGGGCCTAGCCCTACTAGTCTCAATCTCCAACACATATGGCCTAGACTACGTA 10670
Sample 2        GCAGCGGTAGGCCTAGCCCTACTAGTCTCAATCTCCAACACATATGGCCTAGACTACGTA
                ******** ********************************************************

Sample 1        CATAACCTAAACCTACTCCAATGCTAAAACTAATCGTCCCAACAATTATATTACTACCAC 10730
Sample 2        CATAACCTAAACCTACTCCAATGCTAAAACTAATCGTCCCAACAATTATATTACTACCAC
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Sample 1        TGACATGACTTTCCAAAAAACACATAATTTGAATCAACACAACCACCCACAGCCTAATTA 10790
Sample 2        TGACATGACTCTCCAAAAAACACATAATTTGAATCAACACAACCACCCACAGCCTAATTA
                ********** **************************************************

Sample 1        TTAGCATCATCCCTCTACTATTTTTTAACCAAATCAACAACAACCTATTTAGCTGTTCCC 10850
Sample 2        TTAGCATCATCCCCCTACTATTTTTTAACCAAATCAACAACAACCTATTTAGCTGCTCCC
                ************ ****************************************** ****

Sample 1        CAACCTTTTCCTCCGACCCCCTAACAACCCCCCTCCTAATACTAACTACCTGACTCCTAC 10910
Sample 2        CAACCTTTTCCTCCGACCCCCTAACAACCCCCCTCCTAATACTAACTACCTGACTCCTAC
                ************************************************************

Sample 1        CCCTCACAATCATGGCAAGCCAACGCCACTTATCCAGTGAACCACTATCACGAAAAAAAC 10970
Sample 2        CCCTCACAATCATGGCAAGCCAACGCCACTTATCCAGTGAACCACTATCACGAAAAAAAC
                ************************************************************

Sample 1        TCTACCTCTCTATACTAATCTCCCTACAAATCTCCTTAATTATAACATTCACAGCCACAG 11030
Sample 2        TCTACCTCTCTATACTAATCTCCCTACAAATCTCCTTAATTATAACATTCACAGCCACAG
                ************************************************************

Sample 1        AACTAATCATATTTTATATCTTCTTCGAAACCACACTTATCCCCACCTTGGCTATCATCA 11090
Sample 2        AACTAATCATATTTTATATCTTCTTCGAAACCACACTTATCCCCACCTTGGCTATCATCA
                ************************************************************

Sample 1        CCCGATGAGGCAACCAGCCAGAACGCCTGAACGCAGGCACATACTTCCTATTCTACACCC 11150
Sample 2        CCCGATGAGGCAACCAACCAGAACGCCTGAACGCAGGCACATACTTCCTATTCTACACCC
                *************** ****************************************

Sample 1        TAGTAGGCTCCCTTCCCCTACTCATCGCACTAATTTACACTCACAACACCCTAGGCTCAC 11210
Sample 2        TAGTAGGCTCCCTTCCCCTACTCATCGCACTAATTTACACTCACAACACCCTAGGCTCAC
                ************************************************************

Sample 1        TAAACATTCTACTACTCACTCTCACTGCCCAAGAACTATCAAACTCCTGAGCCAACAACT 11270
Sample 2        TAAACATTCTACTACTCACTCTCACTGCCCAAGAACTATCAAACTCCTGAGCCAACAACT
                ************************************************************

Sample 1        TAATATGACTAGCTTACACAATAGCTTTTATAGTAAAGATACCTCTTTACGGACTCCACT 11330
Sample 2        TAATATGACTAGCTTACACAATAGCTTTTATAGTAAAGATACCTCTTTACGGACTCCACT
                ************************************************************

Sample 1        TATGACTCCCTAAAGCCCATGTCGAAGCCCCCATCGCTGGGTCAATAGTACTTGCCGCAG 11390
Sample 2        TATGACTCCCTAAAGCCCATGTCGAAGCCCCCATCGCTGGGTCAATAGTACTTGCCGCAG
                ************************************************************

Sample 1        TACTCTTAAAACTAGGCGGCTATGGTATAATACGCCTCACACTCATTCTCAACCCCCTGA 11450
Sample 2        TACTCTTAAAACTAGGCGGCTATGGTATAATACGCCTCACACTCATTCTCAACCCCCTGA
                ************************************************************

Sample 1        CAAAACACATAGCCTACCCCTTCCTTGTACTATCCCTATGAGGCATAATTATAACAAGCT 11510
Sample 2        CAAAACACATAGCCTACCCCTTCCTTGTACTATCCCTATGAGGCATAATTATAACAAGCT
                ************************************************************

Sample 1        CCATCTGCCTACGACAAACAGACCTAAAATCGCTCATTGCATACTCTTCAATCAGCCACA 11570
Sample 2        CCATCTGCCTACGACAAACAGACCTAAAATCGCTCATTGCATACTCTTCAATCAGCCACA
                ************************************************************

Sample 1        TAGCCCTCGTAGTAACAGCCATTCTCATCCAAACCCCCTGAAGCTTCACCGGCGCAGTCA 11630
Sample 2        TGGCCCTCGTAGTAACAGCCATTCTCATCCAAACCCCCTGAAGCTTCACCGGCGCAGTCA
                * ************************************************************

Sample 1        TTCTCATAATCGCCCACGGGCTTACATCCTCATTACTATTCTGCCTAGCAAACTCAAACT 11690
Sample 2        TTCTCATAATCGCCCACGGACTTACATCCTCATTACTATTCTGCCTAGCAAACTCAAACT
                ****************** ****************************************

Sample 1        ACGAACGCACTCACAGTCGCATCATAATCCTCTCTCAAGGACTTCAAACTCTACTCCCAC 11750
Sample 2        ACGAACGCACTCACAGTCGCATCATAATCCTCTCTCAAGGACTTCAAACTCTACTCCCAC
                ************************************************************

Sample 1        TAATAGCTTTTTGATGACTTCTAGCAAGCCTCGCTAACCTCGCCTTACCCCCCACTATTA 11810
Sample 2        TAATAGCTTTTTGATGACTTCTAGCAAGCCTCGCTAACCTCGCCTTACCCCCCACTATTA
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Sample 1        ACCTACTGGGAGAACTCTCTGTGCTAGTAACCACGTTCTCCTGATCAAATATCACTCTCC 11870
Sample 2        ACCTACTGGGAGAACTCTCTGTGCTAGTAACCACATTCTCCTGATCAAATATCACTCTCC
                ********************************* ************************

Sample 1        TACTTACAGGACTCAACATACTAGTCACAGCCCTATACTCCCTCTACATATTTACCACAA 11930
Sample 2        TACTTACAGGACTCAACATACTAGTCACAGCCCTATACTCCCTCTACATATTTACCACAA
                ************************************************************

Sample 1        CACAATGGGGCTCACTCACCCACCACATTAACAACATAAAACCCTCATTCACACGAGAAA 11990
Sample 2        CACAATGAGGCTCACTCACCCACCACATTAACAACATAAAACCCTCATTCACACGAGAAA
                ******* ****************************************************

Sample 1        ACACCCTCATGTTCATACACCTATCCCCCATTCTCCTCCTATCCCTCAACCCCGACATCA 12050
Sample 2        ACACCCTCATGTTCATACACCTATCCCCCATTCTCCTCCTATCCCTCAACCCCGACATCA
                ************************************************************

Sample 1        TTACCGGGTTTTCCTCTTGTAAATATAGTTTAACCAAAACATCAGATTGTGAATCTGACA 12110
Sample 2        TTACCGGGTTTTCCTCTTGTAAATATAGTTTAACCAAAACATCAGATTGTGAATCTGACA
                ************************************************************

Sample 1        ACAGAGGCTTACGACCCCTTATTTACCGAGAAAGCTCACAAGAACTGCTAACTCATGCCC 12170
Sample 2        ACAGAGGCTTACGACCCCTTATTTACCGAGAAAGCTCACAAGAACTGCTAACTCATGCCC
                ************************************************************

Sample 1        CCATGTCTAACAACATGGCTTTCTCAACTTTTAAAGGATAACAGCTATCCATTGGTCTTA 12230
Sample 2        CCATGTCTAACAACATGGCTTTCTCAACTTTTAAAGGATAACAGCTATCCATTGGTCTTA
                ************************************************************

Sample 1        GGCCCCAAAAATTTTGGTGCAACTCCAAATAAAAGTAATAACCATGCACACTACTATAAC 12290
Sample 2        GGCCCCAAAAATTTTGGTGCAACTCCAAATAAAAGTAATAACCATGCACACTACTATAAC
                ************************************************************

Sample 1        CACCCTAACCCTGACTTCCCTAATTCCCCCCATCCTTACCACCCTCGTTAACCCTAACAA 12350
Sample 2        CACCCTAACCCTGACTTCCCTAATTCCCCCCATCCTTACCACCCTCGTTAACCCTAACAA
                ************************************************************

Sample 1        AAAAAACTCATACCCCCATTATGTAAAATCCATTGTCGCATCCACCTTTATTATCAGTCT 12410
Sample 2        AAAAAACTCATACCCCCATTATGTAAAATCCATTGTCGCATCCACCTTTATTATCAGTCT
                ************************************************************

Sample 1        CTTCCCCACAACAATATTCATGTGCCTAGACCAAGAAGTTATTATCTCGAACTGACACTG 12470
Sample 2        CTTCCCCACAACAATATTCATGTGCCTAGACCAAGAAGTTATTATCTCGAACTGACACTG
                ************************************************************

Sample 1        AGCCACAACCCAAACAACCCAGCTCTCCCTAAGCTTCAAACTAGACTACTTCTCCATAAT 12530
Sample 2        AGCCACAACCCAAACAACCCAGCTCTCCCTAAGCTTCAAACTAGACTACTTCTCCATAAT
                ************************************************************

Sample 1        ATTCATCCCTGTAGCATTGTTCGTTACATGGTCCATCATAGAATTCTCACTGTGATATAT 12590
Sample 2        ATTCATCCCTGTAGCATTGTTCGTTACATGGTCCATCATAGAATTCTCACTGTGATATAT
                ************************************************************

Sample 1        AAACTCAGACCCAAACATTAATCAGTTCTTCAAATATCTACTCATCTTCCTAATTACCAT 12650
Sample 2        AAACTCAGACCCAAACATTAATCAGTTCTTCAAATATCTACTCATTTTCCTAATTACCAT
                ******************************************* **************

Sample 1        ACTAATCTTAGTTACCGCTAACAACCTATTCCAACTGTTCATCGGCTGAGAGGGCGTAGG 12710
Sample 2        GCTAATCTTAGTTACCGCTAACAACCTATTCCAACTGTTCATCGGCTGAGAGGGCGTAGG
                 ************************************************************

Sample 1        AATTATATCCTTCTTGCTCATCAGTTGATGATACGCCCGAGCAGATGCCAACACAGCAGC 12770
Sample 2        AATTATATCCTTCTTGCTCATCAGTTGATGATACGCCCGAGCAGATGCCAACACAGCAGC
                ************************************************************

Sample 1        CATTCAAGCAATCCTATACAACCGTATCGGCGATATCGGTTTCATCCTCGCCTTAGCATG 12830
Sample 2        CATTCAAGCAATCCTATACAACCGTATCGGCGATATCGGTTTCATCCTCGCCTTAGCATG
                ************************************************************

Sample 1        ATTTATCCTACACTCCAACTCATGAGACCCACAACAAATAGCCCTTCTAAACGCTAATCC 12890
Sample 2        ATTTATCCTACACTCCAACTCATGAGACCCACAACAAATAGCCCTTCTAAACGCTAATCC
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Sample 1        AAGCCTCACCCCACTACTAGGCCTCCTCCTAGCAGCAGCAGGCAAATCAGCCCAATTAGG 12950
Sample 2        AAGCCTCACCCCACTACTAGGCCTCCTCCTAGCAGCAGCAGGCAAATCAGCCCAATTAGG
                ************************************************************

Sample 1        TCTCCACCCCTGACTCCCCTCAGCCATAGAAGGCCCCACCCCAGTCTCAGCCCTACTCCA 13010
Sample 2        TCTCCACCCCTGACTCCCCTCAGCCATAGAAGGCCCCACCCCAGTCTCAGCCCTACTCCA
                ************************************************************

Sample 1        CTCAAGCACTATAGTTGTAGCAGGAATCTTCTTACTCATCCGCTTCCACCCCCTAGCAGA 13070
Sample 2        CTCAAGCACTATAGTTGTAGCAGGAGTCTTCTTACTCATCCGCTTCCACCCCCTAGCAGA
                ************************ *********************************

Sample 1        AAATAGCCCACTAATCCAAACTCTAACACTATGCTTAGGCGCTATCACCACTCTGTTCGC 13130
Sample 2        AAATAGCCCACTAATCCAAACTCTAACACTATGCTTAGGCGCTATCACCACTCTGTTCGC
                ************************************************************

Sample 1        AGCAGTCTGCGCCCTTACACAAAATGACATCAAAAAAATCGTAGCCTTCTCCACTTCAAG 13190
Sample 2        AGCAGTCTGCGCCCTTACACAAAATGACATCAAAAAAATCGTAGCCTTCTCCACTTCAAG
                ************************************************************

Sample 1        TCAACTAGGACTCATAATAGTTACAATCGGCATCAACCAACCACACCTAGCATTCCTGCA 13250
Sample 2        TCAACTAGGACTCATAGTAGTTACAATCGGCATCAACCAACCACACCTAGCATTCCTGCA
                *************** ******************************************

Sample 1        CATCTGTACCCACGCCTTCTTCAAAGCCATACTATTTATGTGCTCCGGGTCCATCATCCA 13310
Sample 2        CATCTGTACCCACGCCTTCTTCAAAGCCATACTATTTATGTGCTCCGGGTCCATCATCCA
                ************************************************************

Sample 1        CAACCTTAACAATGAACAAGATATTCGAAAAATAGGAGGACTACTCAAAACCATACCTCT 13370
Sample 2        CAACCTTAACAATGAACAAGATATTCGAAAAATAGGAGGACTACTCAAAACCATACCTCT
                ************************************************************

Sample 1        CACTTCAACCTCCCTCACCATTGGCAGCCTAGCATTAGCAGGAATACCTTTCCTCACAGG 13430
Sample 2        CACTTCAACCTCCCTCACCATTGGCAGCCTAGCATTAGCAGGAATACCTTTCCTCACAGG
                ************************************************************

Sample 1        TTTCTACTCCAAAGACCACATCATCGAAACCGCAAACATATCATACACAAACGCCTGAGC 13490
Sample 2        TTTCTATTCCAAAGACCACATCATCGAAACCGCAAACATATCATACACAAACGCCTGAGC
                ****** *****************************************************

Sample 1        CCTATCTATTACTCTCATCGCTACCTCCCTGACAAGCGCCTATAGCACTCGAATAATTCT 13550
Sample 2        CCTATCTATTACTCTCATCGCTACCTCCCTGACAAGCGCCTATAGCACTCGAATAATTCT
                ************************************************************

Sample 1        TCTCACCCTAACAGGTCAACCTCGCTTCCCCACCCTTACTAACATTAACGAAAATAACCC 13610
Sample 2        TCTCACCCTAACAGGTCAACCTCGCTTCCCTACCCTTACTAACATTAACGAAAATAACCC
                ***************************** ****************************

Sample 1        CACCCTACTAAACCCCATTAAACGCCTGGCAGCCGGAAGCCTATTCGCAGGATTTCTCAT 13670
Sample 2        CACCCTACTAAACCCCATTAAACGCCTGGCAGCCGGAAGCCTATTCGCAGGATTTCTCAT
                ************************************************************

Sample 1        TACTAACAACATTTCCCCCGCATCCCCCTTCCAAACAACAATCCCCCTCTACCTAAAACT 13730
Sample 2        TACTAACAACATTTCCCCCGCATCCCCCTTCCAAACAACAATCCCCCTCTACCTAAAACT
                ************************************************************

Sample 1        CACAGCCCTCGCTGTCACTTTCCTAGGACTTCTAACAGCCCTAGACCTCAACTACCTAAC 13790
Sample 2        CACAGCCCTCGCTGTCACTTTCCTAGGACTTCTAACAGCCCTAGACCTCAACTACCTAAC
                ************************************************************

Sample 1        CAACAAACTTAAAATAAAATCCCCACTATGCACATTTTATTTCTCCAACATACTCGGATT 13850
Sample 2        CAACAAACTTAAAATAAAATCCCCACTATGCACATTTTATTTCTCCAACATACTCGGATT
                ************************************************************

Sample 1        CTACCCTAGCATCACACACCGCACAATCCCCTATCTAGGCCTTCTTACGAGCCAAAACCT 13910
Sample 2        CTACCCTAGCATCACACACCGCACAATCCCCTATCTAGGCCTTCTTACGAGCCAAAACCT
                ************************************************************

Sample 1        GCCCCTACTCCTCCTAGACCTAACCTGACTAGAAAAGCTATTACCTAAAACAATTTCACA 13970
Sample 2        GCCCCTACTCCTCCTAGACCTAACCTGACTAGAAAAGCTATTACCTAAAACAATTTCACA
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Sample 1        GCACCAAATCTCCACCTCCATCATCACCTCAACCCAAAAAGGCATAATTAAACTTTACTT 14030
Sample 2        GCACCAAATCTCCACCTCCATCATCACCTCAACCCAAAAAGGCATAATTAAACTTTACTT
                ************************************************************

Sample 1        CCTCTCTTTCTTCTTCCCACTCATCCTAACCCTACTCCTAATCACATAACCTATTCCCCC 14090
Sample 2        CCTCTCTTTCTTCTTCCCACTCATCCTAACCCTACTCCTAATCACATAACCTATTCCCCC
                ************************************************************

Sample 1        GAGCAATCTCAATTACAATATATACACCAACAAACAATGTTCAACCAGTAACTACTACTA 14150
Sample 2        GAGCAATCTCAATTACAATATATACACCAACAAACAATGTTCAACCAGTAACTACTACTA
                ************************************************************

Sample 1        ATCAACGCCCATAATCATACAAAGCCCCCGCACCAATAGGATCCTCCCGAATCAACCCTG 14210
Sample 2        ATCAACGCCCATAATCATACAAAGCCCCCGCACCAATAGGATCCTCCCGAATCAACCCTG
                ************************************************************

Sample 1        ACCCCTCTCCTTCATAAATTATTCAGCTTCCTACACTATTAAAGTTTACCACAACCACCA 14270
Sample 2        ACCCCTCTCCTTCATAAATTATTCAGCTCCCTACACTATTAAAGTTTACCACAACCACCA
                *************************** ******************************

Sample 1        CCCCATCATACTCTTTCACCCACAGCACCAATCCTACCTCCATCGCTAACCCCACTAAAA 14330
Sample 2        CCCCATCATACTCTTTCACCCACAGCACCAATCCTACCTCCATCGCTAACCCCACTAAAA
                ************************************************************

Sample 1        CACTCACCAAGACCTCAACCCCTGACCCCCATGCCTCAGGATACTCCTCAATAGCCATCG 14390
Sample 2        CACTCACCAAGACCTCAACCCCTGACCCCCATGCCTCAGGATACTCCTCAATAGCCATCG
                ************************************************************

Sample 1        CTGTAGTATATCCAAAGACAACCATCATTCCCCCTAAATAAATTAAAAAAACTATTAAAC 14450
Sample 2        CTGTAGTATATCCAAAGACAACCATCATTCCCCCTAAATAAATTAAAAAAACTATTAAAC
                ************************************************************

Sample 1        CCATATAACCTCCCCCAAAATTCAGAATAATAACACACCCGACCACACCGCTAACAATCA 14510
Sample 2        CCATATAACCTCCCCCAAAATTCAGAATAATAACACACCCGACCACACCGCTAACAATCA
                ************************************************************

Sample 1        ATACTAAACCCCCATAAATAGGAGAAGGCTTAGAAGAAAACCCCACAAACCCCATTACTA 14570
Sample 2        ATACTAAACCCCCATAAATAGGAGAAGGCTTAGAAGAAAACCCCACAAACCCCATTACTA
                ************************************************************

Sample 1        AACCCACACTCAACAGAAACAAAGCATACATCATTATTCTCGCACGGACTACAACCACGA 14630
Sample 2        AACCCACACTCAACAGAAACAAAGCATACATCATTATTCTCGCACGGACTACAACCACGA
                ************************************************************

Sample 1        CCAATGATATGAAAAACCATCGTTGTATTTCAACTACAAGAACACCAATGACCCCAATAC 14690
Sample 2        CCAATGATATGAAAAACCATCGTTGTATTTCAACTACAAGAACACCAATGACCCCAATAC
                ************************************************************

Sample 1        GCAAAACTAACCCCCTAATAAAATTAATTAACCACTCATTCATCGACCTCCCCACCCCAT 14750
Sample 2        GCAAAATTAACCCCCTAATAAAATTAATTAACCACTCATTCATCGACCTCCCCACCCCAT
                ****** ***************************************************

Sample 1        CCAACATCTCCGCATGATGAAACTTCGGCTCACTCCTTGGCGCCTGCCTGATCCTCCAAA 14810
Sample 2        CCAACATCTCCGCATGATGAAACTTCGGCTCACTCCTTGGCGCCTGCCTGATCCTCCAAA
                ************************************************************

Sample 1        TCACCACAGGACTATTCCTAGCCATGCACTACTCACCAGACGCCTCAACCGCCTTTTCAT 14870
Sample 2        TCACCACAGGACTATTCCTAGCCATGCACTACTCACCAGACGCCTCAACCGCCTTTTCAT
                ************************************************************

Sample 1        CAATCGCCCACATCACTCGAGACGTAAATTATGGCTGAATCATCCGCTACCTTCACGCCA 14930
Sample 2        CAATCGCCCACATCACTCGAGACGTAAATTATGGCTGAATCATCCGCTACCTTCACGCCA
                ************************************************************

Sample 1        ATGGCGCCTCAATATTCTTTATCTGCCTCTTCCTACACATCGGGCGAGGCCTATATTACG 14990
Sample 2        ATGGCGCCTCAATATTCTTTATCTGCCTCTTCCTACACATCGGGCGAGGCCTATATTACG
                ************************************************************

Sample 1        GATCATTTCTCTACTCAGAAACCTGAAACATCGGCATTATCCTCCTGCTTGCAACTATAG 15050
Sample 2        GATCATTTCTCTACTCAGAAACCTGAAACATCGGCATTATCCTCCTGCTTGCAACTATAG
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Sample 1        CAACAGCCTTCATAGGCTATGTCCTCCCGTGAGGCCAAATATCATTCTGAGGGGCCACAG 15110
Sample 2        CAACAGCCTTCATAGGTTATGTCCTCCCGTGAGGCCAAATATCATTCTGAGGGGCCACAG
                *************** ********************************************

Sample 1        TAATTACAAACTTACTATCCGCCATCCCATACATTGGGACAGACCTAGTTCAATGAATCT 15170
Sample 2        TAATTACAAACTTACTATCCGCCATCCCATACATTGGGACAGACCTAGTTCAATGAATCT
                ************************************************************

Sample 1        GAGGAGGCTACTCAGTAGACAGTCCCACCCTCACACGATTCTTTACCTTTCACTTCATCT 15230
Sample 2        GAGGAGGCTACTCAGTAGACAGTCCCACCCTCACACGATTCTTTACCTTTCACTTCATCT
                ************************************************************

Sample 1        TGCCCTTCATTATTGCAGCCCTAGCAGCACTCCACCTCCTATTCTTGCACGAAACGGGAT 15290
Sample 2        TGCCCTTCATTATTGCAGCCCTAGCAGCACTCCACCTCCTATTCTTGCACGAAACGGGAT
                ************************************************************

Sample 1        CAAACAACCCCCTAGGAATCACCTCCCATTCCGATAAAATCACCTTCCACCCTTACTACA 15350
Sample 2        CAAACAACCCCCTAGGAATCACCTCCCATTCCGATAAAATCACCTTCCACCCTTACTACA
                ************************************************************

Sample 1        CAATCAAAGACGCCCTCGGCTTACTTCTCTTCCTTCTCTCCTTAATGACATTAACACTAT 15410
Sample 2        CAATCAAAGACACCCTCGGCTTACTTCTCTTCCTTCTCTCCTTAATGACATTAACACTAT
                *********** ************************************************

Sample 1        TCTCACCAGACCTCCTAGGCGACCCAGACAATTATACCCTAGCCAACCCCTTAAACACCC 15470
Sample 2        TCTCACCAGACCTCCTAGGCGACCCAGACAATTATACCCTAGCCAACCCCTTAAACACCC
                ************************************************************

Sample 1        CTCCCCACATCAAGCCCGAATGATATTTCCTATTCGCCTACACAATTCTCCGATCCGTCC 15530
Sample 2        CTCCCCACATCAAGCCCGAATGATATTTCCTATTCGCCTACACAATTCTCCGATCCGTCC
                ************************************************************

Sample 1        CTAACAAACTAGGAGGCGTCCTTGCCCTATTACTATCCATCCTCATCCTAGCAATAATCC 15590
Sample 2        CTAACAAACTAGGAGGCGTCCTTGCCCTATTACTATCCATCCTCATCCTAGCAATAATCC
                ************************************************************

Sample 1        CCATCCTCCATATATCCAAACAACAAAGCATAATATTTCGCCCACTAAGCCAATCACTTT 15650
Sample 2        CCATCCTCCATATATCCAAACAACAAAGCATAATATTTCGCCCACTAAGCCAATCACTTT
                ************************************************************

Sample 1        ATTGACTCCTAGCCGCAGACCTCCTCATTCTAACCTGAATCGGAGGACAACCAGTAAGCT 15710
Sample 2        ATTGACTCCTAGCCGCAGACCTCCTCATTCTAACCTGAATCGGAGGACAACCAGTAAGCT
                ************************************************************

Sample 1        ACCCTTTTACCATCATTGGACAAGTAGCATCCGTACTATACTTCACAACAATCCTAATCC 15770
Sample 2        ACCCTTTTACCATCATTGGACAAGTAGCATCCGTACTATACTTCACAACAATCCTAATCC
                ************************************************************

Sample 1        TAATACCAACTATCTCCCTAATTGAAAACAAAATACTCAAATGGGCCTGTCCTTGTAGTA 15830
Sample 2        TAATACCAACTATCTCCCTAATTGAAAACAAAATACTCAAATGGGCCTGTCCTTGTAGTA
                ************************************************************

Sample 1        TAAATTAATACACCAGTCTTGTAAACCGGAGATGAAAACCTTTTTCCAAGGACAAATCAG 15890
Sample 2        TAAACTAATACACCAGTCTTGTAAGCCGGAGATGAAAACCTTTTTCCAAGGACAAATCAG
                **** ****************** **********************************

Sample 1        AGAAAAAGTCTTTAACTCCACCATTAGCACCCAAAGCTAAGATTCTAATTTAAACTATTC 15950
Sample 2        AGAAAAAGTCTTTAACTCCACCATTAGCACCCAAAGCTAAGATTCTAATTTAAACTATTC
                ************************************************************

Sample 1        TCTGTTCTTTCATGGGGAAGCAGATTTGGGTACCACCCAAGTATTGACTCACCCATCAAC 16010
Sample 2        TCTGTTCTTTCATGGGGAAGCAGATTTGGGTACCACCCAAGTATTGACTCACCCATCAAC
                ************************************************************

Sample 1        AACCGCTATGTATTTCGTACATTACTGCCAGCCACCATGAATATTGTACGGTACCATAAA 16070
Sample 2        AACCGCTATGTATTTCGTACATTACTGCCAGCCACCATGAATATTGTACAGTACCATAAA
                ************************************************** **********

Sample 1        TACTTGACCACCTGTAGTACATAAAAACCCAATCCACATCAAAACCCCCTCCCCATGCTT 16130
Sample 2        TACTTGACTACCTGTAGTACATAAAAACTCAACCCACATCAAAACCCTGCCCCCATGCTT
                ******** ****************** *** **************   **********
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Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1       GCAATACACTGAAAATGTTTAGACGGGCTCACATCACCCCATAAACAAATAGGTTTGGTC 660
Sample 3       GCAATACACTGAAAATGTTTCGACGGGTTTACATCACCCCATAAACAAACAGGTTTGGTC
               ******************** ****** * ****************** **********  _

Sample 1       CTAGCCTTTCTATTAGCTCTTAGTAAGATTACACATGCAAGCATCCCCGTTCCAGTGAGT 720
Sample 3       CTAGCCTTTCTATTAGCTCTTAGTAAGATTACACATGCAAGCATCCCCGCCCC-GTGAGT
               ********************************************  ** ******

Sample 1       TCACCCTCTAAATCACCACGATCAAAAGGGACAAGCATCAAGCACGCAGCAATGCAGCTC 780
Sample 3       -CACCCTCTAAATCGCCATGATCAAAAGGAACAAGTATCAAGCACGCAGCAATGCAGCTC
                ************* *** ********** ***** ***********************

Sample 1       AAAACGCTTAGCCTAGCCACACCCCCACGGGAAACAGCAGTGATTAACCTTTAGCAATAA 840
Sample 3       AAAACGCTTAGCCTAGCCACACCCCCACGGGAGACAGCAGTGATAAACCTTTAGCAATAA
               ******************************** *********** ***************

Sample 1       ACGAAAGTTTAACTAAGCTATACTAACCCCAGGGTTGGTCAATTTCGTGCCAGCCACCGC 900
Sample 3       ACGAAAGTTTAACTAAGCCATACTAACCTCAGGGTTGGTCAATTTCGTGCTAGCCACCGC
               ***************** ********* ******************** *********

Sample 1       GGTCACACGATTAACCCAAGTCAATAGAAGCCGGCGTAAAGAGTGTTTTAGATCACCCCC 960
Sample 3       GGTCATACGATTAACCCAAGTCAATAGAAACCGGCGTAAAGAGTGTTTTAGATCACCCCC
               ***** ********************** ******************************

Sample 1       TCCCCAATAAAGCTAAAACTCACCTGAGTTGTAAAAAACTCCAGTTGACACAAAATAGAC 1020
Sample 3       CC----ATAAAGCTAAAATTCACCTGAGTTGTAAAAAACTCCAGCTGATACAAAATAAAC
                *    ************ ************************ *** ******** **

Sample 1       TACGAAAGTGGCTTTAACATATCTGAACACACAATAGCTAAGACCCAAACTGGGATTAGA 1080
Sample 3       TACGAAAGTGGCTTTAACACATCTGAATACACAATAGCTAAGACCCAAACTGGGATTAGA
               ****************** ******* ********************************

Sample 1       TACCCCACTATGCTTAGCCCTAAACCTCAACAGTTAAATCAACAAAACTGCTCGCCAGAA 1140
Sample 3       TACCCCACTATGCTTAGCCCTAAACTTCAACAGTTAAATTAACAAAACTGCTCGCCAGAA
               ************************ ************* ********************

Sample 1       CACTACGAGCCACAGCTTAAAACTCAAAGGACCTGGCGGTGCTTCATATCCCTCTAGAGG 1200
Sample 3       CACTACGAGCCACAGCTTAAAACTCAAAGGACCTGGCGGTGCTTCATATCCCTCTAGAGG
               ************************************************************

Sample 1       AGCCTGTTCTGTAATCGATAAACCCCGATCAACCTCACCACCTCTTGCTCAGCCTATATA 1260
Sample 3       AGCCTGTTCTGTAATCGATAAACCCCGATCAACCTCACCGCCTCTTGCTCAGCCTATATA
               ************************************ ********************

Sample 1       CCGCCATCTTCAGCAAACCCTGATGAAGGCTACAAAGTAAGCGCAAGTACCCACGTAAAG 1320
Sample 3       CCGCCATCTTCAGCAAACCCTGATGAAGGTTACAAAGTAAGCACAAGTACCCACGTAAAG
               ***************************** ************ *****************

Sample 1       ACGTTAGGTCAAGGTGTAGCCCATGAGGTGGCAAGAAATGGGCTACATTTTCTACCCCAG 1380
Sample 3       ACGTTAGGTCAAGGTGTAGCCTATGAGGTGGCAAGAAATGGGCTACATTTTCTACCCCAG
               ******************** ************************************

Sample 1       AAAACTACGATAGCCCTTATGAAACTTAAGGGTCGAAGGTGGATTTAGCAGTAAACTAAG 1440
Sample 3       AAAATTACGATAACCCTTATGAAACCTAAGGGTCAAAGGTGGATTTAGCAGTAAACTAAG
               **** ******* ************ ******** ************************

Sample 1       AGTAGAGTGCTTAGTTGAACAGGGCCCTGAAGCGCGTACACACCGCCCGTCACCCTCCTC 1500
Sample 3       AGTAGAGTGCTTAGTTGAACAGGGCCCTGAAGCGCGTACACACCGCCCGTCACCCTCCTC
               ************************************************************

Sample 1       AAGTATACTTCAAAGGACATTTAACTAAAACCCC-TACGCATTTATATAGAGGAGACAAG 1560
Sample 3       AAGTATACTTCAAAGGATACTTAACTTAAACCCCCTACGTATTTATATAGAGGAGATAAG
               ***************** * ****** ******* **** **************** ***

Sample 1       TCGTAACATGGTAAGTGTACTGGAAAGTGCACTTGGACGAACCAGAGTGTAGCTTAACAC 1620
Sample 3       TCGTAACATGGTAAGTGTACTGGAAAGTGCACTTGGACGAACCAGAGTGTAGCTTAACAT
               ************************************************************

Sample 1       AAAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTGAGCTAAACCT 1680
Sample 3       AAAGCACCCAACTTACACTTAGGAGATTTCAACTCAACTTGACCACTCTGAGCCAAACCT
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Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        AGCCCCAAACCCACTCCACCTTACTACCAGACAACCTTAGCCAAACCATTTACCCAAATA 1740
Sample 3        AGCCCCAAACCCCCTCCACCCTACTACCAAACAACCTTAACCAAACCATTTACCCAAATA
                ************ ******* ******** ********* ********************

Sample 1        AAGTATAGGCGATAGAAATTGAAACCTGGCGCAATAGATATAGTACCGCAAGGGAAAGAT 1800
Sample 3        AAGTATAGGCGATAGAAATTGTAAACCGGCGCAATAGACATAGTACCGCAAGGGAAAGAT
                ******************** ** * *********** ********************

Sample 1        GAAAAATTATAACCAAGCATAATATAGCAAGGACTAACCCCTATACCTTCTGCATAATGA 1860
Sample 3        GAAAAATTATACCCAAGCATAATACAGCAAGGACTAACCCCTGTACCTTTTGCATAATGA
                *********** ************ ***************** ****** **********

Sample 1        ATTAACTAGAAATAACTTTGCAAGGAGAGCCAAAGCTAAGACCCCCGAAACCAGACGAGC 1920
Sample 3        ATTAACTAGAAATAACTTTGCAAAGAGAACCAAAGCTAAGACCCCCGAAACCAGACGAGC
                ********************** **** ********************************

Sample 1        TACCTAAGAACAGCTAAAAGAGCACACCCGTCTATGTAGCAAAATAGTGGGAAGATTTAT 1980
Sample 3        TACCTAAGAACAGCTAAAAGAGCACACCCGTCTATGTAGCAAAATAGTGGGAAGATTTAT
                ************************************************************

Sample 1        AGGTAGAGGCGACAAACCTACCGAGCCTGGTGATAGCTGGTTGTCCAAGATAGAATCTTA 2040
Sample 3        AGGTAGAGGCGACAAACCTACCGAGCCTGGTGATAGCTGGTTGTCCAAGATAGAATCTTA
                ************************************************************

Sample 1        GTTCAACTTTAAATTTGCCCACAGAACCCTCTAAATCCCCTTGTAAATTTAACTGTTAGT 2100
Sample 3        GTTCAACTTTAAATTTACCTACAGAACCCTCTAAATCCCCTTGTAAACTTAACTGTTAGT
                *************** ** ************************* ************

Sample 1        CCAAAGAGGAACAGCTCTTTGGACACTAGGAAAAAACCTTGTAGAGAGAGTAAAAAATTT 2160
Sample 3        CCAAAGAGGAACAGCTCTTTAGACACTAGGAAAAAACCTTGTAAAGAGAGTAAAAAATTT
                ******************** ********************** ****************

Sample 1        AACACCCATAGTAGGCCTAAAAGCAGCCACCAATTAAGAAAGCGTTCAAGCTCAACACCC 2220
Sample 3        AACACCCATAGTAGGCCTAAAAGCAGCCACCAATTAAGAAAGCGTTCAAGCTCAACACCC
                ************************************************************

Sample 1        ACTACCTAAAAAATCCCAAACATATAACTGAACTCCTCACACCCAATTGGACCAATCTAT 2280
Sample 3        ACAACCTTAAAGATCCCAAACATACAACCGAACTCCTTACACCCAATTGGACCAATCTAT
                ** **** *** ************ *** ******** **********************

Sample 1        CACCCTATAGAAGAACTAATGTTAGTATAAGTAACATGAAAACATTCTCCTCCGCATAAG 2340
Sample 3        TACCCCATAGAAGAACTAATGTTAGTATAAGTAACATGAAAACATTCTCCTCCGCATAAG
                 **** ****************************************************

Sample 1        CCTGCGTCAGATTAAAACACTGAACTGACAATTAACAGCCCAATATCTACAATCAACCAA 2400
Sample 3        CCTACATCAGACCAAAATATTAAACTGACAATTAACAGCCTAATATCTACAATCAACCAA
                *** * *****  **** * * ****************** ******************

Sample 1        CAAGTCATTATTACCCTCACTGTCAACCCAACACAGGCATGCTCATAAGGAAAGGTTAAA 2460
Sample 3        CAAGCCATTATTACCCCCGCTGTTAACCCAACACAGGCATGCCCACAAGGAAAGGTTAAA
                **** *********** * **** ****************** ** **************

Sample 1        AAAAGTAAAAGGAACTCGGCAAATCTTACCCCGCCTGTTTACCAAAAACATCACCTCTAG 2520
Sample 3        AAAAGTAAAAGGAACTCGGCAAATCTTACCCCGCCTGTTTACCAAAAACATCACCTCTAG
                ************************************************************

Sample 1        CATCACCAGTATTAGAGGCACCGCCTGCCCAGTGACACATGTTTAACGGCCGCGGTACCC 2580
Sample 3        CATTACCAGTATTAGAGGCACCGCCTGCCCGGTGACATATGTTTAACGGCCGCGGTACCC
                *** ************************* ****** **********************

Sample 1        TAACCGTGCAAAGGTAGCATAATCACTTGTTCCTTAAATAGGGACCTGTATGAATGGCTC 2640
Sample 3        TAACCGTGCAAAGGTAGCATAATCACTTGTTCCTTAAATAGGGACTTGTATGAATGGCTC
                ******************************************* **************

Sample 1        CACGAGGGTTCAGCTGTCTCTTACTTTTAACCAGTGAAATTGACCTGCCCGTGAAGAGGC 2700
Sample 3        CACGAGGGTTTAGCTGTCTCTTACTTTCAACCAGTGAAATTGACCTACCCGTGAAGAGGC
                ********** *************** ****************** **************

Sample 1        GGGCATAACACAGCAAGACGAGAAGACCCTATGGAGCTTTAATTTATTAATGCAAACAGT 2760
Sample 3        GGGCATAACATAACAAGACGAGAAGACCCTATGGAGCTTTAATTCATTAATGCAAACAAT
                ********** * ****************************** ************* *
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Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        ACCTAACAAACCCACAGGTCCTAAACTACCAAACCTGCATTAAAAATTTCGGTTGGGGCG 2820
Sample 3        ACTTAACAAACCTACAGGTCCTAAACTATTAAACCTGCATTAAAAATTTCGGTTGGGGCG
                ** ********* ***************  ******************************

Sample 1        ACCTCGGAGCAGAACCCAACCTCCGAGCAGTACATGCTAAGACTTCACCAGTCAAAGCGA 2880
Sample 3        ACCTCGGAGCACAACCCAACCTCCGAGCAATACATGCTAAGACCTCACCAGTCAAAGCGA
                *********** ***************** ************* ****************

Sample 1        ACTACTATACTCAATTGATCCAATAACTTGACCAACGGAACAAGTTACCCTAGGGATAAC 2940
Sample 3        ATTACTACATCCAATTGATCCAATGACTTGACCAACGGAACAAGTTACCCTAGGGATAAC
                * ***** *  ************* ***********************************

Sample 1        AGCGCAATCCTATTCTAGAGTCCATATCAACAATAGGGTTTACGACCTCGATGTTGGATC 3000
Sample 3        AGCGCAATCCTATTCCAGAGTCCATATCAACAATAGGGTTTACGACCTCGATGTTGGATC
                *************** ******************************************

Sample 1        AGGACATCCCGATGGTGCAGCCGCTATTAAAGGTTCGTTTGTTCAACGATTAAAGTCCTA 3060
Sample 3        AGGACATCCCGATGGTGCAGCCGCTATTAAAGGTTCGTTTGTTCAACGATTAAAGTCCTA
                ************************************************************

Sample 1        CGTGATCTGAGTTCAGACCGGAGTAATCCAGGTCGGTTTCTATCTACCTTCAAATTCCTC 3120
Sample 3        CGTGATCTGAGTTCAGACCGGAGTAATCCAGGTCGGTTTCTATCTGT-TCTAAATTTCTC
                ******************************************   *  ***** ***

Sample 1        CCTGTACGAAAGGACAAGAGAAATAAGGCCTACTTCACAAAGCGCCTTCCCCCGTAAATG 3180
Sample 3        CCTGTACGAAAGGACAAGAGAAATGAGGCCTACTTCACAAAGCGCCTTCCCCAATAAATG
                ********************** *************************  ******

Sample 1        ATATCATCTCAACTTAGTATTATACCCACACCCACCCAAGAACAGGGTTTGTTAAGATGG 3240
Sample 3        ATATTATCTCAATTTAGCGCCATGCCAACACCCACTCAAGAACAGAGTTTGTTAAGATGG
                **** ******* ****    ** ** ******** ********* **************

Sample 1        CAGAGCCCGGTAATCGCATAAAACTTAAAACTTTACAGTCAGAGGTTCAATTCCTCTTCT 3300
Sample 3        CAGAGCCCGGTAATTGCATAAAACTTAAAACTTTACAATCAGAGGTTCAATTCCTCTTCT
                ************** ********************** **********************

Sample 1        TAACAACATACCCATGGCCAACCTCCTACTCCTCATTGTACCCATTCTAATCGCAATGGC 3360
Sample 3        TGACAACACACCCATGACCAACCTCCTACTCCTCATTGTACCCATCCTAATCGCAATAGC
                * ****** ******* *************************** *********** **

Sample 1        ATTCCTAATGCTTACCGAACGAAAAATTCTAGGCTATATACAACTACGCAAAGGCCCCAA 3420
Sample 3        ATTCCTAATGCTAACCGAACGAAAAATTCTAGGCTACATACAACTACGCAAAGGTCCCAA
                ************ ********************** ***************** *****

Sample 1        CGTTGTAGGCCCCTACGGGCTACTACAACCCTTCGCTGACGCCATAAAACTCTTCACCAA 3480
Sample 3        CATTGTAGGTCCTTACGGGCTATTACAGCCCTTCGCTGACGCCATAAAACTCTTCACTAA
                * ******* ** ********* **** ***************************** **

Sample 1        AGAGCCCCTAAAACCCGCCACATCTACCATCACCCTCTACATCACCGCCCCGACCTTAGC 3540
Sample 3        AGAACCCTTAAAACCCTCCACTTCAACCATTACCCTCTACATCACCGCCCCAACCCTAGC
                *** *** ******** **** ** ***** ******************** *** ****

Sample 1        TCTCACCATCGCTCTTCTACTATGAACCCCCCTCCCCATACCCAACCCCCTGGTCAACCT 3600
Sample 3        CCTCACCATTGCCCTCTTACTATGAACCCCCCTCCCCATACCCAACCCCCTAGTCAATCT
                 ******** ** **  ********************************** ***** **

Sample 1        CAACCTAGGCCTCCTATTTATTCTAGCCACCTCTAGCCTAGCCGTTTACTCAATCCTCTG 3660
Sample 3        TAACTTAGGCCTCCTATTTATTCTAGCCACCTCCAGCCTAGCCGTTTACTCAATCCTCTG
                 *** *************************** *************************

Sample 1        ATCAGGGTGAGCATCAAACTCAAACTACGCCCTGATCGGCGCACTGCGAGCAGTAGCCCA 3720
Sample 3        ATCAGGGTGAGCATCAAACTCGAACTACGCCTTAATCGGTGCACTACGAGCAGTAGCCCA
                ******************** ********* * ***** ***** **************

Sample 1        AACAATCTCATATGAAGTCACCCTAGCCATCATTCTACTATCAACATTACTAATAAGTGG 3780
Sample 3        AACAATCTCATACGAAGTCACTCTAGCCATTATCCTACTGTCAACGCTACTAATAAGTGG
                ************ ******** ******** ** ***** *****  **************

Sample 1        CTCCTTTAACCTCTCCACCCTTATCACAACACAAGAACACCTCTGATTACTCCTGCCATC 3840
Sample 3        CTCCTTCAATCTCTCTACCCTTGTCACAACACAAGAGCACCTCTGACTAATCCTGCCAAC
                ****** ** ***** ****** ************* ********* ** ******** *
```

Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        ATGACCCTTGGCCATAATATGATTTATCTCCACACTAGCAGAGACCAACCGAACCCCCTT 3900
Sample 3        ATGACCCCTGGCCATAATATGATTTATCTCTACACTAGCAGAGACCAACCGAACTCCCTT
                ******* ********************** ********************** *****

Sample 1        CGACCTTGCCGAAGGGGAGTCCGAACTAGTCTCAGGCTTCAACATCGAATACGCCGCAGG 3960
Sample 3        CGACCTTACTGAAGGAGAATCTGAACTAGTCTCAGGCTTTAATATCGAGTATGCCGCAGG
                ******* * ***** ** ** ***************** ** ***** ** ********

Sample 1        CCCCTTCGCCCTATTCTTCATAGCCGAATACACAAACATTATTATAATAAACACCCTCAC 4020
Sample 3        CCCCTTTGCCCTATTTTTCATAGCCGAATACATAAACATTATTATAATAAACACCCTCAC
                ****** ******** ********************** **************************

Sample 1        CACTACAATCTTCCTAGGAACAACATATGACGCACTCTCCCCTGAACTCTACACAACATA 4080
Sample 3        TGCTACAATCTTCCTAGGAGCAACATACAATACTCACTCCCCTGAACTCTACACGACATA
                ***************** *******  *  * * ****************** *****

Sample 1        TTTTGTCACCAAGACCCTACTTCTAACCTCCCTGTTCTTATGAATTCGAACAGCATACCC 4140
Sample 3        TTTTGTCACCAAAGCTCTACTTCTAACCTCCCTGTTCCTATGAATTCGAACAGCATATCC
                ************  * ******************** ****************** **

Sample 1        CCGATTCCGCTACGACCAACTCATACACCTCCTATGAAAAAACTTCCTACCACTCACCCT 4200
Sample 3        CCGATTTCGCTACGACCAGCTCATACACCTCCTATGAAAAAACTTCCTACCACTCACCCT
                ****** *********** ****************************************

Sample 1        AGCATTACTTATATGATATGTCTCCATACCCATTACAATCTCCAGCATTCCCCCTCAAAC 4260
Sample 3        AGCATCACTCATGTGATATATCTCCATACCCACTACAATCTCCAGCATCCCCCCTCAAAC
                ***** *** ** ****** ************ *************** ***********

Sample 1        CTAAGAAATATGTCTGATAAAAGAGTTACTTTGATAGAGTAAATAATAGGAGCTTAAACC 4320
Sample 3        CTAAGAAATATGTCTGATAAAAGAATTACTTTGATAGAGTAAATAATAGGAGTTCAAATC
                ************************ ************************** * *** *

Sample 1        CCCTTATTTCTAGGACTATGAGAATCGAACCCATCCCTGAGAATCCAAAATTCTCCGTGC 4380
Sample 3        CCCTTATTTCTAGGACTATAAGAATCGAACTCATCCCTGAGAATCCAAAATTCTCCGTGC
                ******************* ********** *****************************

Sample 1        CACCTATCACACCCCATCCTAAAGTAAGGTCAGCTAAATAAGCTATCGGGCCCATACCCC 4440
Sample 3        CACCTATCACACCCCATCCTAAAGTAAGGTCAGCTAAATAAGCTATCGGGCCCATACCCC
                ************************************************************

Sample 1        GAAAATGTTGGTTATACCCTTCCCGTACTAATTAATCCCCTGGCCCAACCCGTCATCTAC 4500
Sample 3        GAAAATGTTGGTTACACCCTTCCCGTACTAATTAATCCCCTAGCCCAACCCATCATCTAC
                ************** ************************* ********* ********

Sample 1        TCTACCATCTTTGCAGGCACACTCATCACAGCGCTAAGCTCGCACTGATTTTTTACCTGA 4560
Sample 3        TCTACCATCCTTACAGGCACGCTCATTACAGCGCTAAGCTCACACTGATTTTTCACCTGA
                ********* ** ******* ***** ************** ************ ******

Sample 1        GTAGGCCTAGAAATAAACATGCTAGCTTTTATTCCAGTTCTAACCAAAAAAATAAACCCT 4620
Sample 3        GTAGGCCTAGAAATAAATATACTAGCTTTTATCCCAATCCTAACCAAAAAAATAAGCCCC
                ***************** ** ************ *** * ***************** ***

Sample 1        CGTTCCACAGAAGCTGCCATCAAGTATTTCCTCACGCAAGCAACCGCATCCATAATCCTT 4680
Sample 3        CGCTCCACAGAAGCCGCCATCAAATACTTTCTCACACAAGCAACTGCGTCCATAATTCTC
                ** ************ ******** ** ** ***** ******** ** ******** **

Sample 1        CTAATAGCTATCCTCTTCAACAATATACTCTCCGGACAATGAACCATAACCAATACTACC 4740
Sample 3        CTGATAGCTATCCTCTCCAACAGCATACTCTCCGGACAATGAACCATAACCAATACTACC
                ** ************** *****  ************************************

Sample 1        AATCAATACTCATCATTAATAATCATAATAGCTATAGCAATAAAACTAGGAATAGCCCCC 4800
Sample 3        AATCAATACTCATCATTAATAATTATAATAGCAATGGCAATAAAACTAGGAATAGCCCCC
                ********************** ******** ** ************************

Sample 1        TTTCACTTCTGAGTCCCAGAGGTTACCCAAGGCACCCCTCTGACATCCGGCCTGCTTCTT 4860
Sample 3        TTTCACTTTTGAGTTCCAGAAGTTACCCAAGGCACCCCCCTAATATCCGGCCTACTCCTC
                ******** ***** ***** ***************** ** * ********* ** **

Sample 1        CTCACATGACAAAAACTAGCCCCCATCTCAATCATATACCAAATCTCTCCCTCACTAAAC 4920
Sample 3        CTCACATGACAAAAATTAGCCCCTATTTCAATTATATACCAAATCTCCTCATCACTGAAC
                *************** ******* ** ***** **************  * ***** ***
```

Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        GTAAGCCTTCTCCTCACTCTCTCAATCTTATCCATCATAGCAGGCAGTTGAGGTGGATTA 4980
Sample 3        GTAAACCTTCTCCTCACCCTTTCAATCTTGTCCATTATAGCAGGCAGCTGAGGCGGACTA
                **** ************ ** ******** ***** *********** ***** *** **

Sample 1        AACCAGACCCAGCTACGCAAAATCTTAGCATACTCCTCAATTACCCACATAGGATGAATA 5040
Sample 3        AACCAAACCCAACTACGCAAAATCCTAGCATACTCCTCAATCACCCACATAGGCTGAATA
                ***** ***** ************ *************** *********** ******

Sample 1        ATAGCAGTTCTACCGTACAACCCTAACATAACCATTCTTAATTTAACTATTTATATTATC 5100
Sample 3        ATAGCAGTCCTACCATATAACCCTAACATAACCATTCTTAATTTAACCATTTACATCATC
                ******** ***** ** ***************************** ***** ** ***

Sample 1        CTAACTACTACCGCATTCCTACTACTCAACTTAAACTCCAGCACCACGACCCTACTACTA 5160
Sample 3        CTAACTACTACCGCATTTCTGCTACTCAACTTAAACTCCAGCACCACAACCCTACTACTA
                ***************** ** ************************** ************

Sample 1        TCTCGCACCTGAAACAAGCTAACATGACTAACACCCTTAATTCCATCCACCCTCCTCTCC 5220
Sample 3        TCTCGCACCTGAAACAAGCTAACATGATTAACTCCCCTAATTCCATCCACCCTCCTCTCC
                ************************** **** *** **********************

Sample 1        CTAGGAGGCCTGCCCCCGCTAACCGGCTTTTTGCCCAAATGGGCCATTATCGAAGAATTC 5280
Sample 3        CTAGGAGGCCTACCCCCACTAACTGGCTTCTTACCCAAATGAGTTATCATCGAAGAATTC
                *********** ***** ***** ***** ** ******** *  ** ************

Sample 1        ACAAAAAACAATAGCCTCATCATCCCCACCATCATAGCCACCATCACCCTCCTTAACCTC 5340
Sample 3        ACAAAAAATAATAGCCTCATCATCCCCACCATCATAGCCATCATCACTCTCCTTAACCTC
                ******** ****************************** ****** ************

Sample 1        TACTTCTACCTACGCCTAATCTACTCCACCTCAATCACACTACTCCCCATATCTAACAAC 5400
Sample 3        TATTTCTACCTACGCCTAATCTACTCCACCTCAATTACACTACTTCCCATATCTAATAAC
                ** ******************************** ******** *********** ***

Sample 1        GTAAAAATAAAATGACAGTTTGAACATACAAAACCCACCCCATTCCTCCCCACACTCATC 5460
Sample 3        GTAAAAATAAAATGACAATTCGAACATACAAAACCCACCCCCTTCCTCCCTACACTCATC
                ***************** ** ******************** ******** *********

Sample 1        GCCCTTACCACGCTACTCCTACCTATCTCCCCTTTTATACTAATAATCTTATAGAAATTT 5520
Sample 3        ACCCTTACCACACTGCTTCTACCCATCTCCCCCTTCATACTAATAATCTTATAGAAATTT
                 ********** ** ** ***** ******** ** ************************

Sample 1        AGGTTAAATACAGACCAAGAGCCTTCAAAGCCCTCAGTAAGTTGCAATACTTAATTTCTG 5580
Sample 3        AGGTTAAGCACAGACCAAGAGCCTTCAAAGCCCTCAGCAAGTTACAATACTTAATTTCTG
                *******  **************************** ***** ****************

Sample 1        TAACAGCTAAGGACTGCAAAACCCCACTCTGCATCAACTGAACGCAAATCAGCCACTTTA 5640
Sample 3        CAACAACTAAGGACTGCAAAACCCCACTCTGCATCAACTGAACGCAAATCAGCCACTTTA
                 **** ****************************************************

Sample 1        ATTAAGCTAAGCCCTTACTAGACCAATGGGACTTAAACCCACAAACACTTAGTTAACAGC 5700
Sample 3        ATTAAGCTAAGCCCTTACTAGATTAATGGGACTTAAACCCACAAACATTTAGTTAACAGC
                **********************  ********************** ************

Sample 1        TAAGCACCCTAATCAACTGGCTTCAATCTACTTCTCCCGCCGCCGGGAAAAAAGGCGGGA 5760
Sample 3        TAAACACCCTAATCAACTGGCTTCAATCTACTTCTCCCGCCGCAAGAAAAAAAGGCGGGA
                *** ************************************  * **************

Sample 1        GAAGCCCCGGCAGGTTTGAAGCTGCTTCTTCGAATTTGCAATTCAATATGAAAATCACCT 5820
Sample 3        GAAGCCCCGGCAGGTTTGAAGCTGCTTCTTCGAATTTGCAATTCAATATGAAAATCACCT
                ************************************************************

Sample 1        CGGAGCTGGTAAAAAGAGGCCTAACCCCTGTCTTTAGATTTACAGTCCAATGCTTCACTC 5880
Sample 3        CAGAGCTGGTAAAAAGAGGCTTAACCCCTGTCTTTAGATTTACAGTCCAATGCTTCACTC
                * ****************** ***************************************

Sample 1        AGCCATTTTACCTCACCCCCACTGATGTTCGCCGACCGTTGACTATTCTCTACAAACCAC 5940
Sample 3        AGCCATTTTACCCCACCCT-ACTGATGTTCACCGACCGCTGACTATTCTCTACAAACCAC
                ************ *****  ********** ******* **********************

Sample 1        AAAGACATTGGAACACTATACCTATTATTCGGCGCATGAGCTGGAGTCCTAGGCACAGCT 6000
Sample 3        AAAGATATTGGAACACTATACCTACTATTCGGTGCATGAGCTGGAGTCCTGGGCACAGCC
                ***** ****************** ******* ***************** ********
```

Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        CTAAGCCTCCTTATTCGAGCCGAGCTGGGCCAGCCAGGCAACCTTCTAGGTAACGACCAC 6060
Sample 3        CTAAGTCTCCTTATTCGGGCTGAACTAGGCCAACCAGGCAACCTCCTAGGTAATGACCAC
                ***** ********** ** ** ** ***** ********** ******** ******

Sample 1        ATCTACAACGTTATCGTCACAGCCCATGCATTTGTAATAATCTTCTTCATAGTAATACCC 6120
Sample 3        ATCTACAATGTCATCGTCACAGCCCATGCATTCGTAATAATCTTCTTCATAGTAATGCCT
                ******** ** ****************** ********************** **

Sample 1        ATCATAATCGGAGGCTTTGGCAACTGACTAGTTCCCCTAATAATCGGTGCCCCCGATATG 6180
Sample 3        ATTATAATCGGAGGCTTTGGCAACTGGCTAGTTCCCTTGATAATTGGTGCCCCCGACATG
                ** ********************** ********* * ***** ********** ***

Sample 1        GCGTTTCCCCGCATAAACAACATAAGCTTCTGACTCTTACCTCCCTCTCTCCTACTCCTG 6240
Sample 3        GCATTCCCCCGCATAAACAACATAAGCTTCTGGCTCCTGCCCCCTTCTCTCCTACTTCTA
                ** ** ************************** *** * ** ** ********** **

Sample 1        CTCGCATCTGCTATAGTGGAGGCCGGAGCAGGAACAGGTTGAACAGTCTACCCTCCCTTA 6300
Sample 3        CTTGCATCTGCCATAGTAGAAGCCGGCGCGGGAACAGGTTGAACAGTCTACCCTCCCTTA
                ** ******** ***** ** ***** ** ******************************

Sample 1        GCAGGGAACTACTCCCACCCTGGAGCCTCCGTAGACCTAACCATCTTCTCCTTACACCTA 6360
Sample 3        GCGGGAAACTACTCGCATCCTGGAGCCTCCGTAGACCTAACCATCTTCTCCTTACATCTG
                ** ** ******** ** ************************************ **

Sample 1        GCAGGTGTCTCCTCTATCTTAGGGGCCATCAATTTCATCACAACAATTATCAATATAAAA 6420
Sample 3        GCAGGCATCTCCTCTATCCTAGGAGCCATTAACTTCATCACAACAATTATTAATATAAAA
                *****  ********** **** ***** ** ***************** *********

Sample 1        CCCCCTGCCATAACCCAATACCAAACGCCCCTCTTCGTCTGATCCGTCCTAATCACAGCA 6480
Sample 3        CCTCCTGCCATGACCCAATACCAAACACCCCTCTTCGTCTGATCCGTCCTAATCACAGCA
                ** ******** ************** ********************************

Sample 1        GTCCTACTTCTCCTATCTCTCCCAGTCCTAGCTGCTGGCATCACTATACTACTAACAGAC 6540
Sample 3        GTCTTACTTCTCCTATCCCTCCCAGTCCTAGCTGCTGGCATCACCATACTATTGACAGAT
                *** ************* ************************** ****** * *****

Sample 1        CGCAACCTCAACACCACCTTCTTCGACCCCGCCGGAGGAGGAGACCCCATTCTATACCAA 6600
Sample 3        CGTAACCTCAACACTACCTTCTTCGACCCAGCCGGGGGAGGAGACCCTATTCTATATCAA
                ** ************ ************** ***** ************ ******** ***

Sample 1        CACCTATTCTGATTTTTCGGTCACCCTGAAGTTTATATTCTTATCCTACCAGGCTTCGGA 6660
Sample 3        CACTTATTCTGATTTTTTGGCCACCCCGAAGTTTATATTCTTATCCTACCAGGCTTCGGA
                *** ************* ** ***** *********************************

Sample 1        ATAATCTCCCATATTGTAACTTACTACTCCGGAAAAAAAGAACCATTTGGATACATAGGT 6720
Sample 3        ATAATTTCCCACATTGTAACTTATTACTCCGGAAAAAAAGAACCATTTGGATATATAGGC
                ***** ***** ********** ***************************** *****

Sample 1        ATGGTCTGAGCTATGATATCAATTGGCTTCCTAGGGTTTATCGTGTGAGCACACCATATA 6780
Sample 3        ATGGTTTGAGCTATAATATCAATTGGCTTCCTAGGGTTTATCGTGTGAGCACACCATATA
                ***** ******** ********************************************

Sample 1        TTTACAGTAGGAATAGACGTAGACACACGAGCATATTTCACCTCCGCTACCATAATCATC 6840
Sample 3        TTTACAGTAGGGATAGACGTAGACACCCGAGCCTATTTCACCTCCGCTACCATAATCATT
                ********** ************** ***** *************************

Sample 1        GCTATCCCCACCGGCGTCAAAGTATTTAGCTGACTCGCCACACTCCACGGAAGCAATATG 6900
Sample 3        GCTATTCCTACCGGCGTCAAAGTATTCAGCTGACTCGCTACACTTCACGGAAGCAATATG
                ***** ** ***************** ********** ***** ***************

Sample 1        AAATGATCTGCTGCAGTGCTCTGAGCCCTAGGATTCATCTTTCTTTTCACCGTAGGTGGC 6960
Sample 3        AAATGATCTGCCGCAGTACTCTGAGCCCTAGGGTTTATCTTTCTCTTCACCGTAGGTGGC
                ********** ***** ************** ** ******** ***************

Sample 1        CTGACTGGCATTGTATTAGCAAACTCATCACTAGACATCGTACTACACGACACGTACTAC 7020
Sample 3        CTAACCGGCATTGTACTAGCAAACTCATCATTAGACATCGTGCTACACGACACATACTAC
                ** ** ********* ************** ********** ********** ******

Sample 1        GTTGTAGCCCACTTCCACTATGTCCTATCAATAGGAGCTGTATTTGCCATCATAGGAGGC 7080
Sample 3        GTCGTAGCCCACTTCCACTACGTTCTATCAATAGGAGCTGTATTCGCCATCATAGGAGGC
                ** ***************** ** ******************* ***************
```

Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        TTCATTCACTGATTTCCCCTATTCTCAGGCTACACCCTAGACCAAACCTACGCCAAAATC 7140
Sample 3        TTCATTCACTGATTCCCCCTATTCTCAGGCTATACCCTAGACCAAACCTATGCCAAAATC
                ************** ***************** ***************** *********

Sample 1        CATTTCACTATCATATTCATCGGCGTAAATCTAACTTTCTTCCCACAACACTTTCTCGGC 7200
Sample 3        CAATTTGCCATCATGTTCATTGGCGTAAACCTAACCTTCTTCCCACAGCACTTCCTTGGC
                ** **  * ***** ***** ******** ***** *********** ***** ** ***

Sample 1        CTATCCGGAATGCCCCGACGTTACTCGGACTACCCCGATGCATACACCACATGAAACATC 7260
Sample 3        CTATCTGGGATGCCCCGACGTTACTCGGACTACCCCGATGCATACACCACATGAAATGTC
                ***** ** ********************************************  **

Sample 1        CTATCATCTGTAGGCTCATTCATTTCTCTAACAGCAGTAATATTAATAATTTTCATGATT 7320
Sample 3        CTATCATCCGTAGGCTCATTTATCTCCCTGACAGCAGTAATATTAATAATTTTCATGATT
                ******** *********** ** ** ** ******************************

Sample 1        TGAGAAGCCTTCGCTTCGAAGCGAAAAGTCCTAATAGTAGAAGAACCCTCCATAAACCTG 7380
Sample 3        TGAGAAGCCTTTGCTTCAAAACGAAAAGTCCTAATAGTAGAAGAGCCCTCCGCAAACCTG
                *********** ***** ** ********************** ******  *******

Sample 1        GAGTGACTATATGGATGCCCCCCACCCTACCACACATTCGAAGAACCCGTATACATAAAA 7440
Sample 3        GAATGACTATATGGATGCCCCCCACCCTACCACACATTCGAAGAACCCGTATACATAAAA
                ** ********************************************************

Sample 1        TCTAGACAAAAAAGGAAGGAATCGAACCCCCCAAAGCTGGTTTCAAGCCAACCCCATGGC 7500
Sample 3        TCTAGACAAAAAAGGAAGGAATCGAACCCCCTAAAGCTGGTTTCAAGCCAACCCCATGAC
                ***************************** ************************* *

Sample 1        CTCCATGACTTTTTCAAAAAGGTATTAGAAAAACCATTTCATAACTTTGTCAAAGTTAAA 7560
Sample 3        CTCCATGACTTTTTCAAAAAGATATTAGAAAAACTATTTCATAACTTTGTCAAAGTTAAA
                ********************* ************ ************************

Sample 1        TTATAGGCTAAATCCTATATATCTTAATGGCACATGCAGCGCAAGTAGGTCTACAAGACG 7620
Sample 3        TTACAGGTTAACCCCCGTATATCTTAATGGCACATGCAGCGCAAGTAGGTCTACAAGATG
                *** *** ***  **  ****************************************** *

Sample 1        CTACTTCCCCTATCATAGAAGAGCTTATCACCTTTCATGATCACGCCCTCATAATCATTT 7680
Sample 3        CTACTTCCCCTATCATAGAAGAACTTATTATCTTTCACGACCATGCCCTCATAATTATCT
                ********************** ***** * ****** ** ** *********** ** *

Sample 1        TCCTTATCTGCTTCCTAGTCCTGTATGCCCTTTTCCTAACACTCACAACAAAACTAACTA 7740
Sample 3        TTCTCATCTGCTTTCTAGTCCTATACGCCCTTTTCCTAACACTCACAACAAAACTAACTA
                * ** ******** ******** ** **********************************

Sample 1        ATACTAACATCTCAGACGCTCAGGAAATAGAAACCGTCTGAACTATCCTGCCCGCCATCA 7800
Sample 3        ATACTAGTATTTCAGACGCCCAGGAAATAGAAACCGTCTGAACTATCCTGCCCGCCATCA
                ******  ** ******** ****************************************

Sample 1        TCCTAGTCCTCATCGCCCTCCCATCCCTACGCATCCTTTACATAACAGACGAGGTCAACG 7860
Sample 3        TCCTAGTCCTTATTGCCCTACCATCCCTGCGTATCCTTTACATAACAGACGAGGTCAACG
                ********** ** ***** ******** ** ****************************

Sample 1        ATCCCTCCCTTACCATCAAATCAATTGGCCACCAATGGTACTGAACCTACGAGTACACCG 7920
Sample 3        ACCCCTCCTTTACTATTAAATCAATCGGCCATCAATGATATTGAACCTACGAATACACCG
                * ****** **** ** ******** ***** ***** ** *********** *******

Sample 1        ACTACGGCGGACTAATCTTCAACTCCTACATACTTCCCCCATTATTCCTAGAACCAGGCG 7980
Sample 3        ACTACGGCGGGCTAATCTTCAACTCCTACATACTCCCCCCATTATTTCTAGAACCAGGTG
                ********** ********************** *********** *********** *

Sample 1        ACCTGCGACTCCTTGACGTTGACAATCGAGTAGTACTCCCGATTGAAGCCCCCATTCGTA 8040
Sample 3        ATCTACGACTCCTTGACGTTGATAACCGAGTGGTCCTCCCAGTTGAAGCCCCCGTTCGTA
                * ** ***************** ** ***** ** *****  *********** ******

Sample 1        TAATAATTACATCACAAGACGTCTTGCACTCATGAGCTGTCCCCACATTAGGCTTAAAAA 8100
Sample 3        TAATAATTACATCACAAGATGTTCTACACTCATGAGCTGTTCCCACATTAGGCCTAAAAA
                ******************* **  * ************** ************ ******

Sample 1        CAGATGCAATTCCCGGACGTCTAAACCAAACCACTTTCACCGCTACACGACCGGGGGTAT 8160
Sample 3        CAGACGCAATTCCCGGACGCCTAAACCAAACCACTTTCACCGCCACACGACCAGGAGTAT
                **** ************** ********************** ******** ** ****
```

Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        ACTACGGTCAATGCTCTGAAATCTGTGGAGCAAACCACAGTTTCATGCCCATCGTCCTAG 8220
Sample 3        ACTACGGCCAATGCTCAGAAATCTGTGGAGCAAACCACAGTTTTATACCCATCGTCCTAG
                ******* ******** ************************** ** *************

Sample 1        AATTAATTCCCCTAAAAATCTTTGAAATAGGGCCCGTATTTACCCTATAGCACCCCCTCT 8280
Sample 3        AATTAATCCCTCTAAAAATCTTTGAAATAGGACCCGTATTCACTCTATAGCACCTTCTCT
                ******* ** ******************** ******** ** **********  ****

Sample 1        ACCCC-CTCTAGAGCCCACTGTAAAGCTAACTTAGCATTAACCTTTTAAGTTAAAGATTA 8340
Sample 3        ACCCCTCTCCAGAGCTCACTGTAAAGCTAACCTAGCATTAACCTTTTAAGTTAAAGATTA
                ***** *** ***** *************** ****************************

Sample 1        AGAGAACCAACACCTCTTTACAGTGAAATGCCCCAACTAAATACTACCGTATGGCCCACC 8400
Sample 3        AGAGGACCGACACCTCTTTACAGTGAAATGCCCCAACTAAATACCGCCGTATGACCCACC
                **** *** ***********************************  ******* ******

Sample 1        ATAATTACCCCCATACTCCTTACACTATTCCTCATCACCCAACTAAAAATATTAAACACA 8460
Sample 3        ATAATTACCCCCATACTCCTGACACTATTTCTCGTCACCCAACTAAAAATATTAAATTCA
                ******************** ******** *** **********************  **

Sample 1        AACTACCACCTACCTCCCTCACCAAAGCCCATAAAAATAAAAAATTATAACAAACCCTGA 8520
Sample 3        AATTACCATCTACCCCCCTCACCAAAACCCATAAAAATAAAAAACTACAATAAACCCTGA
                ** ***** ***** *********** ***************** ** ** *********

Sample 1        GAACCAAAATGAACGAAAATCTGTTCGCTTCATTCATTGCCCCCACAATCCTAGGCCTAC 8580
Sample 3        GAACCAAAATGAACGAAAATCTATTCGCTTCATTCGCTGCCCCCACAATCCTAGGCTTAC
                ********************** ************  ****************** ***

Sample 1        CCGCCGCAGTACTGATCATTCTATTTCCCCCTCTATTGATCCCCACCTCCAAATATCTCA 8640
Sample 3        CCGCCGCAGTACTAATCATTCTATTCCCCCCTCTACTGGTCCCCACTTCTAAACATCTCA
                ************* *********** ********* ** ******* ** *** ******

Sample 1        TCAACAACCGACTAATCACCACCCAACAATGACTAATCAAACTAACCTCAAAACAAATGA 8700
Sample 3        TCAACAACCGACTAATTACCACCCAACAATGACTAATTCAACTGACCTCAAAACAAATAA
                **************** ********************  **** ************** *

Sample 1        TAACCATACACAACACTAAAGGACGAACCTGATCTCTTATACTAGTATCCTTAATCATTT 8760
Sample 3        TAACTATACACAGCACTAAAGGACGAACCTGATCTCTCATACTAGTATCCTTAATCATTT
                **** ******* ************************ **********************

Sample 1        TTATTGCCACAACTAACCTCCTCGGACTCCTGCCTCACTCATTTACACCAACCACCCAAC 8820
Sample 3        TTATTACCACAACCAATCTTCTTGGGCTTCTACCCCACTCATTCACACCAACCACCCAAC
                ***** ******* ** ** ** ** ** ** ** ******** ****************

Sample 1        TATCTATAAACCTAGCCATGGCCATCCCCTTATGAGCGGGCACAGTGATTATAGGCTTTC 8880
Sample 3        TATCTATAAACCTAGCCATGGCTATCCCCCTATGAGCAGGCGCAGTAGTCATAGGCTTTC
                ********************** ****** ******* *** ****  * **********

Sample 1        GCTCTAAGATTAAAAATGCCCTAGCCCACTTCTTACCACAAGGCACACCTACACCCCTTA 8940
Sample 3        GCTTTAAGACTAAAAATGCCCTAGCCCACTTCTTACCGCAAGGCACACCTACACCCCTTA
                *** ***** ************************** **********************

Sample 1        TCCCCATACTAGTTATTATCGAAACCATCAGCCTACTCATTCAACCAATAGCCCTGGCCG 9000
Sample 3        TCCCCATACTAGTTATCATCGAAACTATTAGCCTACTCATTCAACCAATAGCCTTAGCCG
                **************** ******** ** ************************ * ****

Sample 1        TACGCCTAACCGCTAACATTACTGCAGGCCACCTACTCATGCACCTAATTGGAAGCGCCA 9060
Sample 3        TACGTCTAACCGCTAACATTACTGCAGGCCACCTACTCATGCACCTAATTGGAAGCGCCA
                **** ****************************************************

Sample 1        CCCTAGCAATATCAACCATTAACCTTCCCTCTACACTTATCATCTTCACAATTCTAATTC 9120
Sample 3        CACTAGCATTATCAACTATCAATCTACCCTATGCACTCATTATCTTCACAATTCTAATCC
                * ****** ******* ** ** ** **** * **** ** ***************** *

Sample 1        TACTGACTATCCTAGAAATCGCTGTCGCCTTAATCCAAGCCTACGTTTTCACACTTCTAG 9180
Sample 3        TACTGACTATTCTAGAGATCGCCGTCGCCTTAATCCAAGCCTACGTTTTTACACTTCTAG
                ********** ***** ***** ************************** **********

Sample 1        TAAGCCTCTACCTGCACGACAACACATAATGACCCACCAATCACATGCCTATCATATAGT 9240
Sample 3        TGAGCCTCTACCTGCACGACAACACATAATGACCCACCAATCACATGCCTACCACATAGT
                * ********************************************** ** *****
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Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        AAAACCCAGCCCATGACCCCTAACAGGGGCCCTCTCAGCCCTCCTAATGACCTCCGGCCT 9300
Sample 3        AAAACCCAGCCCATGACCCCTAACAGGGGCCCTCTCGGCCCTCCTAATAACCTCCGGCCT
                ********************************** ********** **********

Sample 1        AGCCATGTGATTTCACTTCCACTCCATAACGCTCCTCATACTAGGCCTACTAACCAACAC 9360
Sample 3        GGCCATATGATTCCACTTCTACTCCACAACACTACTCACACTAGGCTTACTAACTAACAC
                 ***** ***** ****** ****** *** ** **** ******* ******* *****

Sample 1        ACTAACCATATACCAATGATGGCGCGATGTAACACGAGAAAGCACATACCAAGGCCACCA 9420
Sample 3        ATTGACCATATATCAATGATGACGCGATGTTATACGAGAAGGCACATACCAAGGCCACCA
                * * ******** ******** ******** * ******* ******************

Sample 1        CACACCACCTGTCCAAAAAGGCCTTCGATACGGGATAATCCTATTTATTACCTCAGAAGT 9480
Sample 3        CACACCACCCGTCCAAAAAGGTCTCCGATATGGGATAATTCTTTTTATTACCTCAGAAGT
                ********* ********** ** ***** ******** ** *****************

Sample 1        TTTTTTCTTCGCAGGATTTTTCTGAGCCTTTTACCACTCCAGCCTAGCCCCTACCCCCCA 9540
Sample 3        TTTTTTCTTTGCAGGATTTTTTTGAGCTTTCTACCACTCCAGCCTAGCCCCTACCCCCCA
                ********* ********** ***** ** ****************************

Sample 1        ATTAGGAGGGCACTGGCCCCCAACAGGCATCACCCCGCTAAATCCCCTAGAAGTCCCACT 9600
Sample 3        GCTAGGAGGACACTGGCCCCCAACAGGTATTACCCCACTAAATCCCCTAGAAGTCCCACT
                  ******* ***************** ** ***** **********************

Sample 1        CCTAAACACATCCGTATTACTCGCATCAGGAGTATCAATCACCTGAGCTCACCATAGTCT 9660
Sample 3        CCTAAACACATCTGTATTACTCGCATCAGGAGTATCAATTACTTGAGCCCATCACAGCTT
                ************ ************************* ** ***** ** ** **  *

Sample 1        AATAGAAAACAACCGAAACCAAATAATTCAAGCACTGCTTATTACAATTTTACTGGGTCT 9720
Sample 3        AATAGAAAATAACCGAAACCAAATAATTCAAGCACTGCTTATTACGATTCTACTAGGTCT
                ********* ********************************** *** **** *****

Sample 1        CTATTTTACCCTCCTACAAGCCTCAGAGTACTTCGAGTCTCCCTTCACCATTTCCGACGG 9780
Sample 3        TTATTTTACCCTCCTACAAGCCTCAGAATATTTCGAATCCCCTTTTACCATTTCCGATGG
                 ************************** ** ***** ** ** ** *********** **

Sample 1        CATCTACGGCTCAACATTTTTTGTAGCCACAGGCTTCCACGGACTTCACGTCATTATTGG 9840
Sample 3        CATCTACGGCTCAACATTCTTTGTAGCCACAGGCTTCCACGGACTCCACGTCATTATTGG
                ****************** ************************* **************

Sample 1        CTCAACTTTCCTCACTATCTGCTTCATCCGCCAACTAATATTTCACTTTACATCCAAACA 9900
Sample 3        ATCAACTTTCCTCACTATCTGCCTCATCCGCCAACTAATATTTCACTTCACATCCAAACA
                 ********************** ************************ ***********

Sample 1        TCACTTTGGCTTCGAAGCCGCCGCCTGATACTGGCATTTTGTAGATGTGGTTTGACTATT 9960
Sample 3        TCACTTCGGCTTTCAAGCCGCCGCCTGATACTGACACTTCGTAGATGTAGTCTGACTATT
                ****** *****  ******************* ** ** ******** ** ********

Sample 1        TCTGTATGTCTCCATCTATTGATGAGGGTCTTACTCTTTTAGTATAAATAGTACCGTTAA 10020
Sample 3        TCTATATGTCTCTATTTACTGATGAGGATCTTACTCTTTTAGTATAAGTAGTACCGTTAA
                *** ******** ** ** ******** ******************* ************

Sample 1        CTTCCAATTAACTAGTTTTGACAACATTCAAAAAAGAGTAATAAACTTCGCCTTAATTTT 10080
Sample 3        CTTCCAATTAACTAGTTTTGACAACATTCAAAAAAGAGTAATAAACTTCGTCCTAATTTT
                ************************************************ * *******

Sample 1        AATAATCAACACCCTCCTAGCCTTACTACTAATAATTATTACATTTTGACTACCACAACT 10140
Sample 3        AATAACCAATACCCTTCTAGCCCTACTACTGATAATTATCACATTCTGACTACCACAACT
                ***** *** ***** ****** ******* ******** ***** **************

Sample 1        CAACGGCTACATAGAAAAATCCACCCCTTACGAGTGCGGCTTCGACCCTATATCCCCCGC 10200
Sample 3        CAACAGCTACATAGAAAAATCTACCCCTTACGAATGTGGCTTCGACCCTATATCCCCCGC
                **** ***************** ********** ** **********************

Sample 1        CCGCGTCCCTTTCTCCATAAAATTCTTCTTAGTAGCTATTACCTTCTTATTATTTGATCT 10260
Sample 3        CCGCGTCCCCTTCTCCATAAAATTTTTCCTAGTAGCCATCACCTTCCTATTATTTGACCT
                ********* ************** *** ******* ** ****** ********** **

Sample 1        AGAAATTGCCCTCCTTTTACCCCTACCATGAGCCCTACAAACAACTAACCTGCCACTAAT 10320
Sample 3        AGAAATTGCCCTCCTATTGCCCTTACCTTGAGCCCTACAAACGGCCAACCTACCACTAAT
                *************** ** *** **** **************  * ***** ********
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Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        AGTTATGTCATCCCTCTTATTAATCATCATCCTAGCCCTAAGTCTGGCCTATGAGTGACT 10380
Sample 3        AGTCACATCATCCCTCTTATTAATTACTATCCTAGCCCTAAGCCTCGCCTACGAATGATT
                *** *  ***************** *  ************** ** ***** ** *** *

Sample 1        ACAAAAAGGATTAGACTGAACCGAATTGGTATATAGTTTAAACAAAACGAATGATTTCGA 10440
Sample 3        ACAAAAAGGGTTAGACTGAACCGAATTGGTATATAGTTTAAATAAAACGAATGATTTCGA
                ********* ******************************** *****************

Sample 1        CTCATTAAATTATGATAATCATATTTACCAAATGCCCCTCATTTACATAAATATTATACT 10500
Sample 3        CTCATTAAATTATGATAATCATATTTACCAAATGCCCCTTATTTATATAAATATTATACT
                ************************************* ***** **************

Sample 1        AGCATTTACCATCTCACTTCTAGGAATACTAGTATATCGCTCACACCTCATATCCTCCCT 10560
Sample 3        AGCATTTACCATCTCACTTCTAGGAATACTAGTATATCGCTCACACCTAATATCTTCCCT
                ********************************************** ***** *****

Sample 1        ACTATGCCTAGAAGGAATAATACTATCGCTGTTCATTATAGCTACTCTCATAACCCTCAA 10620
Sample 3        ACTATGCCTAGAAGGAATAATACTATCACTGTTCATCATAGCCACCCTCATAACCCTCAA
                ************************** ******** ***** ** **************

Sample 1        CACCCACTCCCTCTTAGCCAATATTGTGCCTATTGCCATACTAGTCTTTGCCGCCTGCGA 10680
Sample 3        TACTCACTCCCTCTTAGCCAATATTGTACCCATCACCATACTAGTCTTTGCTGCCTGCGA
                 ** ********************** ** **  ***************** ********

Sample 1        AGCAGCGGTGGGCCTAGCCCTACTAGTCTCAATCTCCAACACATATGGCCTAGACTACGT 10740
Sample 3        AGCAGCAGTAGGTCTAGCACTACTAGTTTCAATCTCTAACACATATGGCTTAGACTACGT
                ****** ** ** ***** ******** ******** ************ **********

Sample 1        ACATAACCTAAACCTACTCCAATGCTAAAACTAATCGTCCCAACAATTATATTACTACCA 10800
Sample 3        ACATAACCTAAACCTACTCCAATGCTAAAACTAATCATCCCGACAATTATATTACTACCA
                ********************************** **** ******************

Sample 1        CTGACATGACTTTCCAAAAAACACATAATTTGAATCAACACAACCACCCACAGCCTAATT 10860
Sample 3        CTAACATGATTCTCTAAAAAACGTATAATTTGAATCAACACAACCACTCACAGCCTAATT
                ** ****** * ** *******  ********************** ************

Sample 1        ATTAGCATCATCCCTCTACTATTTTTTAACCAAATCAACAACAACCTATTTAGCTGTTCC 10920
Sample 3        ATCAGCACCATTCCCTTACTATTTTTTAACCAAATTAACAACAACCTATTCAGCTGTTCC
                ** **** *** **  ****************** ************** *********

Sample 1        CCAACCTTTTCCTCCGACCCCCTAACAACCCCCCTCCTAATACTAACTACCTGACTCCTA 10980
Sample 3        CTGCCCTTCTCCTCCGACCCCTTAACAACTCCCCTCCTAATATTAACTGCTTGACTTCTA
                *   **** ************ ******* ************ ***** * ***** ***

Sample 1        CCCCTCACAATCATGGCAAGCCAACGCCACTTATCCAGTGAACCACTATCACGAAAAAAA 11040
Sample 3        CCCCTCACAATCATAGCAAGCCAGCGCCACCTATCCAACGAACCACTATCACGAAAAAAA
                ************** ******** ****** ******  **********************

Sample 1        CTCTACCTCTCTATACTAATCTCCCTACAAATCTCCTTAATTATAACATTCACAGCCACA 11100
Sample 3        CTCTACCTCTCCATGCTAATTTCCCTCCAAATCTCCTTAATTATAACATTCTCGGCCACA
                *********** ** ***** ***** ************************ * ******

Sample 1        GAACTAATCATATTTTATATCTTCTTCGAAACCACACTTATCCCCACCTTGGCTATCATC 11160
Sample 3        GAGCTAATTATATTTTATATCTTCTTCGAAACCACACTTATCCCCACCCTGGCTATCATC
                ** ***** ************************************** ***********  _

Sample 1        ACCCGATGAGGCAACCAGCCAGAACGCCTGAACGCAGGCACATACTTCCTATTCTACACC 11220
Sample 3        ACCCGATGGGGTAACCAACCAGAACGCCTGAACGCAGGTACATACTTCCTATTCTATACC
                ******** ** ***** ******************** ***************** ***

Sample 1        CTAGTAGGCTCCCTTCCCCTACTCATCGCACTAATTTACACTCACAACACCCTAGGCTCA 11280
Sample 3        CTAGTAGGCTCCCTCCCCCTACTCATCGCACTAATCTATACCCACAACACCCTAGGCTCA
                ************** ******************* ** ** ******************

Sample 1        CTAAACATTCTACTACTCACTCTCACTGCCCAAGAACTATCAAACTCCTGAGCCAATAAC 11340
Sample 3        CTAAATATCCTATTACTCACTCTTACAACCCAAGAACTATCAAACACCTGAGCCAACAAC
                ***** ** *** ********** **  ***************** ********** ***

Sample 1        TTAATATGACTAGCTTACACAATAGCTTTTATAGTAAAGATACCTCTTTACGGACTCCAC 11400
Sample 3        TTAATATGACTAGCGTACACGATGGCTTTCATGGTAAAAATACCCCTTTACGGACTCCAC
                ************** ***** ** ***** ** ***** ***** ***************
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Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        TTATGACTCCCTAAAGCCCATGTCGAAGCCCCCATCGCTGGGTCAATAGTACTTGCCGCA 11460
Sample 3        CTATGACTCCCTAAAGCCCATGTCGAAGCCCCTATTGCCGGGTCAATGGTACTTGCTGCA
                 ******************************** ** ** ******** ******** ***

Sample 1        GTACTCTTAAAACTAGGCGGCTATGGTATAATACGCCTCACACTCATTCTCAACCCCCTG 11520
Sample 3        GTACTCTTAAAATTAGGTGGCTATGGCATAATACGCCTCACACTCATCCTCAACCCCCTA
                ************ **** ******** ******************** ***********

Sample 1        ACAAAACACATAGCCTACCCCTTCCTTGTACTATCCCTATGAGGCATAATTATAACAAGC 11580
Sample 3        ACAAAACATATAGCCTATCCCTTCCTCATGTTGTCCTTATGAGGTATAATCATAACAAGC
                ******** ******** ********  *  * *** ******* ***** *********

Sample 1        TCCATCTGCCTACGACAAACAGACCTAAAATCGCTCATTGCATACTCTTCAATCAGCCAC 11640
Sample 3        TCCATCTGCCTGCGACAAACAGACCTAAAATCGCTCATTGCATACCCTTCAGTCAGCCAC
                *********** ********************************** ***** ********

Sample 1        ATAGCCCTCGTAGTAACAGCCATTCTCATCCAAACCCCCTGAAGCTTCACCGGCGCAGTC 11700
Sample 3        ATAGCCCTCGTAGTAACAGCCATTCTCATCCAAACCCCCTGAAGCTTCACCGGCGCAATT
                ********************************************************* *

Sample 1        ATTCTCATAATCGCCCACGGGCTTACATCCTCATTACTATTCTGCCTAGCAAACTCAAAC 11760
Sample 3        ATCCTCATAATCGCCCACGGACTTACATCCTCATTATTATCCTGCCTAGCAAACTCAAAT
                ** ***************** *************** *** ******************

Sample 1        TACGAACGCACTCACAGTCGCATCATAATCCTCTCTCAAGGACTTCAAACTCTACTCCCA 11820
Sample 3        TATGAACGCACCCACAGTCGCATCATAATTCTCTCCCAAGGACTTCAAACTCTACTCCCA
                ** ******** ***************** ***** ************************

Sample 1        CTAATAGCTTTTTGATGACTTCTAGCAAGCCTCGCTAACCTCGCCTTACCCCCCACTATT 11880
Sample 3        CTAATAGCCTTTTGATGACTCCTGGCAAGCCTCGCTAACCTCGCCCTACCCCCTACCATT
                ******** ************ ** ********************** ******* ** ***

Sample 1        AACCTACTGGGAGAACTCTCTGTGCTAGTAACCACGTTCTCCTGATCAAATATCACTCTC 11940
Sample 3        AATCTCCTAGGGGAACTCTCCGTGCTAGTAACCTCATTCTCCTGATCAAATACCACTCTC
                ** ** ** ** ******** ************ * ***************** *******

Sample 1        CTACTTACAGGACTCAACATACTAGTCACAGCCCTATACTCCCTCTACATATTTACCACA 12000
Sample 3        CTACTCACAGGATTCAACATACTAATCACAGCCCTGTACTCCCTCTACATGTTTACCACA
                ***** ****** *********** ********** ************** *********

Sample 1        ACACAATGGGGCTCACTCACCCACCACATTAACAACATAAAACCCTCATTCACACGAGAA 12060
Sample 3        ACACAATGAGGCTCACTCACCCACCACATTAATAGCATAAAGCCCTCATTCACACGAGAA
                ******** ********************** * ****** ******************

Sample 1        AACACCCTCATGTTCATACACCTATCCCCCATTCTCCTCCTATCCCTCAACCCCGACATC 12120
Sample 3        AACACTCTCATATTTTTACACCTATCCCCCATCCTCCTTCTATCCCTCAATCCTGATATC
                ***** ***** **  ***************** ***** *********** ** ** ***

Sample 1        ATTACCGGGTTTTCCTCTTGTAAATATAGTTTAACCAAAACATCAGATTGTGAATCTGAC 12180
Sample 3        ATCACTGGATTCACCTCCTGTAAATATAGTTTAACCAAAACATCAGATTGTGAATCTGAC
                ** ** ** **  **** ****************************************

Sample 1        AACAGAGGCTTACGACCCCTTATTTACCGAGAAAGCTCACAAGAACTGCTAACTCATGCC 12240
Sample 3        AACAGAGGCTCACGACCCCTTATTTACCGAGAAAGCTTATAAGAACTGCTAACTCGTATT
                ********** ************************* * *************** *

Sample 1        CCCATGTCTAACAACATGGCTTTCTCAACTTTTAAAGGATAACAGCTATCCATTGGTCTT 12300
Sample 3        CCCATGCCTAACAACATGGCTTTCTCAACTTTTAAAGGATAACAGTTATCCATTGGTCTT
                ****** ************************************* **************

Sample 1        AGGCCCCAAAAATTTTGGTGCAACTCCAAATAAAAGTAATAACCATGCACACTACTATAA 12360
Sample 3        AGGCCCCAAAAATTTTGGTGCAACTCCAAATAAAAGTAATAACCATGTATGCTACCATAA
                ********************************************* *  **** ****

Sample 1        CCACCCTAACCCTGACTTCCCTAATTCCCCCCATCCTTACCACCCTCGTTAACCCTAACA 12420
Sample 3        CCACCTTAGCCCTAACTTCCTTAATTCCCCCCATCCTCGGCGCCCTCATTAACCCTAACA
                ***** ** **** ****** ****************   * ***** ************

Sample 1        AAAAAAACTCATACCCCCATTATGTAAAATCCATTGTCGCATCCACCTTTATTATCAGTC 12480
Sample 3        AAAAAAACTCATACCCCCATTACGTGAAATCCATTATCGCATCCACCTTTATCATTAGCC
                ********************** ** ********* *************** ** ** *
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Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        TCTTCCCCACAACAATATTCATGTGCCTAGACCAAGAAGTTATTATCTCGAACTGACACT 12540
Sample 3        TTTTCCCCACAACAATATTCATATGCCTAGACCAAGAAACTATTATCTCGAACTGACACT
                * ******************** ***************  ********************

Sample 1        GAGCCACAACCCAAACAACCCAGCTCTCCCTAAGCTTCAAACTAGACTACTTCTCCATAA 12600
Sample 3        GAGCAACAACCCAAACAACCCAACTCTCCCTGAGCTTTAAACTAGACTATTTCTCCATAA
                **** ***************** ******** ***** *********** **********

Sample 1        TATTCATCCCTGTAGCATTGTTCGTTACATGGTCCATCATAGAATTCTCACTGTGATATA 12660
Sample 3        CATTTATCCCCGTAGCACTGTTCGTTACATGATCCATCATAGAATTCTCACTATGATATA
                 *** ***** ****** ************* ******************** *******

Sample 1        TAAACTCAGACCCAAACATTAATCAGTTCTTCAAATATCTACTCATCTTCCTAATTACCA 12720
Sample 3        TAGACTCAGACCCCAACATCAACCAATTCTTCAAATACTTACTTATCTTCCTAATTACTA
                ** ********** ***** ** ** ***********  **** ************** *

Sample 1        TACTAATCTTAGTTACCGCTAACAACCTATTCCAACTGTTCATCGGCTGAGAGGGCGTAG 12780
Sample 3        TACTAATCCTAGTCACCGCTAACAACCTATTCCAACTCTTCATCGGCTGAGAAGGCGTAG
                ******** **** ********************** ************** *******

Sample 1        GAATTATATCCTTCTTGCTCATCAGTTGATGATACGCCCGAGCAGATGCCAACACAGCAG 12840
Sample 3        GAATTATATCCTTTCTACTCATTAGCTGATGGTACGCCCGAACAGATGCCAACACAGCAG
                *************  * ***** ** ***** ********* ******************

Sample 1        CCATTCAAGCAATCCTATACAACCGTATCGGCGATATCGGTTTCATCCTCGCCTTAGCAT 12900
Sample 3        CCATCCAAGCAATCCTATATAACCGTATCGGTGATATTGGTTTTGTCCTAGCCCTAGCAT
                **** ************** ************ ***** *****  **** *** ******

Sample 1        GATTTATCCTACACTCCAACTCATGAGACCCACAACAAATAGCCCTTCTAAACGCTAATC 12960
Sample 3        GATTTCTCCTACACTCCAACTCATGAGATCCACAACAAATAATCCTCCTAAGTACTAATA
                ***** ********************** ************  *** ****   *****

Sample 1        CAAGCCTCACCCCACTACTAGGCCTCCTCCTAGCAGCAGCAGGCAAATCAGCCCAATTAG 13020
Sample 3        CAGACCTTACTCCACTACTAGGCTTCCTCCTAGCAGCAGCAGGCAAATCAGCTCAACTAG
                **  *** ** ************ ***************************** *** ***

Sample 1        GTCTCCACCCCTGACTCCCCTCAGCCATAGAAGGCCCCACCCCAGTCTCAGCCCTACTCC 13080
Sample 3        GCCTTCACCCCTGACTCCCCTCAGCCATAGAAGGCCCTACCCCTGTTTCAGCCCTACTCC
                * ** ******************************** ***** ** *************

Sample 1        ACTCAAGCACTATAGTTGTAGCAGGAATCTTCTTACTCATCCGCTTCCACCCCCTAGCAG 13140
Sample 3        ACTCAAGCACCATAGTCGTAGCAGGAATCTTCCTACTCATCCGCTTCTACCCCCTAGCAG
                ********** ***** *************** ************** ************

Sample 1        AAAATAGCCCACTAATCCAAACTCTAACACTATGCTTAGGCGCTATCACCACTCTGTTCG 13200
Sample 3        AGAATAACCCACTAATCCAAACTCTCACGCTATGCCTAGGCGCTATCACCACCCTATTCG
                * **** ****************** ** ****** *************** ** ****

Sample 1        CAGCAGTCTGCGCCCTTACACAAAATGACATCAAAAAAATCGTAGCCTTCTCCACTTCAA 13260
Sample 3        CAGCAGTCTGCGCCCTCACACAAAATGACATCAAAAAAATCGTGGCCTTCTCCACTTCAA
                *************** ************************** ****************

Sample 1        GTCAACTAGGACTCATAATAGTTACAATCGGCATCAACCAACCACACCTAGCATTCCTGC 13320
Sample 3        GCCAACTAGGACTCATAATAGTTACAATCGGTATCAACCAACCACACCTAGCATTCCTTC
                * ***************************** ************************* *

Sample 1        ACATCTGTACCCACGCCTTCTTCAAAGCCATACTATTTATGTGCTCCGGGTCCATCATCC 13380
Sample 3        ACATCTGCACCCACGCTTTCTTCAAAGCCATACTATTCATATGCTCCGGATCCATTATTC
                ******* ******** ******************** ** ******** ***** ** *

Sample 1        ACAACCTTAACAATGAACAAGATATTCGAAAAATAGGAGGACTACTCAAAACCATACCTC 13440
Sample 3        ACAACCTCAATAATGAGCAAGACATTCGAAAAATAGGAGGATTACTCAAAACCATACCCC
                ******* ** ***** ***** ***************** *************** *

Sample 1        TCACTTCAACCTCCCTCACCATTGGCAGCCTAGCATTAGCAGGAATACCTTTCCTCACAG 13500
Sample 3        TCACTTCAACCTCCCTCACCATTGGGAGCCTAGCATTAGCAGGAATACCCTTCCTCACAG
                ************************ ********************** **********

Sample 1        GTTTCTACTCCAAAGACCACATCATCGAAACCGCAAACATATCATACACAAACGCCTGAG 13560
Sample 3        GTTTCTACTCCAAAGACCTCATCATCGAAACCGCTAACATATCATACACAAACGCCTGAG
                ***************** *************** ************************
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Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        CCCTATCTATTACTCTCATCGCTACCTCCCTGACAAGCGCCTATAGCACTCGAATAATTC 13620
Sample 3        CCCTATCTATTACTCTCATCGCCACCTCTCTGACAAGCGCCTACAGCACCCGAATAATCC
                ********************** ***** ************** ***** ******** *

Sample 1        TTCTCACCCTAACAGGTCAACCTCGCTTCCCCACCCTTACTAACATTAACGAAAATAACC 13680
Sample 3        TCCTCACCCTAACAGGTCAACCTCGCTTCCCAACCCTCACCAACATTAACGAAAACAACC
                * ***************************** ***** ** ************** ****

Sample 1        CCACCCTACTAAACCCCATTAAACGCCTGGCAGCCGGAAGCCTATTCGCAGGATTTCTCA 13740
Sample 3        CCACTCTGTTAAATCCCATTAAACGCCTAACCATTGGAAGCTTATTTGCAGGATTTCTCA
                **** **  **** **************  *    ****** **** *************

Sample 1        TTACTAACAACATTTCCCCCGCATCCCCCTTCCAAACAACAATCCCCCTCTACCTAAAAC 13800
Sample 3        TTACCAACAACATTCTCCCCATATCTACTCCCCAAGTGACAATTCCCCTTTACTTAAAAC
                **** *********  ****  ***  *   ****   ***** ***** *** ******

Sample 1        TCACAGCCCTCGCTGTCACTTTCCTAGGACTTCTAACAGCCCTAGACCTCAACTACCTAA 13860
Sample 3        TTACAGCCCTAGGCGTTACTTCCCTAGGACTTCTAACAGCCCTAGACCTCAATTACCTAA
                * ******** *  ** **** ****************************** *******

Sample 1        CCAACAAACTTAAAATAAAATCCCCACTATGCACATTTTATTTCTCCAACATACTCGGAT 13920
Sample 3        CCAGCAAGCTCAAAATAAAATCCCCACTATATACATTTCACTTCTCTAATATACTCGGAT
                *** *** ** ******************  ****** * ***** ** **********

Sample 1        TCTACCCTAGCATCACACACCGCACAATCCCCTATCTAGGCCTTCTTACGAGCCAAAACC 13980
Sample 3        TCTACCCTAACATTATACACCGCTCGATCCCCTATCTAGGCCTTCTTACAAGCCAAAACC
                ********* *** * ******* * ********************** **********

Sample 1        TGCCCCTACTCCTCCTAGACCTAACCTGACTAGAAAAGCTATTACCTAAAACAATTTCAC 14040
Sample 3        TACCCCTACTTCTTCTAGACCTGACCTGACTAGAGAAACTATTACCTAAAACAATTTCAC
                * ******** ** ******** ********** ** **********************

Sample 1        AGCACCAAATCTCCACCTCCATCATCACCTCAACCCAAAAAGGCATAATTAAACTTTACT 14100
Sample 3        AGTACCAAATCTCCGCTTCCATTACCACCTCAACCCAAAAAGGCATGATCAAACTTTATT
                ** *********** * ***** * ********************** ** ******** *

Sample 1        TCCTCTCTTTCTTCTTCCCACTCATCCTAACCCTACTCCTAATCACATAACCTATTCCCC 14160
Sample 3        TCCTCTCTTTTTTCTTCCCTCTCATCTTAACCTTACTCCTAATCACATAACCTATTCCCC
                ********** ******** ****** ***** **************************

Sample 1        CGAGCAATCTCAATTACAATATATACACCAACAAACAATGTTCAACCAGTAACTACTACT 14220
Sample 3        CGAGCAATCTCAATCACAATGTATACACCAACAAACAATGTCCAACCAGTAACTACTACT
                ************** ***** ******************** ******************

Sample 1        AATCAACGCCCATAATCATACAAAGCCCCCGCACCAATAGGATCCTCCCGAATCAACCCT 14280
Sample 3        AACCAACGCCCATAATCATATAAGGCCCCCGCACCAATAGGATCCTCCCGAATCAGCCCT
                ** ***************** ** ******************************** ****

Sample 1        GACCCCTCTCCTTCATAAATTATTCAGCTTCCTACACTATTAAAGTTTACCACAACCACC 14340
Sample 3        GGCCCCTCCCCTTCATAAATTATTCAACTTCCCACGCTATTAAAATTTACCACAACCACC
                * ****** ***************** ***** ** ******** ***************

Sample 1        ACCCCATCATACTCTTTCACCCACAGCACCAATCCTACCTCCATCGCTAACCCCACTAAA 14400
Sample 3        ATCCCATCATACCCTTTTACCCATAACACTAATCCTACCTCCATCGCCAGTCCTACTAAA
                * ********** **** ***** * *** ***************** *  ** ******

Sample 1        ACACTCACCAAGACCTCAACCCCTGACCCCCATGCCTCAGGATACTCCTCAATAGCCATC 14460
Sample 3        ACACTAACCAAAACCTCAACCCCTGACCCCCATGCCTCAGGATACTCCTCAATAGCCATA
                ***** ***** ********************************************

Sample 1        GCTGTAGTATATCCAAAGACAACCATCATTCCCCCTAAATAAATTAAAAAAACTATTAAA 14520
Sample 3        GCCGTAGTATACCCAAAAACAACCATTATTCCCCCCAAATAAATTAAAAAAACCATTAAA
                ** ******** ***** ******** ******** ***************** ******

Sample 1        CCCATATAACCTCCCCCAAAATTCAGAATAATAACACACCCGACCACACCGCTAACAATC 14580
Sample 3        CCTATATAACCTCCCCCATAATTCAAAATGATGGCACACCCAACTACACCACTAACAATC
                ** *************** ****** *** **  ******* ** ***** *********

Sample 1        AATACTAAACCCCCATAAATAGGAGAAGGCTTAGAAGAAAACCCCACAAACCCCATTACT 14640
Sample 3        AATACTAAACCCCCATAAATGGGAGAAGGCTTAGAAGAAAACCCCACAAACCCTATCACT
                ******************** ******************************** ** ***
```

Comparison of DNA from Sample 1 and Sample 3 (Please don't write on this page)

```
Sample 1        AAACCCACACTCAACAGAAACAAAGCATACATCATTATTCTCGCACGGACTACAACCACG 14700
Sample 3        AAACTCACACTCAATAAAAATAAAGCATATGTCATTATTCTCGCACGGACTACAACCACG
                **** ********* * *** ********  ****************************

Sample 1        ACCAATGATATGAAAAACCATCGTTGTATTTCAACTACAAGAACACCAATGACCCCAATA 14760
Sample 3        ACCAATGATATGAAAAACCATCGTTGTATTTCAACTACAAGAACACCAATGACCCCGACA
                ********************************************************* * *

Sample 1        CGCAAAATTAACCCCCTAATAAAATTAATTAACCACTCATTCATCGACCTCCCCACCCCA 14820
Sample 3        CGCAAAATTAACCCACTAATAAAATTAATTAATCACTCATTTATCGACCTCCCCACCCCA
                ************** ***************** ******** ******************

Sample 1        TCCAACATCTCCGCATGATGAAACTTCGGCTCACTCCTTGGCGCCTGCCTGATCCTCCAA 14880
Sample 3        TCCAACATTTCCGCATGATGGAACTTCGGCTCACTTCTCGGCGCCTGCCTAATCCTTCAA
                ******** *********** ************** ** *********** ***** ***

Sample 1        ATCACCACAGGACTATTCCTAGCCATGCACTACTCACCAGACGCCTCAACCGCCTTTTCA 14940
Sample 3        ATTACCACAGGATTATTCCTAGCTATACACTACTCACCAGACGCCTCAACCGCCTTCTCG
                ** ********* ********** ** ***************************** **

Sample 1        TCAATCGCCCACATCACTCGAGACGTAAATTATGGCTGAATCATCCGCTACCTTCACGCC 15000
Sample 3        TCGATCGCCCACATCACCCGAGACGTAAACTATGGTTGGATCATCCGCTACCTCCACGCT
                ** ************** *********** ***** ** ************** *****

Sample 1        AATGGCGCCTCAATATTCTTTATCTGCCTCTTCCTACACATCGGGCGAGGCCTATATTAC 15060
Sample 3        AACGGCGCCTCAATATTTTTTATCTGCCTCTTCCTACACATCGGCCGAGGTCTATATTAC
                ** ************** ************************* ***** *********

Sample 1        GGATCATTTCTCTACTCAGAAACCTGAAACATCGGCATTATCCTCCTGCTTGCAACTATA 15120
Sample 3        GGCTCATTTCTCTACCTAGAAACCTGAAACATTGGCATTATCCTCTTGCTCACAACCATA
                ** ************  *************** ************ ****  **** ***

Sample 1        GCAACAGCCTTCATAGGCTATGTCCTCCCGTGAGGCCAAATATCATTCTGAGGGGCCACA 15180
Sample 3        GCAACAGCCTTTATGGGCTATGTCCTCCCATGAGGCCAAATATCCTTCTGAGGAGCCACA
                *********** ** ************** ************** ******** ******

Sample 1        GTAATTACAAACTTACTATCCGCCATCCCATACATTGGGACAGACCTAGTTCAATGAATC 15240
Sample 3        GTAATTACAAACCTACTGTCCGCTATCCCATACATCGGAACAGACCTGGTCCAGTGAGTC
                ************ **** ***** *********** ** ******** ** ** *** **

Sample 1        TGAGGAGGCTACTCAGTAGACAGTCCCACCCTCACACGATTCTTTACCTTTCACTTCATC 15300
Sample 3        TGAGGAGGCTACTCAGTAGACAGCCCTACCCTTACACGATTCTTCACCTTCCACTTTATC
                ********************** ** ***** *********** ***** ***** ***

Sample 1        TTGCCCTTCATTATTGCAGCCCTAGCAACACTCCACCTCCTATTCTTGCACGAAACGGGA 15360
Sample 3        TTACCCTTCATCATCACAGCCCTAACAACACTTCATCTCCTATTCTTACACGAAACAGGA
                ** ******** **  ******** ******* ** *********** ******** ***

Sample 1        TCAAACAACCCCCTAGGAATCACCTCCCATTCCGATAAAATCACCTTCCACCCTTACTAC 15420
Sample 3        TCAAATAACCCCCTAGGAATCACCTCCCACTCCGACAAAATTACCTTCCACCCCTACTAC
                ***** ********************** ***** ***** *********** ******

Sample 1        TTCTCACCAGACCTCCTAGGCGACCCAGACAATTATACCCTAGCCAACCCCTTAAACACC 15540
Sample 3        TTCTCACCAGGCCTCCTAGGCGATCCAGACAACTATACCCTAGCTAACCCCCTAAACACC
                ********** ************ ******** *********** ****** ********

Sample 1        CCTCCCCACATCAAGCCCGAATGATATTTCCTATTCGCCTACACAATTCTCCGATCCGTC 15600
Sample 3        CCACCCCACATTAAACCCGAGTGATACTTTCTATTTGCCTACACAATCCTCCGATCCATC
                ** ******** ** ***** ***** ** ***** *********** ********* **

Sample 1        CCTAACAAACTAGGAGGCGTCCTTGCCCTATTACTATCCATCCTCATCCTAGCAATAATC 15660
Sample 3        CCCAACAAACTAGGAGGCGTCCTCGCCCTACTACTATCTATCCTAATCCTAACAGCAATC
                ** ******************** ****** ******* ***** ****** **  ****

Sample 1        CCCATCCTCCATATATCCAAACAACAAAGCATAATATTTCGCCCACTAAGCCAATCACTT 15720
Sample 3        CCTGTCCTCCACACATCCAAACAACAAAGCATAATATTTCGCCCACTAAGCCAACTGCTT
                **  ******* * ****************************************   ***

Sample 1        TATTGACTCCTAGCCGCAGACCTCCTCATTCTAACCTGAATCGGAGGACAACCAGTAAGC 15780
Sample 3        TACTGACTCCTAGCCACAGACCTCCTCATCCTAACCTGAATCGGAGGACAACCAGTAAGC
                ** ************ ************* ****************************
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Research Project - Poster or Brochure

Student Name: _____

CATEGORY	4	3	2	1
Required Elements	The poster or brochure includes all required elements as well as additional information.	All required elements are included on the poster or brochure.	All but 1 of the required elements are included on the poster or brochure.	Several required elements were missing.
Knowledge Gained	Student can accurately answer all questions related to facts in the poster or brochure and processes used to create the poster or brochure.	Student can accurately answer most questions related to facts in the poster or brochure and processes used to create the poster or brochure.	Student can accurately answer about 75% of questions related to facts in the poster or brochure and processes used to create the poster or brochure.	Student appears to have insufficient knowledge about the facts or processes used in the poster or brochure.
Content - Accuracy	All or almost all of the facts are accurate.	Most of the facts are accurate.	Some of the facts are accurate.	Few of the facts are accurate.
Citations	3 new sources, not including the source(s) given are used and cited	2 new sources, not including the source(s) given are used and cited	1 new sources, not including the source(s) given are used and cited	only the source(s) given are used and cited
Attractiveness	The poster or brochure is exceptionally attractive in terms of design, layout, and neatness.	The poster or brochure is attractive in terms of design, layout and neatness.	The poster or brochure is acceptably attractive though it may be a bit messy.	The poster or brochure is distractingly messy or very poorly designed. It is not attractive.
Graphics -Clarity	Graphics are all in focus and the content easily viewed and identified.	Most graphics are in focus and the content easily viewed and identified.	Most graphics are in focus and the content is easily viewed and identified.	Many graphics are not clear or are too small.
Graphics - Relevance	All graphics are related to the topic and make it easier to understand. All borrowed graphics have a source citation.	All graphics are related to the topic and most make it easier to understand. All borrowed graphics have a source citation.	All graphics relate to the topic. Most borrowed graphics have a source citation.	Graphics do not relate to the topic OR several borrowed graphics do not have a source citation.
Labels	All items of importance on the poster or brochure are clearly labeled with labels that can be read.	Almost all items of importance on the poster or brochure are clearly labeled with labels that can be read.	Several items of importance on the poster or brochure are clearly labeled with labels that can be read.	Labels are too small to view OR no important items were labeled.

Name _____

Class _____

Teacher _____

Posttest

1. Which one of the following molecules carries out all the work of a cell?

   a. RNA
   b. DNA
   c. Protein
   d. Amino acids

2. Are the cells in your skin different from the cells in your liver?

a. Yes, the cells in my skin have genes that my liver cells don't have.
b. Yes, the cells in my skin turn on genes that my liver cells don't turn on.
c. No, the cells in my skin are the same as the cells in my liver.
d. Both a and b

3. DNA can be compared to a language in which "letters" are arranged in a specific sequence, that provides a specific meaning. How many "letters" are there in the DNA code?

   a. 2
   b. 26
   c. 4
   d. 20

4. List 4 types of cellular activities that are carried out by proteins.

   1. _____
   2. _____
   3. _____
   4. _____

5. Below are parts of an mRNA molecule from four individuals. Person A has the sequence found in most healthy people.

Person A: AUGUUCCAAACUACCGGAAUU (healthy person)
Person B: AUGUUCCAAUCUACCGGAAUU
Person C: AUGUUCCGGCCUACCGGAAUU
Person D: AUGUUCCAAAACUACCGGAAUU

Amino acid sequence for Person A: M F Q T T G I

For Person B, C, and D, put an X where the amino acids will be **DIFFERENT** from person A:

Person B __ __ __ __ __ __ __
Person C __ __ __ __ __ __ __
Person D __ __ __ __ __ __ __

If the gene sequence in Person A is important for a proper functioning heart, which person (Person B, C or D) is MOST likely to have heart problems? _____

Explain why the person you chose is most likely to have heart problems:

_____

_____

_____

6. Which of the follwowing has items ordered from largest to smallest?

a. Human, fly, cell, protein, amino acid
b. Human, cell, fly, protein, amino acid
c. Human, cell, amino acid, protein, fly
d. Human, fly, cell, amino acid, protein

7. What do the A, T, G and C in DNA represent?

a. Different genes
b. Different amino acids
c. Different sugars
d. Different bases

8. Scientists have been studying a particular protein that helps to break down fat. These scientists have found that some people have a larger than normal protein. Which of the following is NOT a likely explanation for why the protein is larger than normal?

a. Extra DNA bases exist

b. Extra RNA bases exist

c. Extra amino acids exist

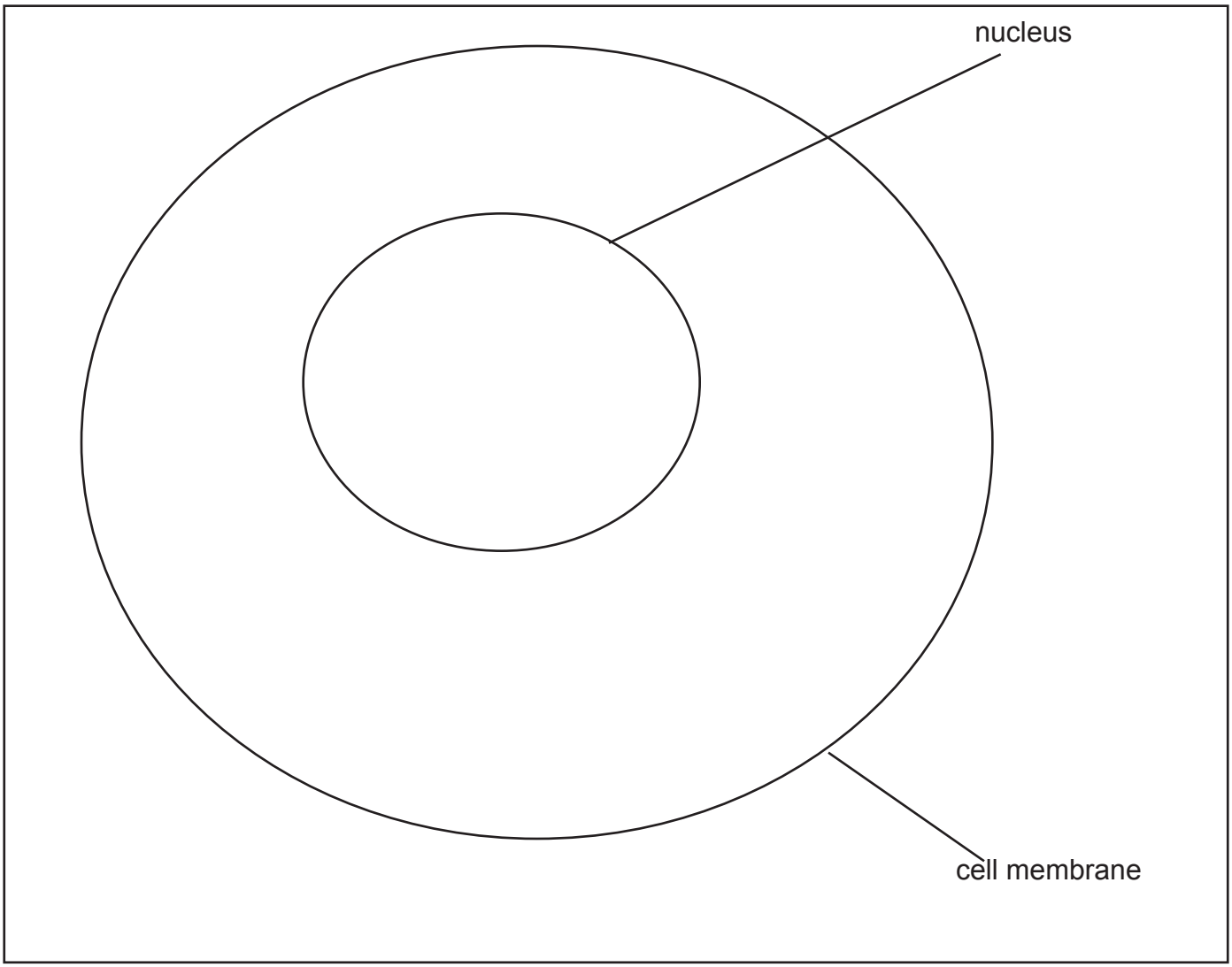
d. Extra genes exist

9. In the space below a cell membrane and a nucleus are drawn. Add the following to the drawing:

chromosome gene RNA amino acid protein

Make sure to label all of the parts you draw.

Label where transcription and translation are happening in the cell.

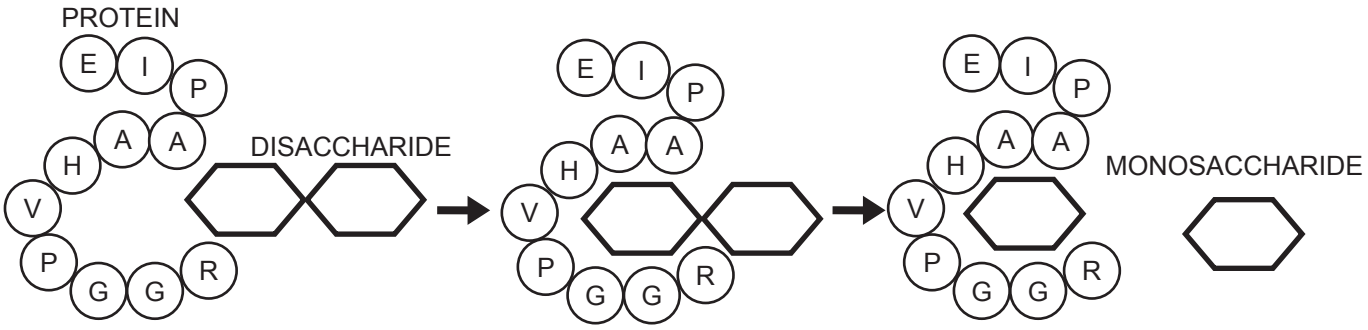


Use this information to answer questions 10 and 11.

Table of Physical Properties of Some Amino Acids

Hydrophobic amino acids	**Hydrophilic amino acids**
A (Alanine)	G (Glycine)
L (Leucine)	Q (Glutamine)
P (Proline)	
V (Valine)	**Charged amino acids**
I (Isoleucine)	E (Glutamic acid): negative charge
	H (Histidine): positive charge
	R (Arginine): positive charge

The illustration below shows a protein that binds a disaccharide molecule and cleaves it into two monosaccharides:



Based on the images and information above, use the following list to answer questions 10 and 11.

a. If the Valine (V) is changed to a Histidine (H)

b. If the Valine (V) is changed to Leucine (L)

c. If the Valine (V) is changed to a Glutamine (Q)

d. If the Valine (V) is deleted

10. Which of the above changes is **LEAST** likely to affect the ability of the protein to break down the sugar? _____

Explain why you chose your answer:

_____

_____

_____

_____

11. Which of the above changes is **MOST** likely to affect the ability of the protein to break down the sugar? _____

Explain why you chose your answer:

_____

_____

_____

_____

12. There is a protein called Lysozyme that can break down a molecule found on the surface of bacteria. Some people have different amino acid sequences for Lysozyme

Explain why some people have proteins with different amino acid sequences:

_____

_____

_____

_____

13. What is a gene?

a. a unit of heredity, passed from parents to their children
b. a set of instructions for making a protein
c. a piece of DNA
d. all of the above

14. What would need to be sequenced in order to sequence all of your genome?

a. Every chromosome in every cell in the body.
b. Every chromosome in one cell in the body.
c. One chromosome in every cell in the body.
d. One chromosome in one cell in the body.

15. Joe lived in Detroit for one year. It was cloudy often and it rained more than 130 days that year. At the end of the year Joe's skin was very light. He decided to move to Los Angeles for a new job. In Los Angeles it was usually sunny and it rained only 35 days during his first year there. After the first year, Joe's skin was much darker.

Explain why Joe's skin is darker. Make sure your explanation includes the relationship between genes and environment:

_____

_____

_____

_____

_____

16. How similar is the entire DNA sequence of any two humans from different places in the world?

    a. 88.9% identical
    b. 79.9% identical
    c. 99.9% identical
    d. 50.0% identical

17. How many genes are found in one cell of your body?

    a. 2 (one from each parent)
    b. 50,000 (25,000 from each parent)
    c. 46 (23 from each parent)
    d. 6 million (3 million from each parent)

18. My health is influenced by:

    A) my genes, but not my environment
    B) my environment, but not my genes
    C) both my genes and my environment
    D) only my diet and exercise

19. Mutations in the DNA are:

a. always bad for a human

b. sometimes bad for a human

c. never bad for a human

d. not found in humans

20. Scientists are working to make a new drug to treat lactose intolerance. This new drug will stick to the DNA near the lactase gene and cause the lactase gene to turn on. Normally, lactase protein breaks down lactose, a disaccharide found in dairy products. Write your answers in complete sentences.

Explain what will happen to the amount of lactase protein:

_____

_____

_____

Do you think this new drug will work to treat lactose intolerance? Explain why or why not:

_____

_____

_____

_____

_____

Name _____

Class _____

Teacher _____

Posttest

1. Which one of the following molecules carries out all the work of a cell?

a. RNA

b. DNA

c. Protein (1 point)

d. Amino acids

2. Are the cells in your skin different from the cells in your liver?

a. Yes, the cells in my skin have genes that my liver cells don't have.

b. Yes, the cells in my skin turn on genes that my liver cells don't turn on. (1 point)

c. No, the cells in my skin are the same as the cells in my liver.

d. Both a and b

3. DNA can be compared to a language in which "letters" are arranged in a specific sequence, that provides a specific meaning. How many "letters" are there in the DNA code?

a. 2

b. 26

c. 4 (1 point)

d. 20

4. List 4 types of cellular activities that are carried out by proteins. (**1 point for each correct answer)**

Break down food/molecules

Build molecules used in the cell (e.g. energy molecules)

Transport molecules into the cell (or within cell) (e.g. cytoplasmic streaming, phagocytosis)

Cellular movement

Cell division (e.g. movement of chromosomes) etc.

[note, students can give general examples or specific examples

5. Below are parts of an mRNA molecule from four individuals. Person A has the sequence found in most healthy people.

Person A: AUGUUCCAAACUACCGGAAUU (healthy person)
Person B: AUGUUCCAAUCUACCGGAAUU
Person C: AUGUUCCGGCCUACCGGAAUU
Person D: AUGUUCCAAAACUACCGGAAUU

Amino acid sequence for Person A: M F Q T T G I

For Person B, C, and D, put an X where the amino acids will be **DIFFERENT** from person A:

Person B	__	__	__	X	__	__	__
Person C	__	__	X	X	__	__	__
Person D	__	__	__	X	X	X	X

If the gene sequence in Person A is important for a proper functioning heart, which person (Person B, C or D) is MOST likely to have heart problems?____**D_ (1 point)**____

Explain why the person you chose is most likely to have heart problems:

Indicates Person D has an extra DNA base or an insertion (1 point), that this causes more than one amino acid to change (1 point), that the protein with the most changes will have a much different shape or will be less likely to work than the other two proteins (1 point).

6. Which of the follwowing has items ordered from largest to smallest?

a. Human, fly, cell, protein, amino acid

b. Human, cell, fly, protein, amino acid

c. Human, cell, amino acid, protein, fly

d. Human, fly, cell, amino acid, protein

7. What do the A, T, G and C in DNA represent?

a. Different genes

b. Different amino acids

c. Different sugars

d. Different bases

8. Scientists have been studying a particular protein that helps to break down fat. These scientists have found that some people have a larger than normal protein. Which of the following is NOT a likely explanation for why the protein is larger than normal?

a. Extra DNA bases exist

b. Extra RNA bases exist

c. Extra amino acids exist

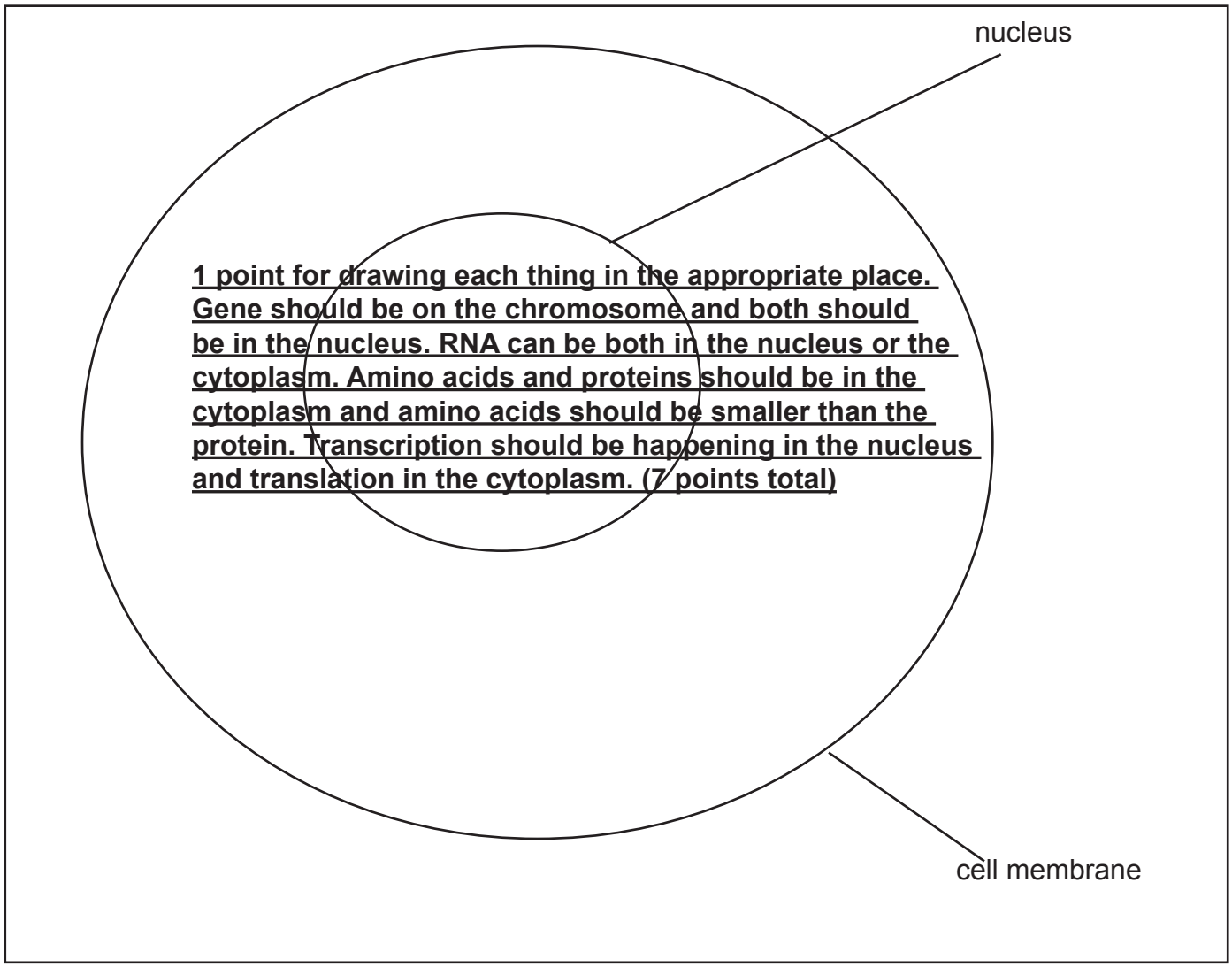
d. Extra genes exist

9. In the space below a cell membrane and a nucleus are drawn. Add the following to the drawing:

chromosome gene RNA amino acid protein

Make sure to label all of the parts you draw.

Label where transcription and translation are happening in the cell.



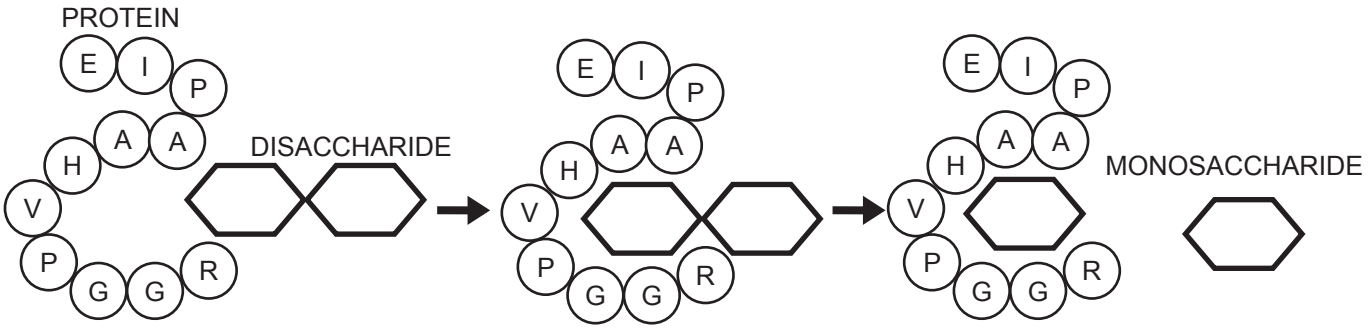
1 point for drawing each thing in the appropriate place. Gene should be on the chromosome and both should be in the nucleus. RNA can be both in the nucleus or the cytoplasm. Amino acids and proteins should be in the cytoplasm and amino acids should be smaller than the protein. Transcription should be happening in the nucleus and translation in the cytoplasm. (7 points total)

Use this information to answer questions 10 and 11.

TABLE OF PHYSICAL PROPERTIES OF SOME AMINO ACIDS

Hydrophobic amino acids	**Hydrophilic amino acids**
A (Alanine)	G (Glycine)
L (Leucine)	Q (Glutamine)
P (Proline)	
V (Valine)	**Charged amino acids**
I (Isoleucine)	E (Glutamic acid): negative charge
	H (Histidine): positive charge
	R (Arginine): positive charge

The illustration below shows a protein that binds a disaccharide molecule and cleaves it into two monosaccharides:



Based on the images and information above, use the following list to answer questions 10 and 11.

a. If the Valine (V) is changed to a Histidine (H)

b. If the Valine (V) is changed to Leucine (L)

c. If the Valine (V) is changed to a Glutamine (Q)

d. If the Valine (V) is deleted

10. Which of the above changes is **LEAST** likely to affect the ability of the protein to break down the sugar? ___**B**_**(1 point)**___

Explain why you chose your answer:

Indicates a change from one hydrophobic amino acid to another hydrophobic amino acid (1 point), that this change is not likely to change the shape of the protein (1 point).

11. Which of the above changes is **MOST** likely to affect the ability of the protein to break down the sugar? ____**D (1 point)**___

Explain why you chose your answer:

Indicates he or she chose D because it took out an amino acid (1 point), that this change is likely to change the shape of the protein or the pocket (1 point), that the protein cannot do its work if it changes shape (1 point).

12. There is a protein called Lysozyme that can break down a molecule found on the surface of bacteria. Some people have different amino acid sequences for Lysozyme

Explain why some people have proteins with different amino acid sequences:

Indicates that different amino acid sequences occur because people have different DNA sequences (1 point).

or

One person has a mutation in the DNA the other does not (1 point).

13. What is a gene?

a. a unit of heredity, passed from parents to their children
b. a set of instructions for making a protein
c. a piece of DNA
d. all of the above (1 point)

14. What would need to be sequenced in order to sequence all of your genome?

a. Every chromosome in every cell in the body.
b. Every chromosome in one cell in the body. (1 point)
c. One chromosome in every cell in the body.
d. One chromosome in one cell in the body.

15. Joe lived in Detroit for one year. It was cloudy often and it rained more than 130 days that year. At the end of the year Joe's skin was very light. He decided to move to Los Angeles for a new job. In Los Angeles it was usually sunny and it rained only 35 days during his first year there. After the first year, Joe's skin was much darker.

Explain why Joe's skin is darker. Make sure your explanation includes the relationship between genes and environment:

Indicates that the environment turns on genes (1 point), that proteins made from those genes build melanin (1 point), that there will be more melanin (1 point).

16. How similar is the entire DNA sequence of any two humans from different places in the world?

a. 88.9% identical

b. 79.9% identical

c. 99.9% identical (1 point)

d. 50.0% identical

17. How many genes are found in one cell of your body?

a. 2 (one from each parent)

b. 50,000 (25,000 from each parent) (1 point)

c. 46 (23 from each parent)

d. 6 million (3 million from each parent)

18. My health is influenced by:

A) my genes, but not my environment

B) my environment, but not my genes

C) both my genes and my environment

D) only my diet and exercise

19. Mutations in the DNA are:

a. always bad for a human

b. sometimes bad for a human

c. never bad for a human

d. not found in humans

20. Scientists are working to make a new drug to treat lactose intolerance. This new drug will stick to the DNA near the lactase gene and cause the lactase gene to turn on. Normally, lactase protein breaks down lactose, a disaccharide found in dairy products. Write your answers in complete sentences.

Explain what will happen to the amount of lactase protein:

Indicates there will be more lactase proteins (1 point).

Do you think this new drug will work to treat lactose intolerance? Explain why or why not:

2 possible answers

Yes, because if there is more lactase proteins, more lactose can be broken down. (2 points)

or

No, because if there is a mutation in the lactase gene, the lactase protein will not work and not be able to break down lactose.

Comparing Humans From Different Places

Ethiopia

Vietnam

India

Iraq

Comparing External Structures

Fruit Fly

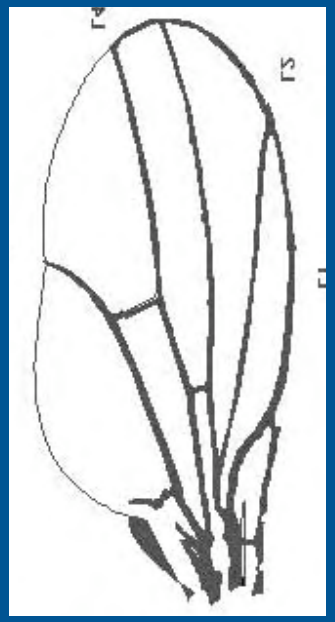
Mouse

Human

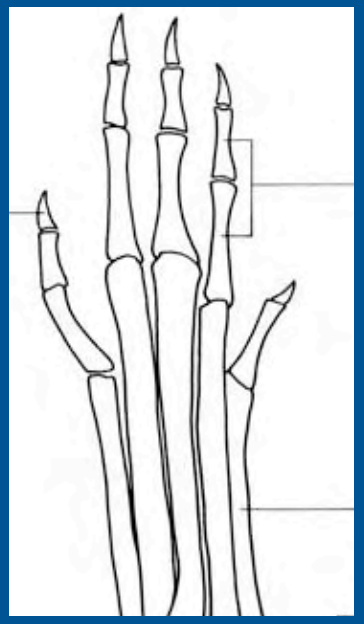
Chimpanzee

Comparing Limbs

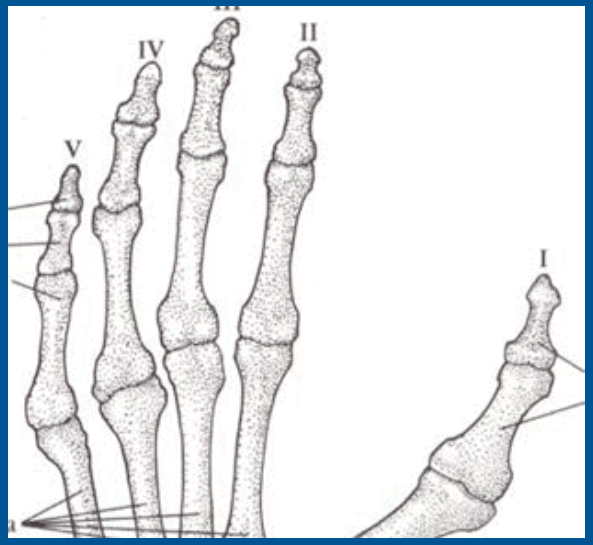
Fruit fly wing



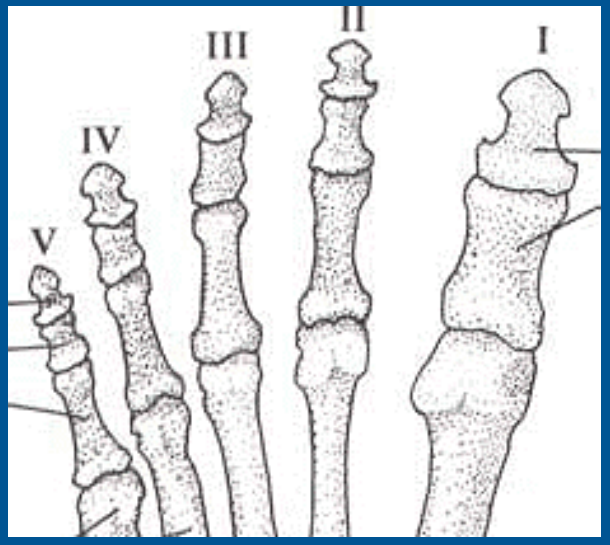
Mouse hind foot



Chimpanzee foot



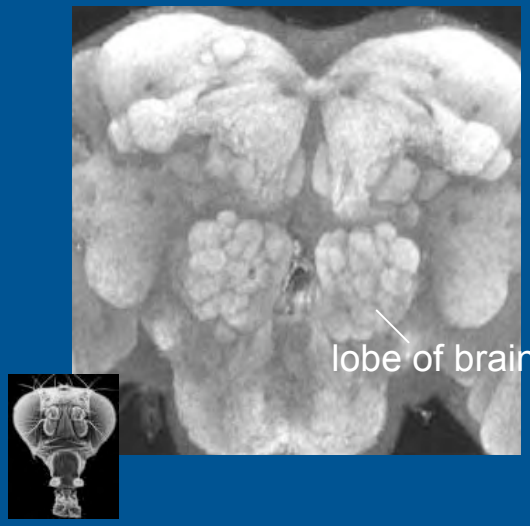
Human foot



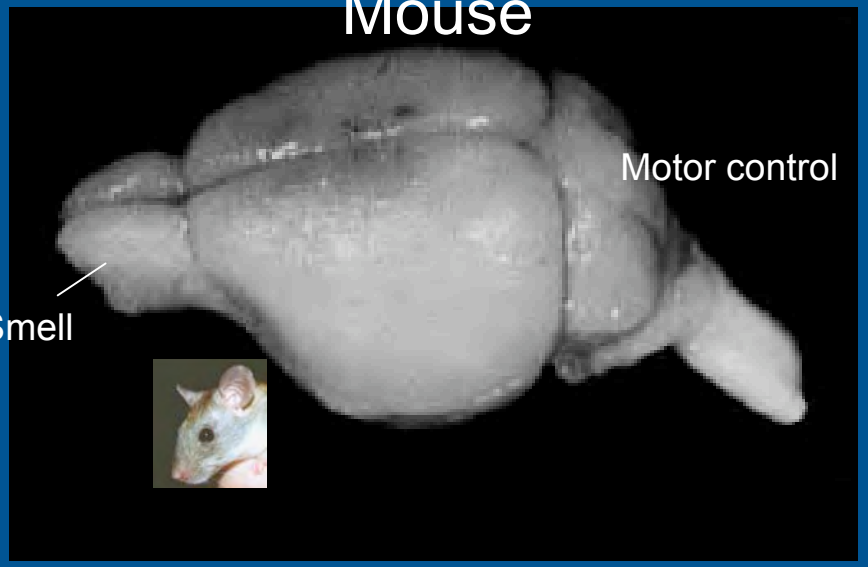
Not to scale!

Comparing Brains

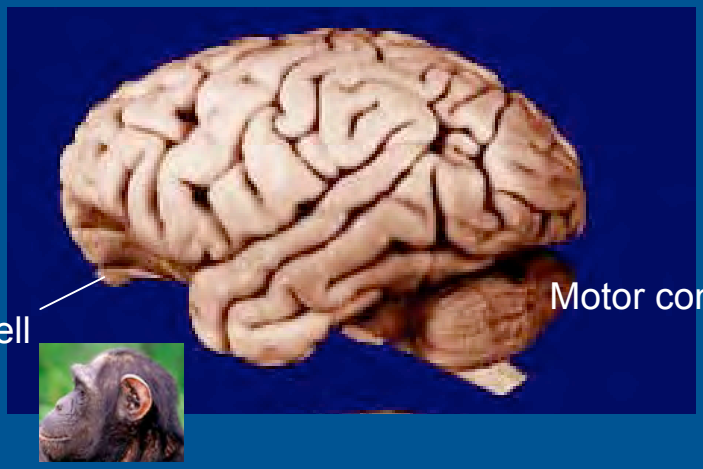
Fly



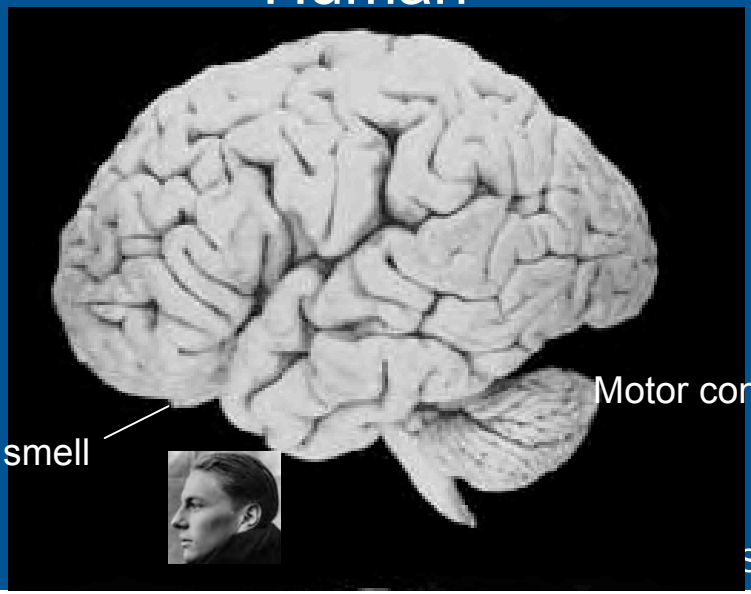
Mouse



Chimpanzee

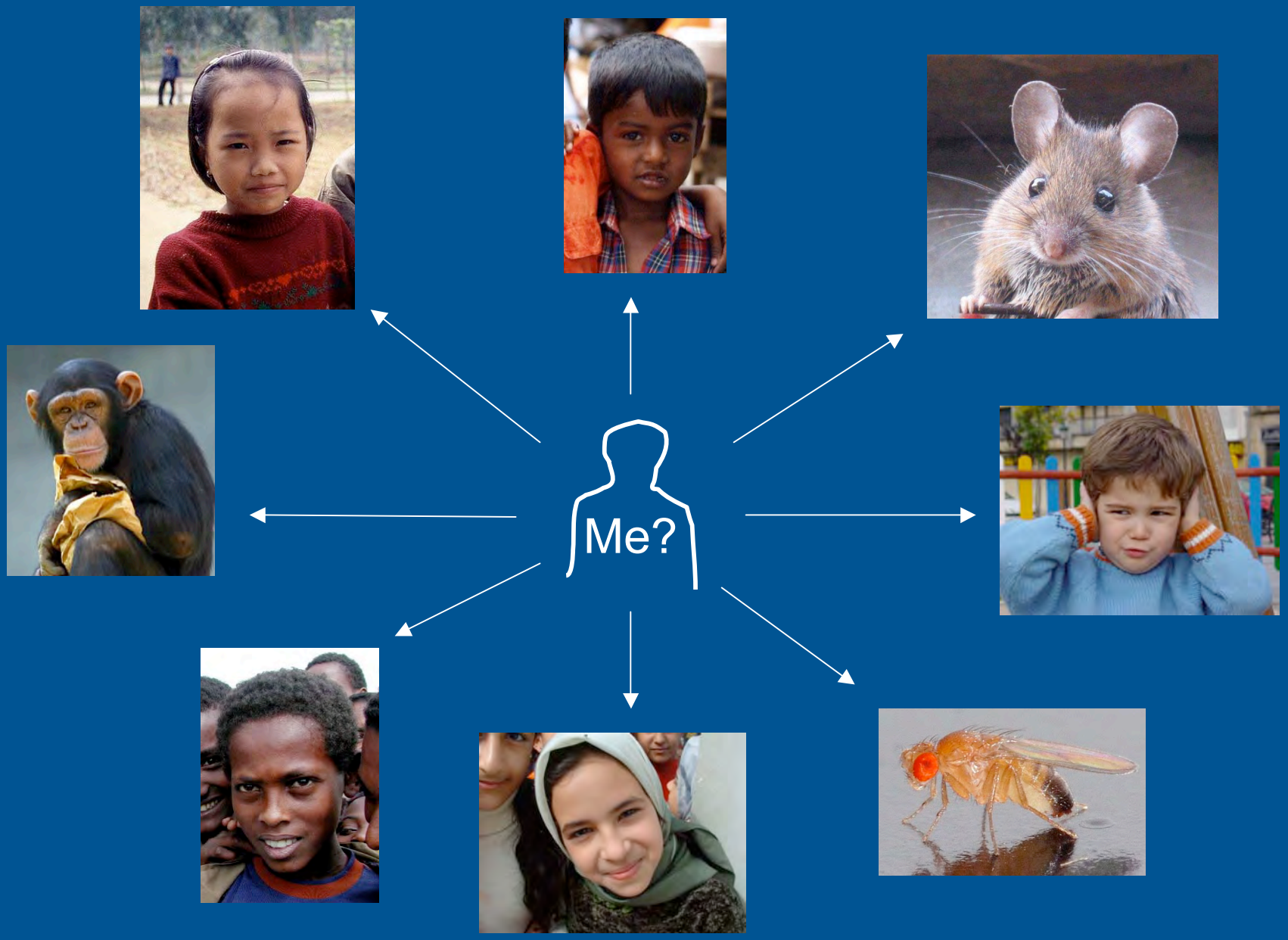


Human

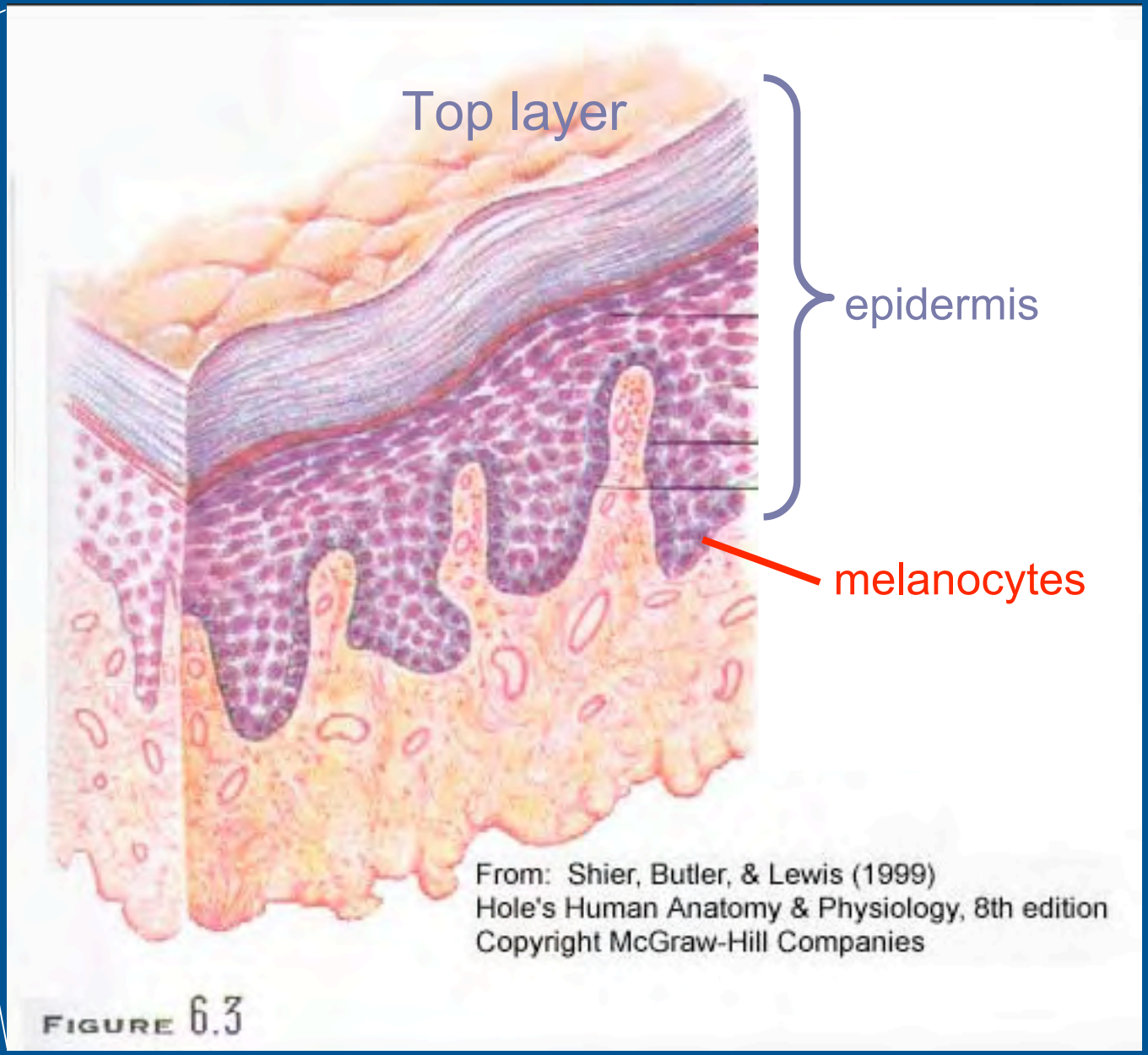


Not to scale!

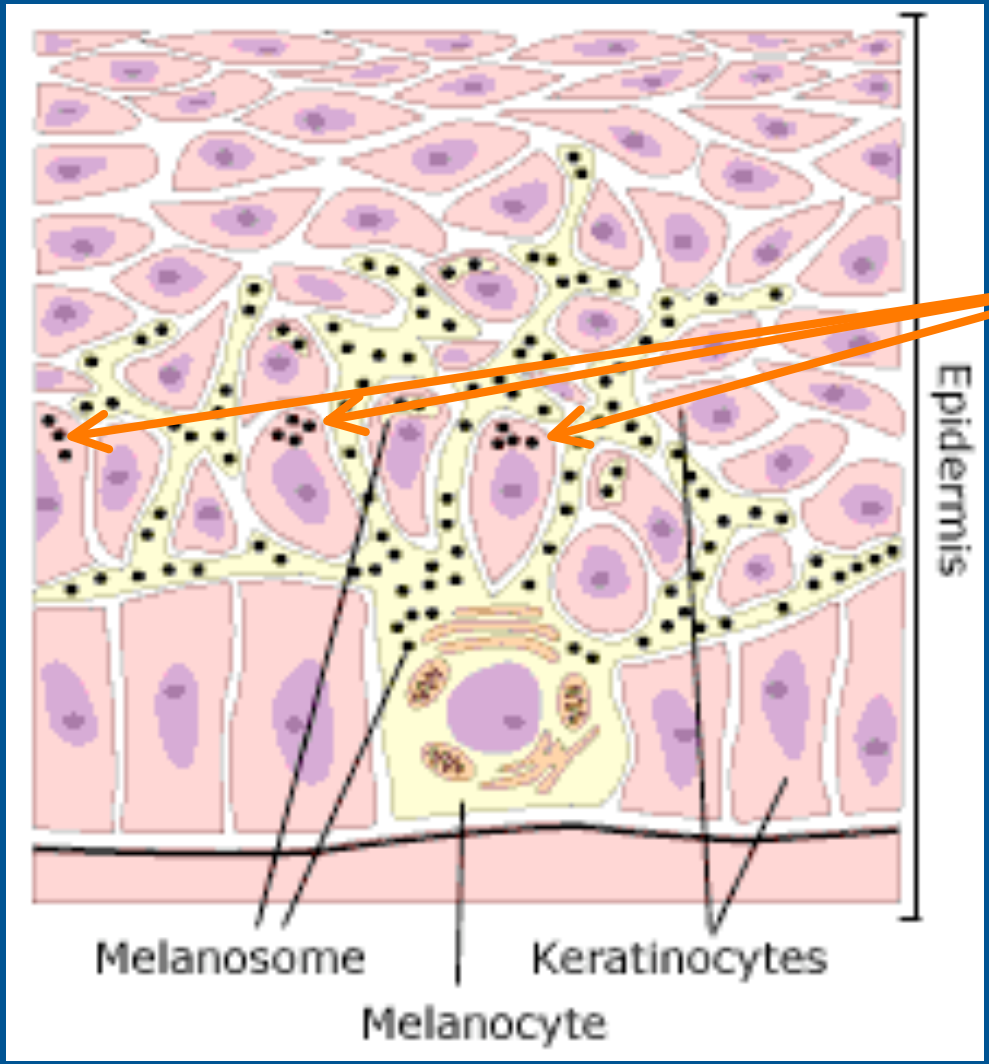
How Similar or Different are We From Each Other?



Cross Section of Skin



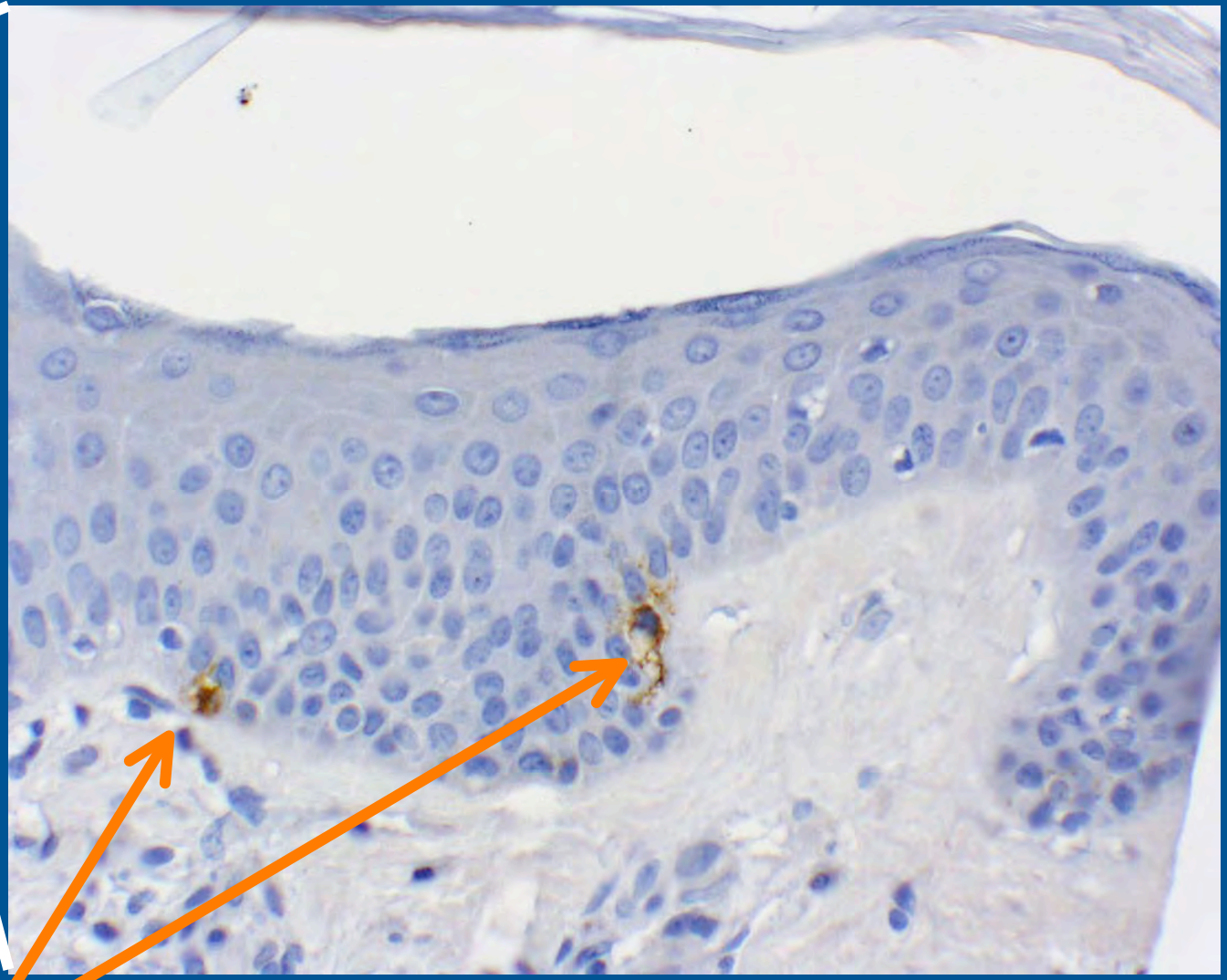
Cross section of Epidermis: Blow up



Melanin taken up by keratinocytes

Based on what you know about skin cells, predict what could be the difference between light skin and dark skin.

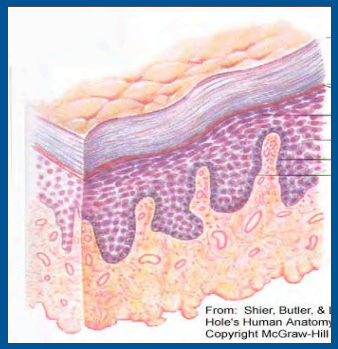
Melanocytes



courtesy of Laura P. Hale, M.D. Ph.D., Duke University

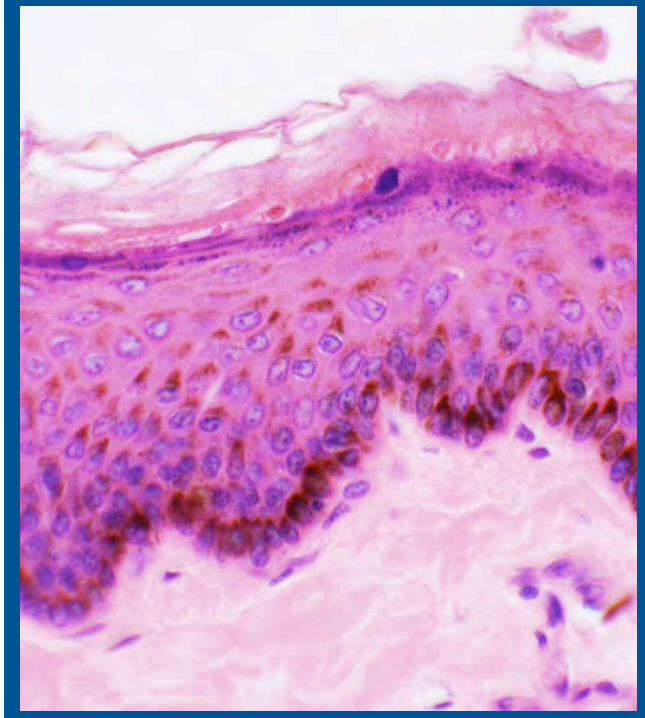
melanocytes

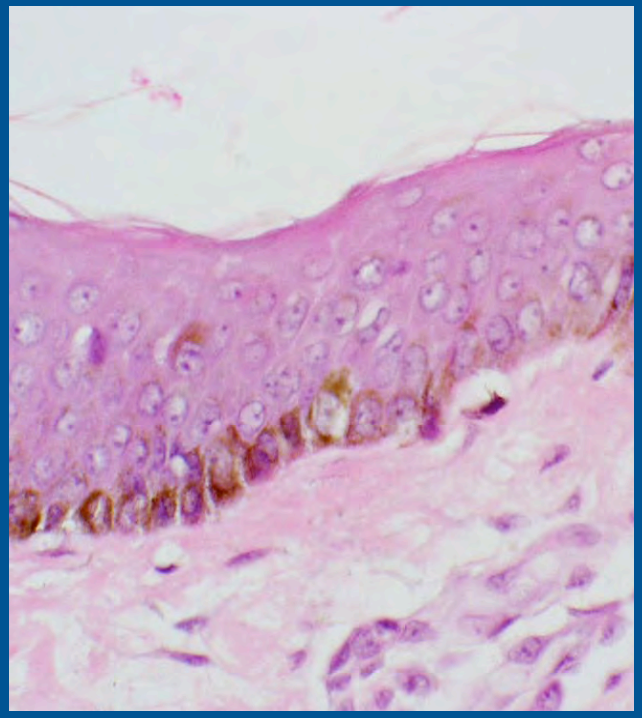
Skin Samples

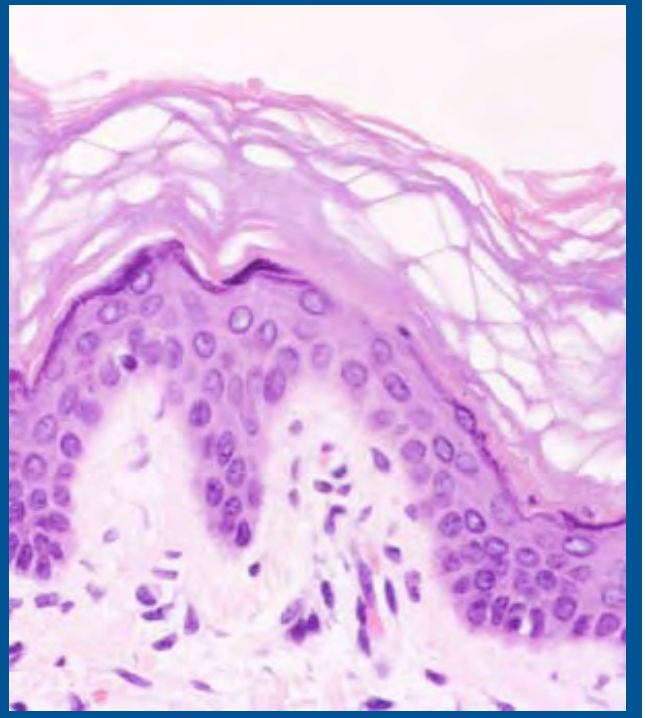


darkest skin color

lightest skin color



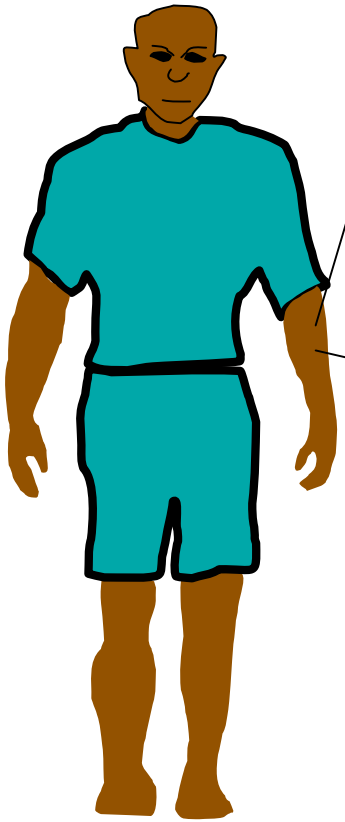




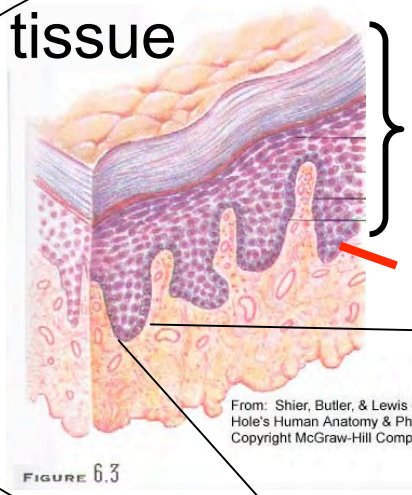
courtesy of Laura P. Hale, M.D. Ph.D., Duke University

Special Skin Cells Make Melanin

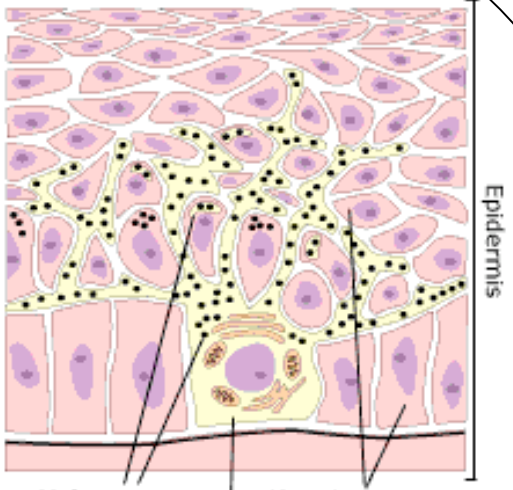
body



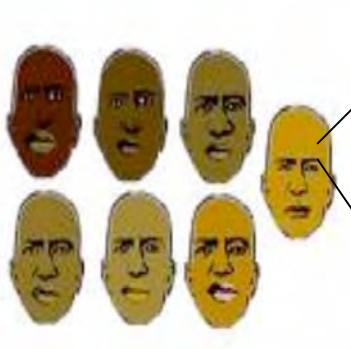
tissue



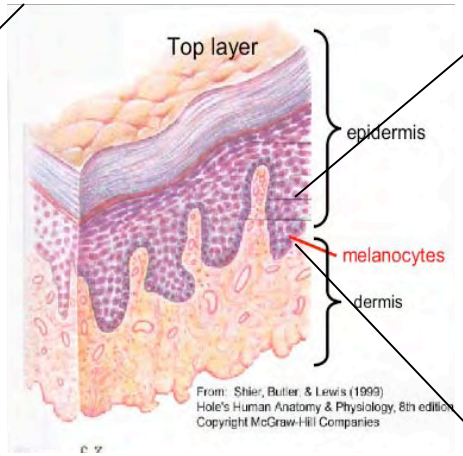
cells



How is melanin made inside the melanocytes?

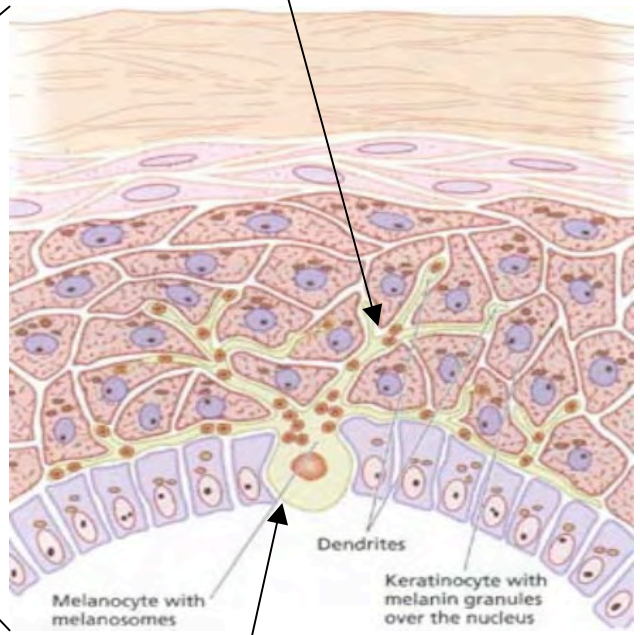


Skin Colors



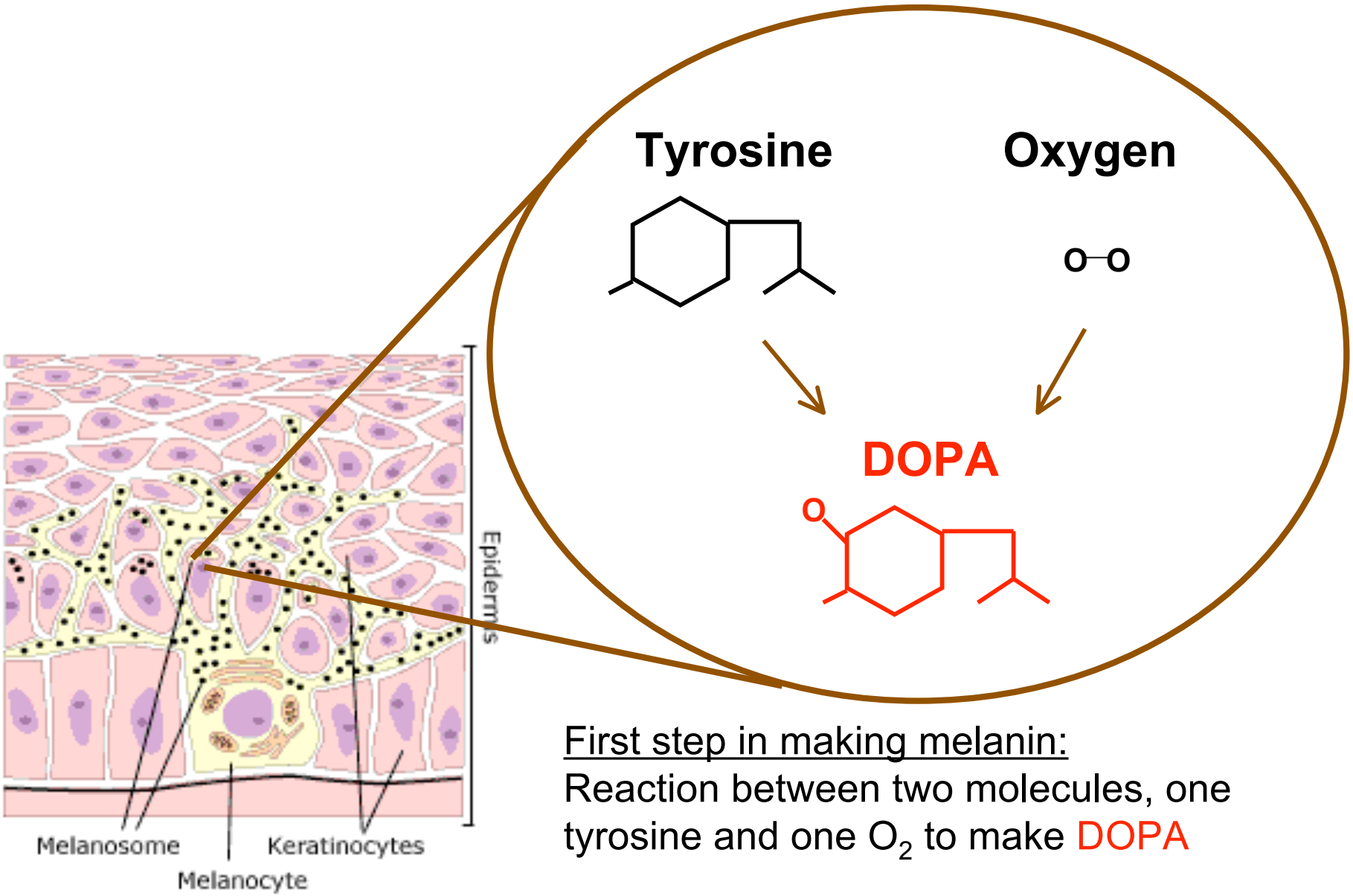
Cross Section of Skin Tissue

Melanin

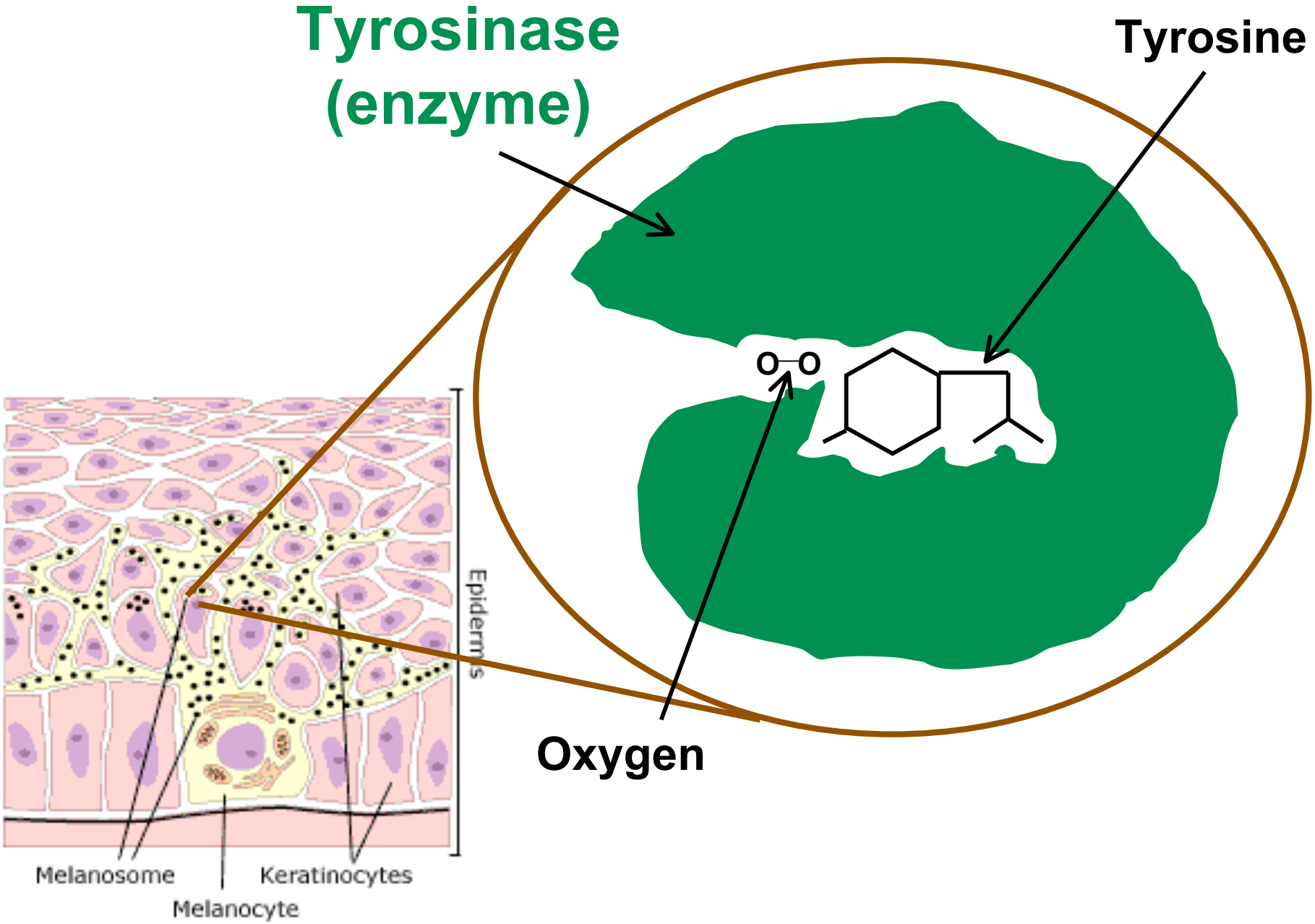


Melanocyte

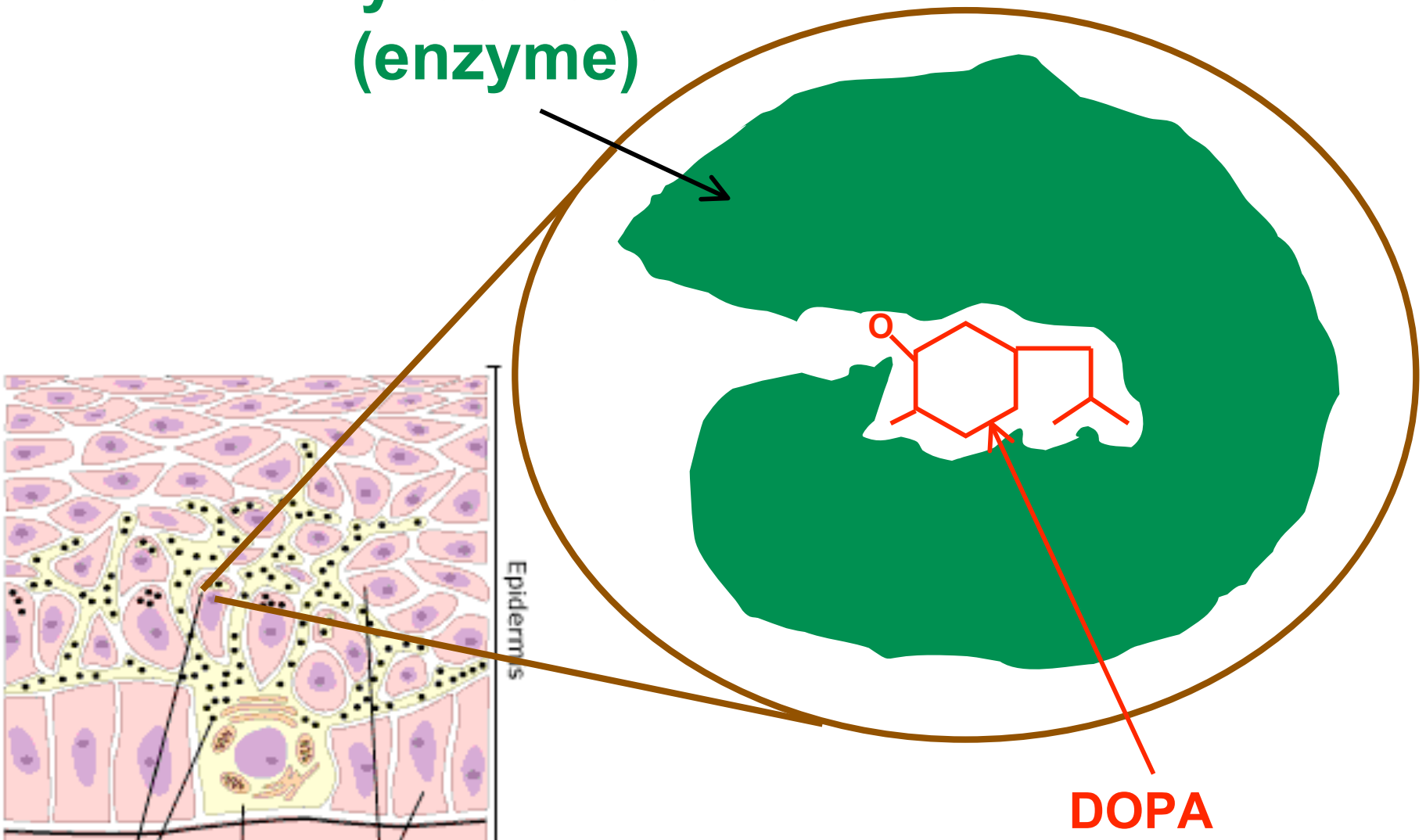
Looking inside a melanosome



<u>First step in making melanin:</u>
Reaction between two molecules, one tyrosine and one O_2 to make DOPA


Tyrosinase
(enzyme)
Tyrosine
Oxygen
Epiderms
Melanosome
Melanocyte
Keratinocytes

Tyrosinase (enzyme)

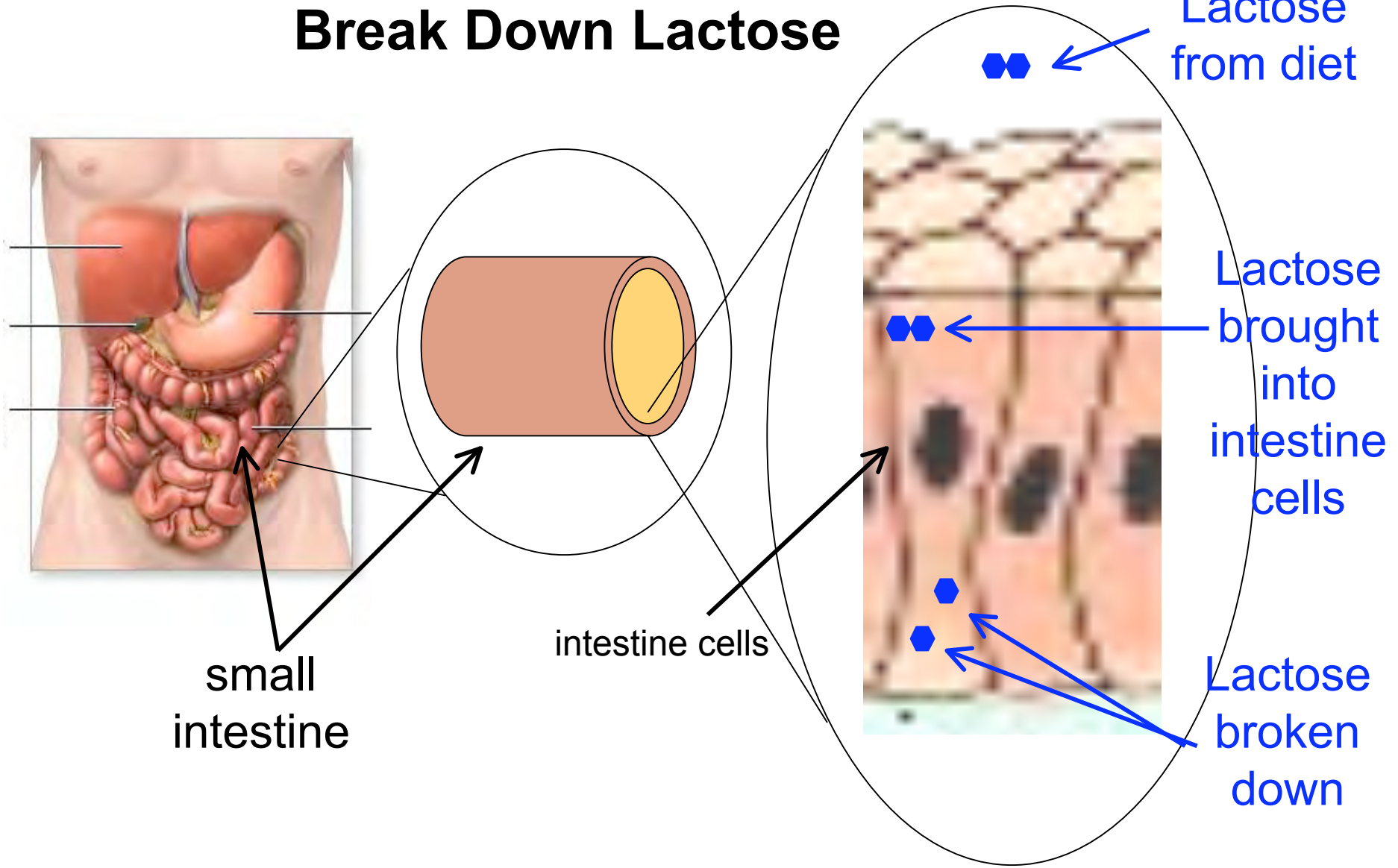


Other enzymes turn help turn DOPA into melanin.

Lactose intolerance

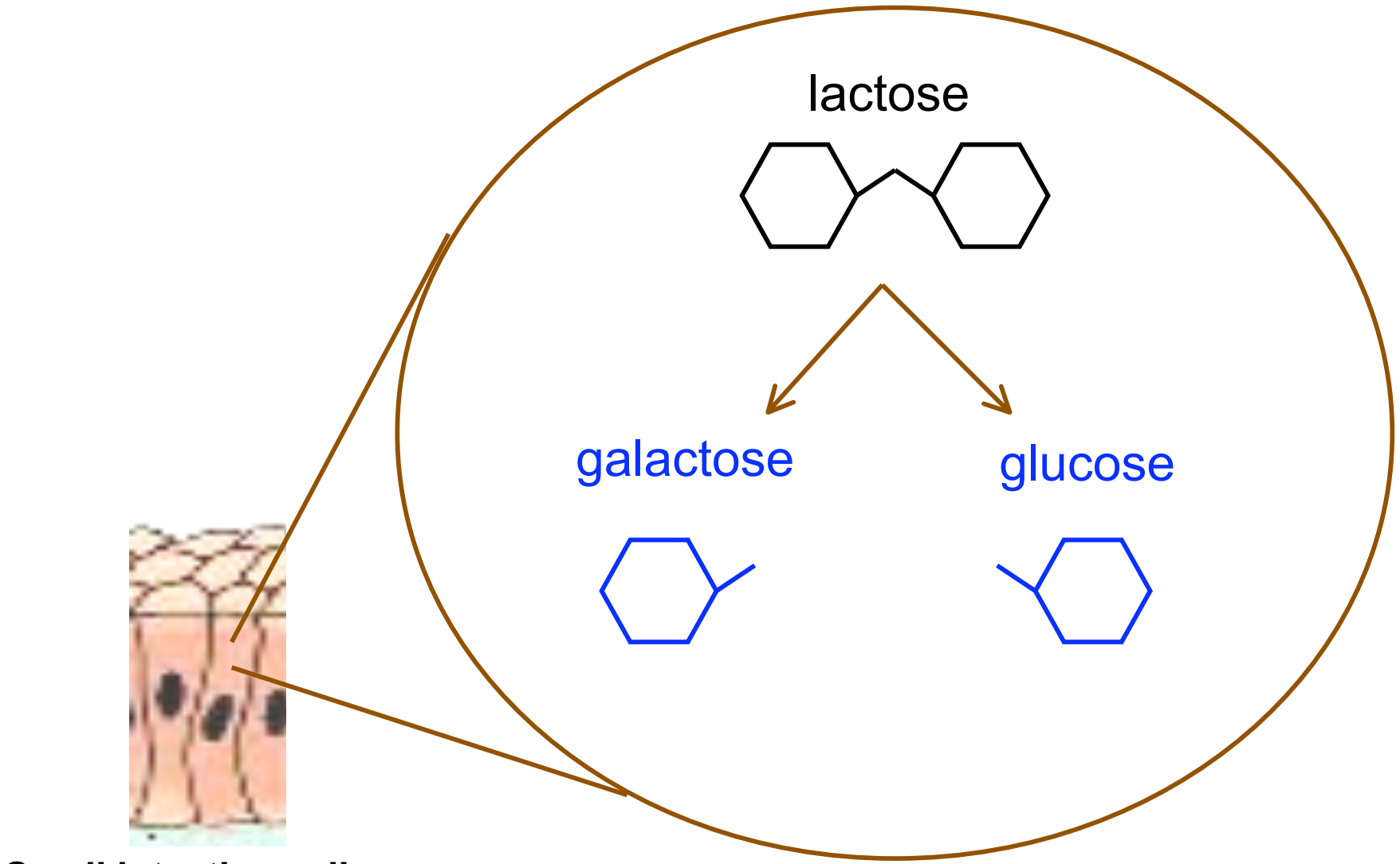
- Cannot break down lactose, a disaccharide found in dairy products
- Instead, bacteria in the intestine break down the lactose, producing gas
- Most children can break down lactose
- Most adults in the world cannot break down lactose - making them *lactose intolerant*

Cells in Small Intestine Break Down Lactose



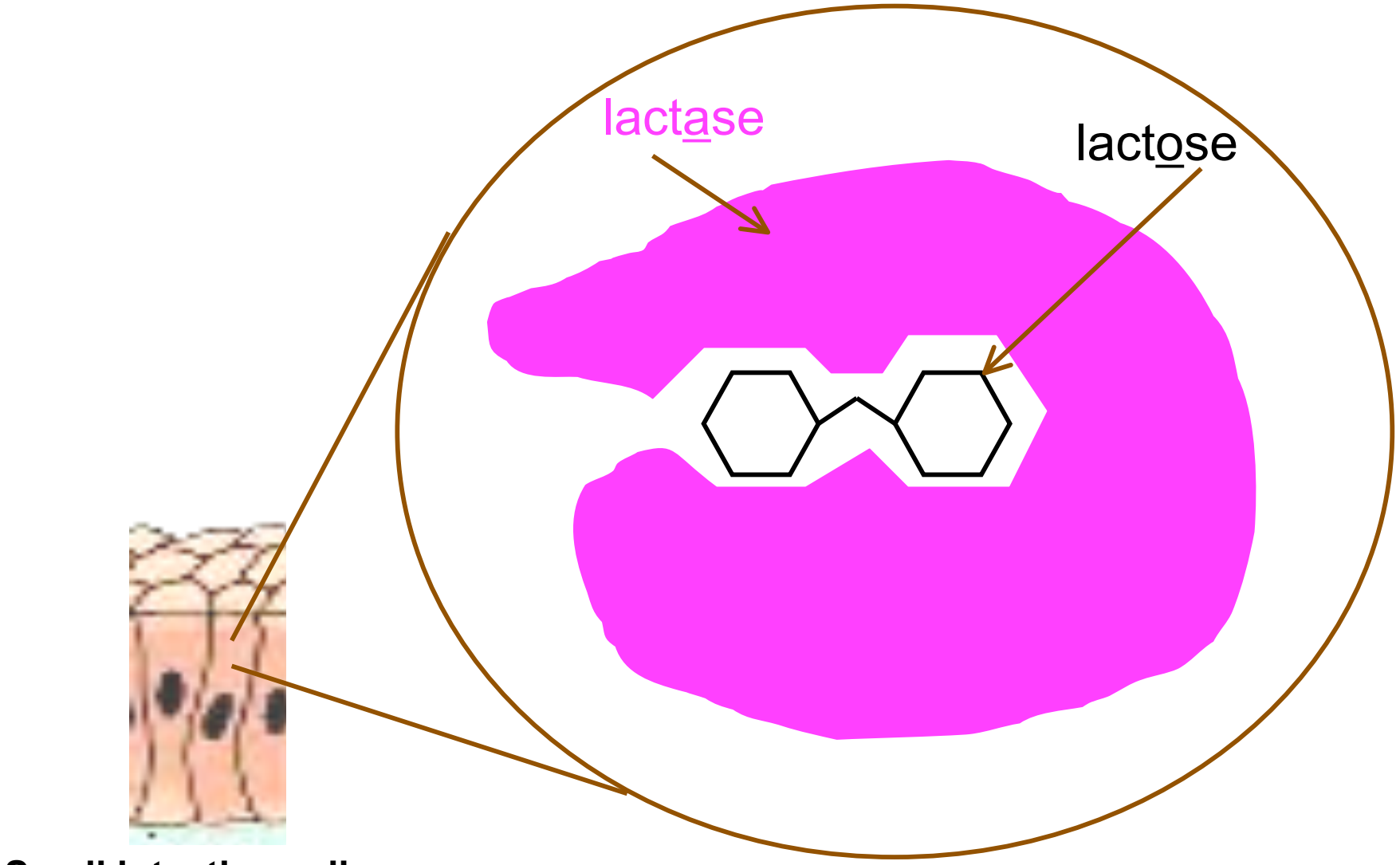
How is lactose broken down in intestine cells?

Looking inside small intestine cells



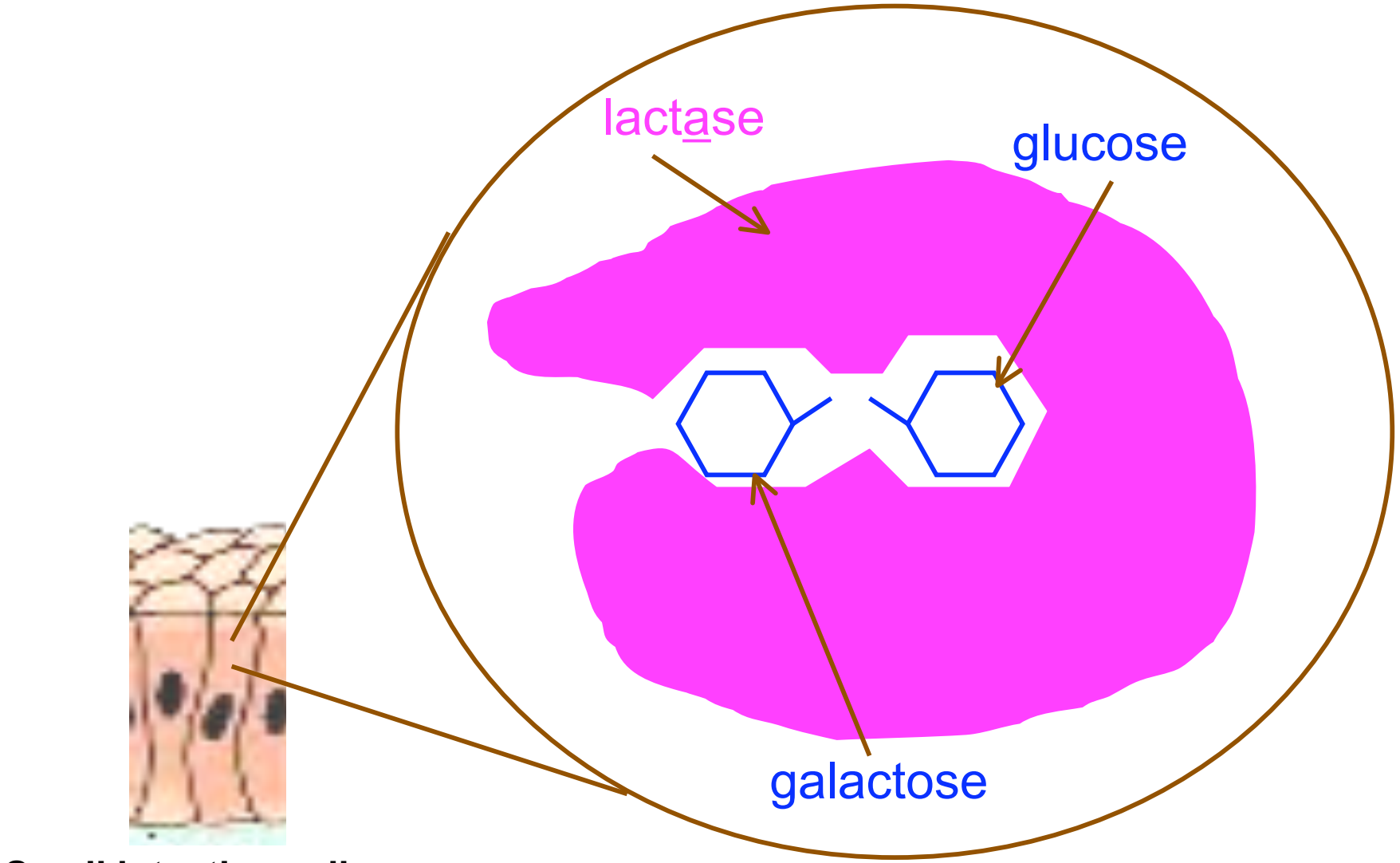
Small intestine cells

Looking inside small intestine cells



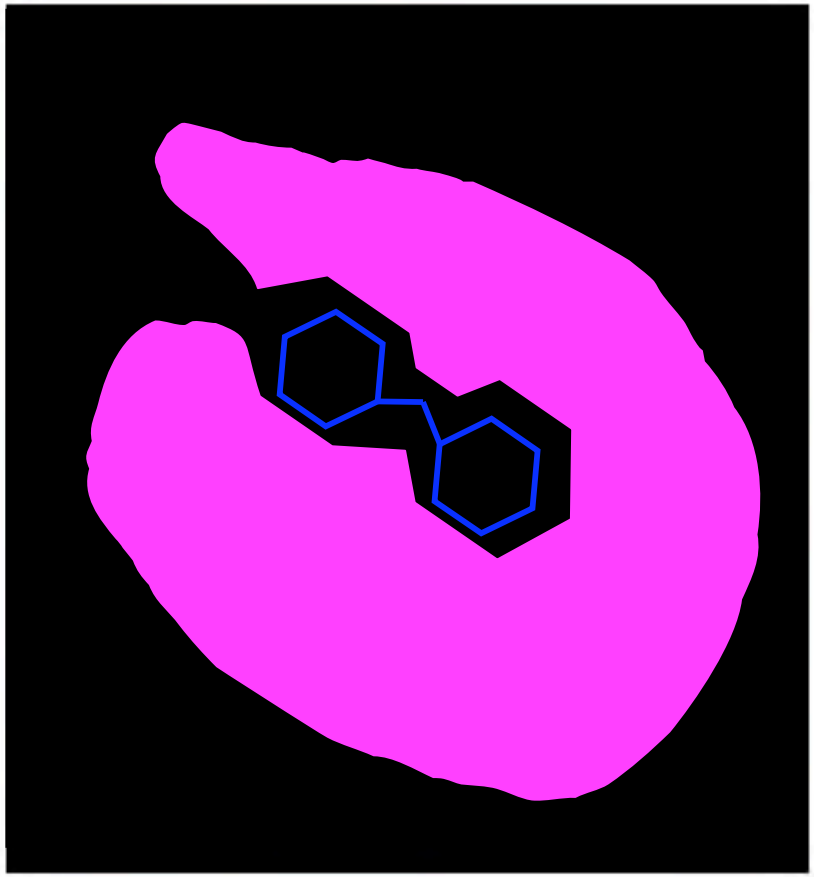
Small intestine cells

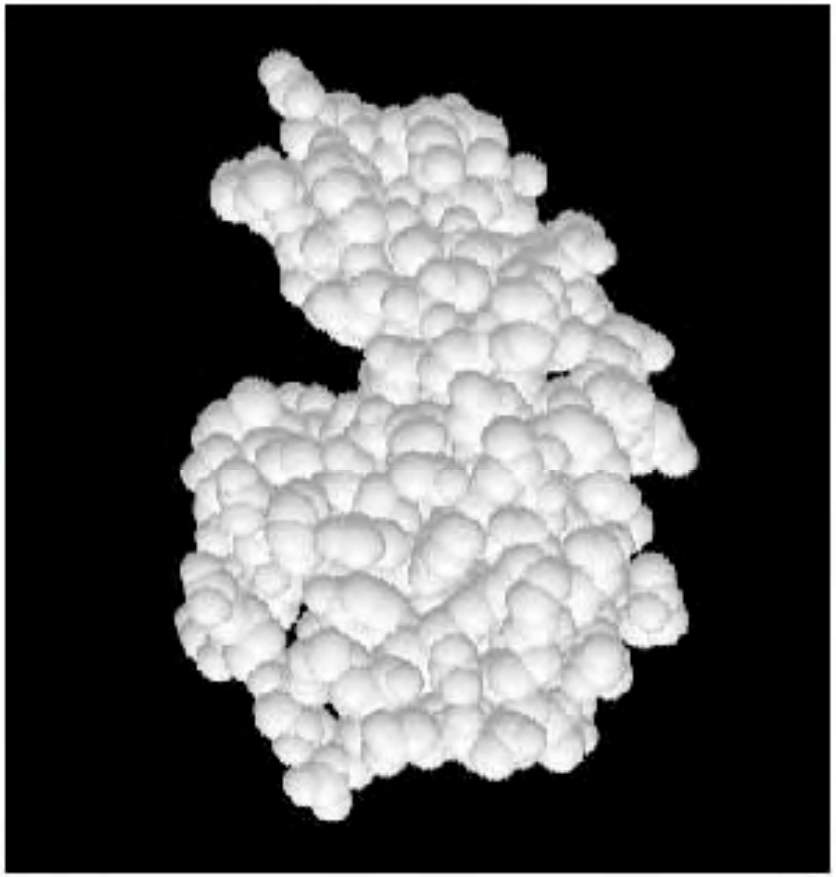
Looking inside small intestine cells



Small intestine cells

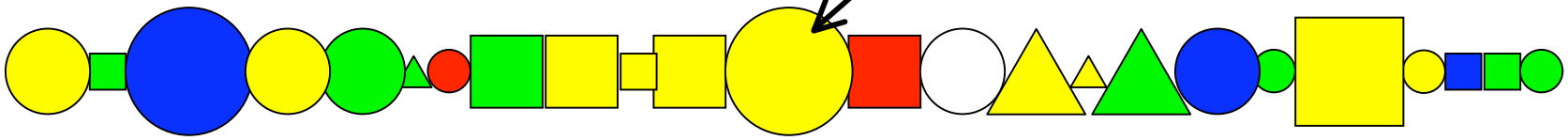
Lactase



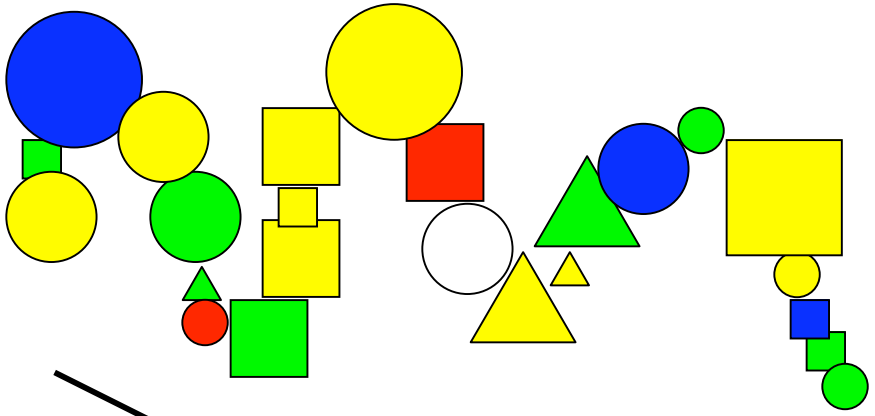


Protein Structure

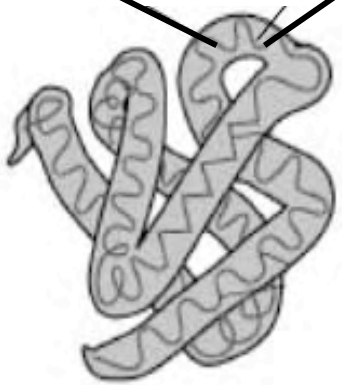
Chain of amino acids



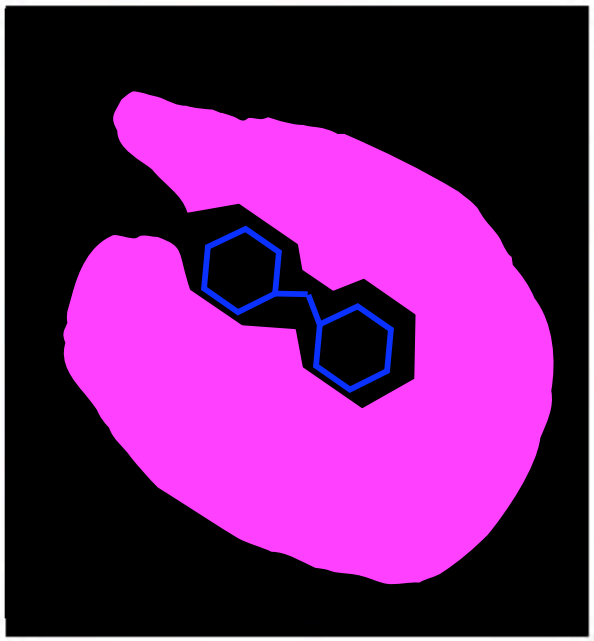
Folded chain of amino acids



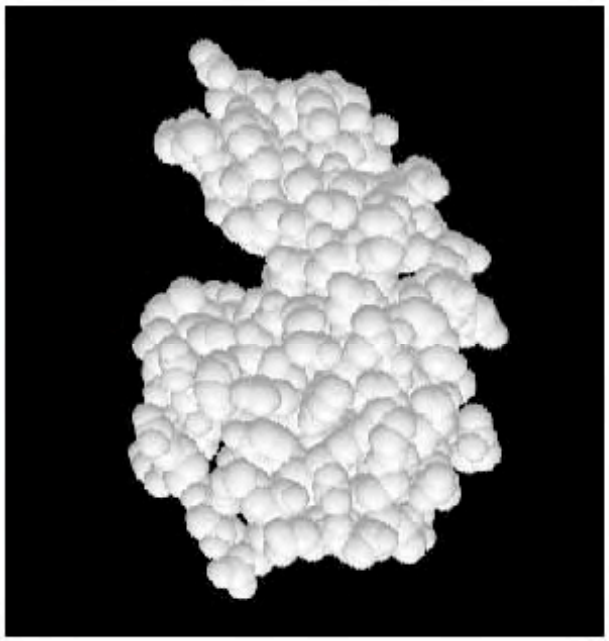
Whole protein



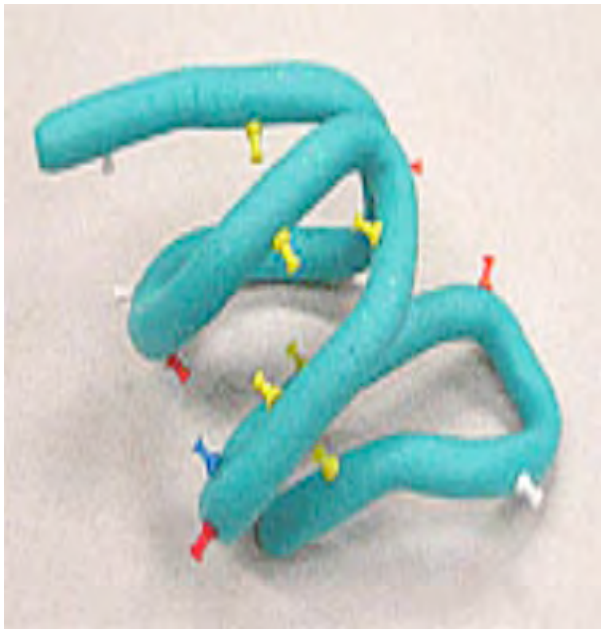
Protein Models



Cartoon model

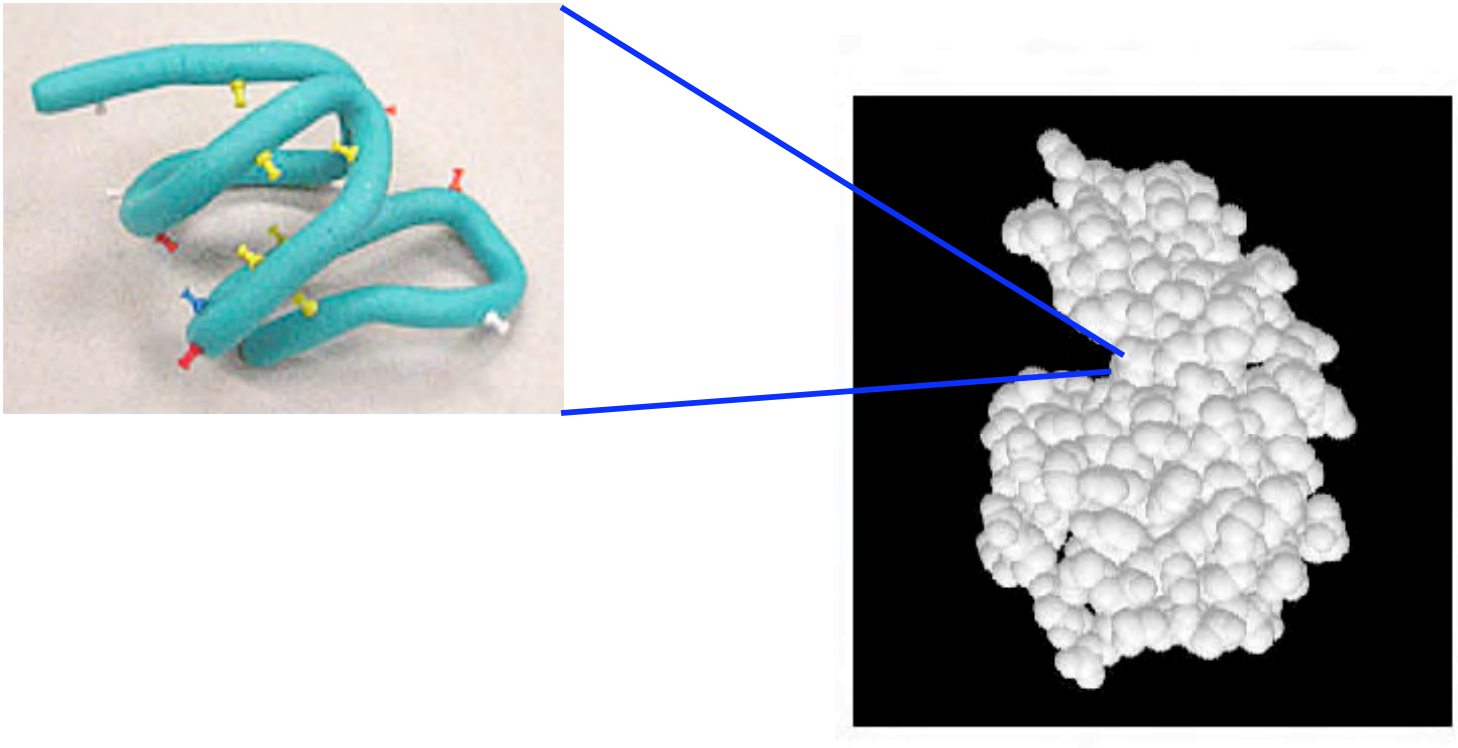


Space-filling model



Toober model

Modeling Lactase



Key to Toobers

Blue=positive charge (+)

K, R, H

Red=negative charge (-)

D, E

Yellow=hydrophobic

A, V, L, I, P, M, F, W

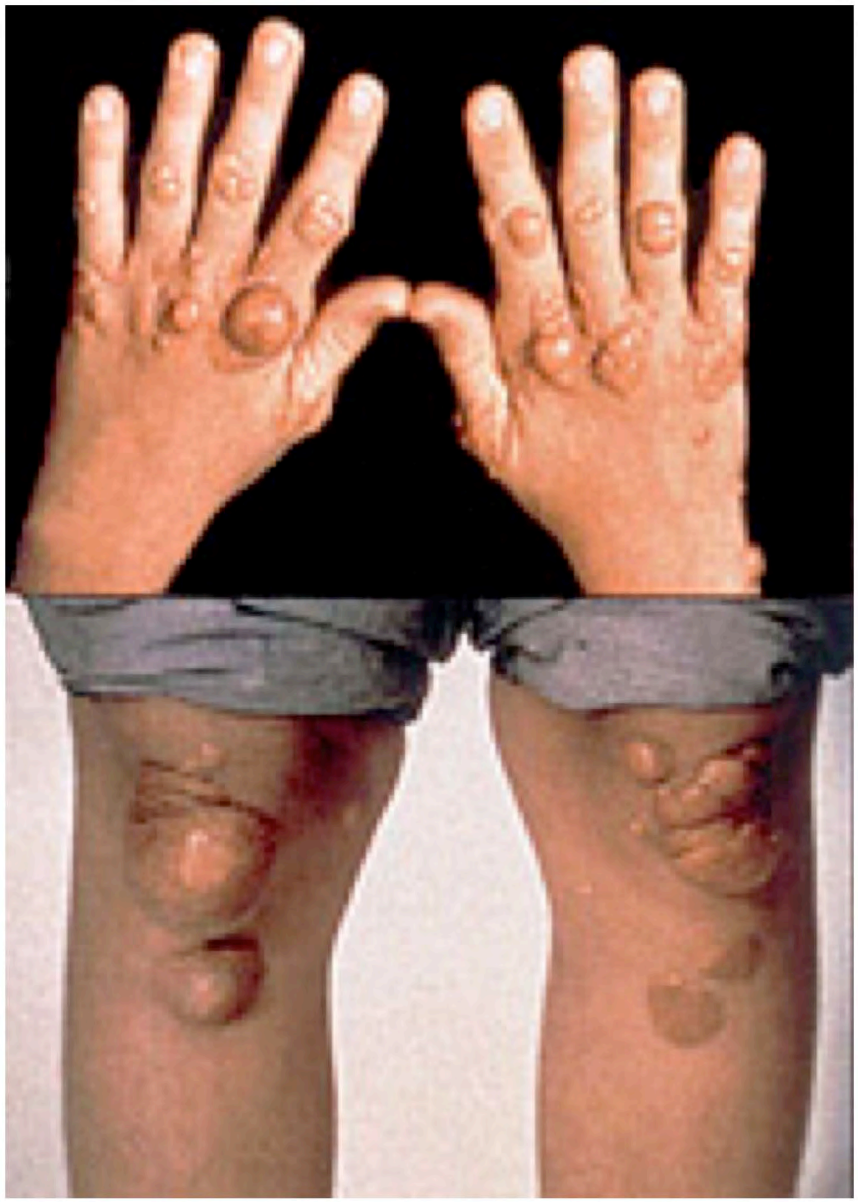
Green=hydrophilic

G, S, T, N, Q, Y

White = cysteine

C

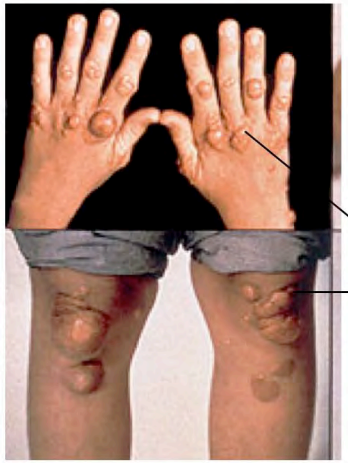
What might cause this disease?



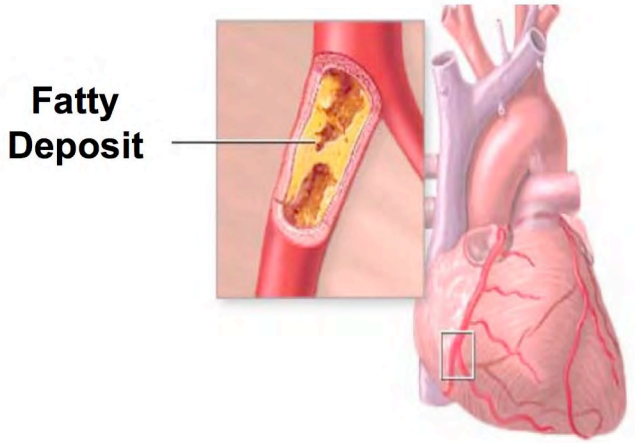
Familial Hypercholesterolemia (FH) Symptoms

- Very high cholesterol in blood
- Chest pain and heart attacks at a young age
- Build up of fatty deposits on under skin and in arteries

Knees and Fingers

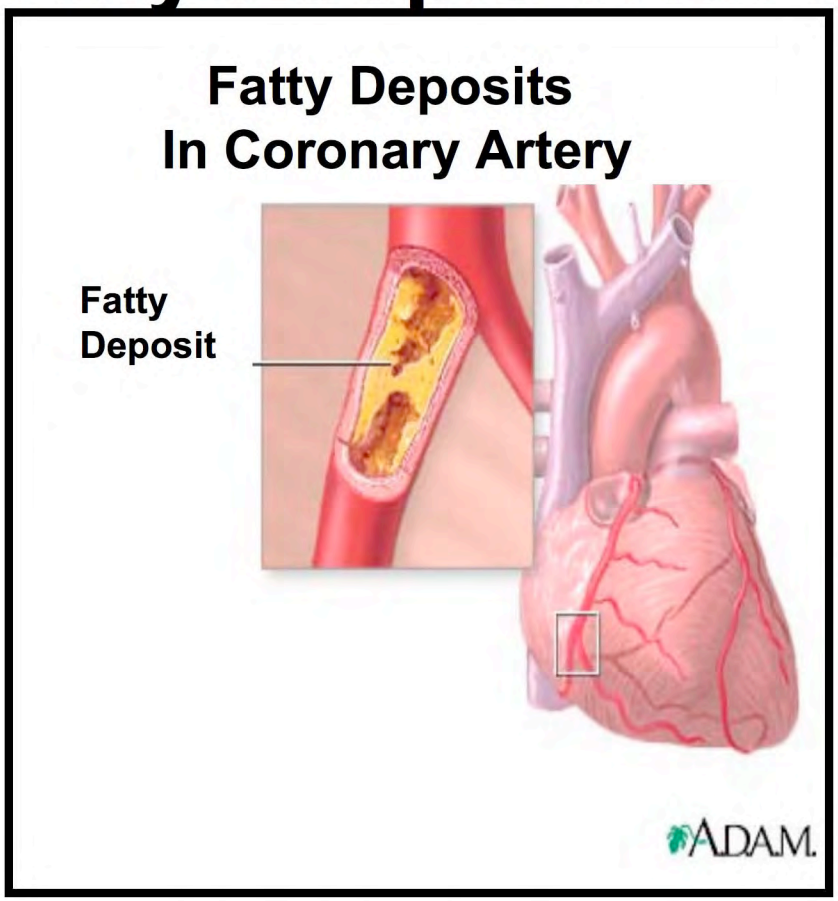


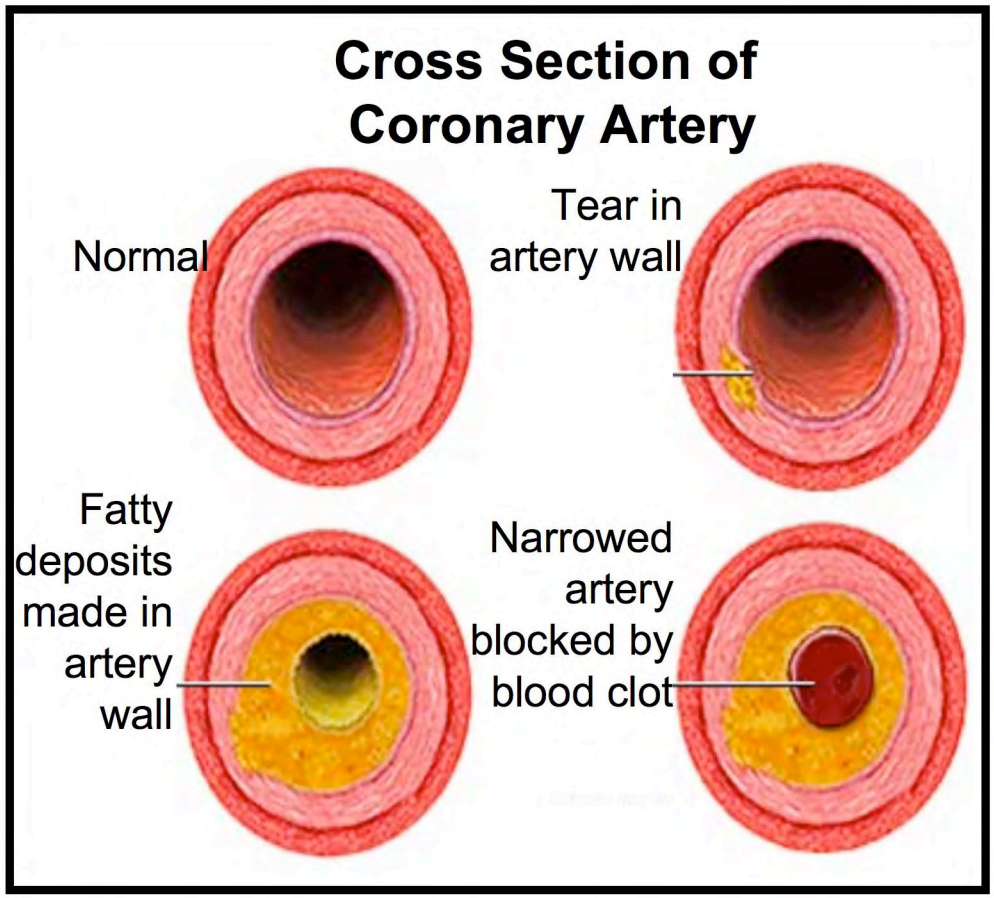
Coronary Artery: a heart artery



A.D.A.M.

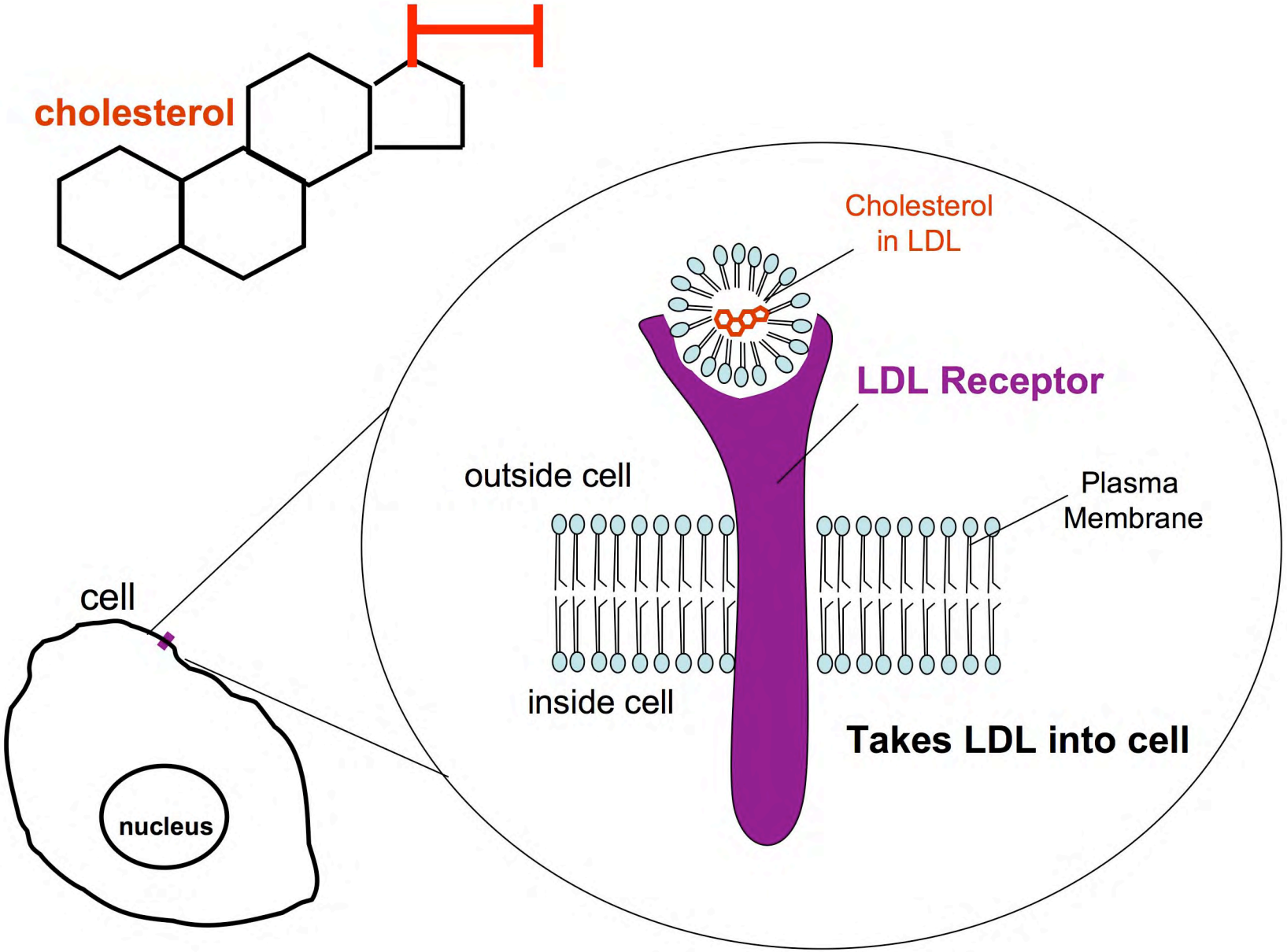
Why People With FH Have Heart Attacks



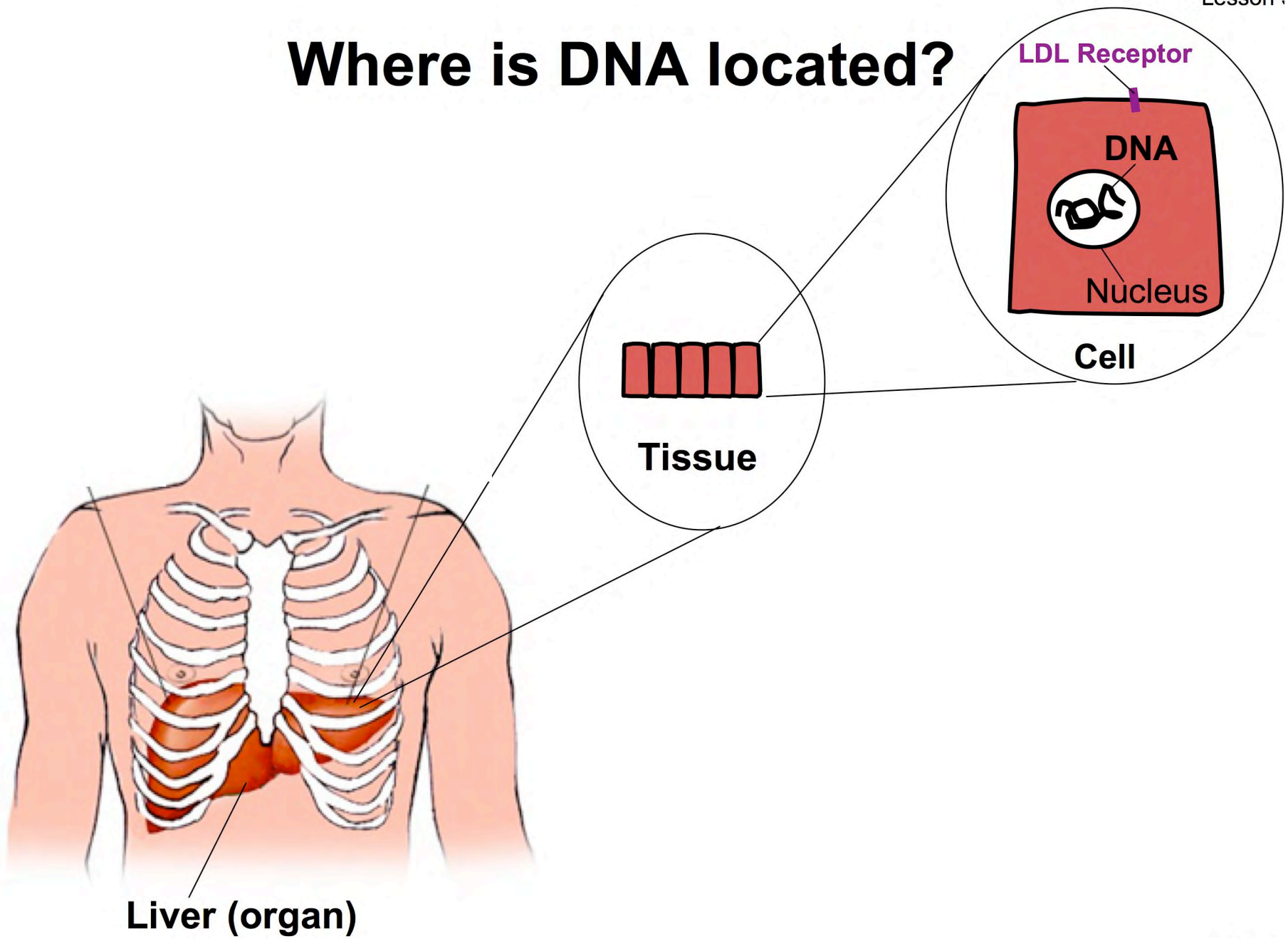


- **Artery wall injured by toxins from smoking, high blood pressure**
- **Arteries harden and narrow due to fat accumulation**
- **Blood flow is reduced**
- **Oxygen supply to heart reduced**
- **Can cause chest pain heart attack or death in severe cases**

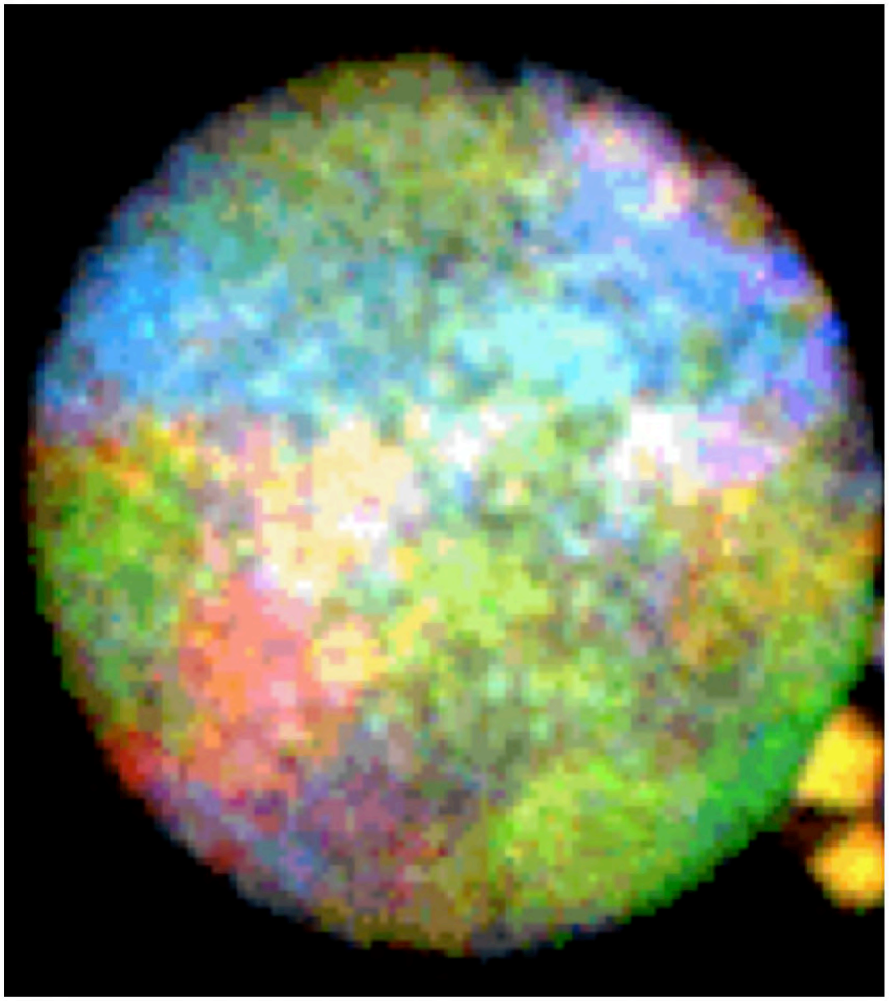
Low density lipoprotein (LDL) Receptor



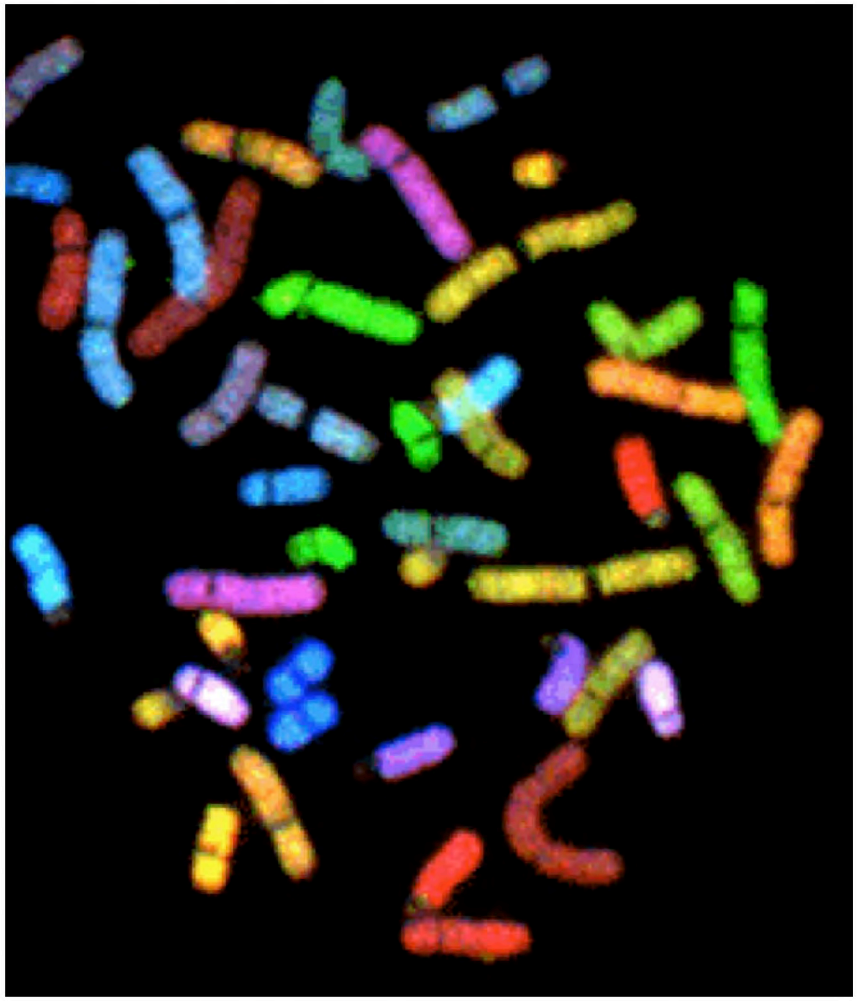
Where is DNA located?



Chromosomes

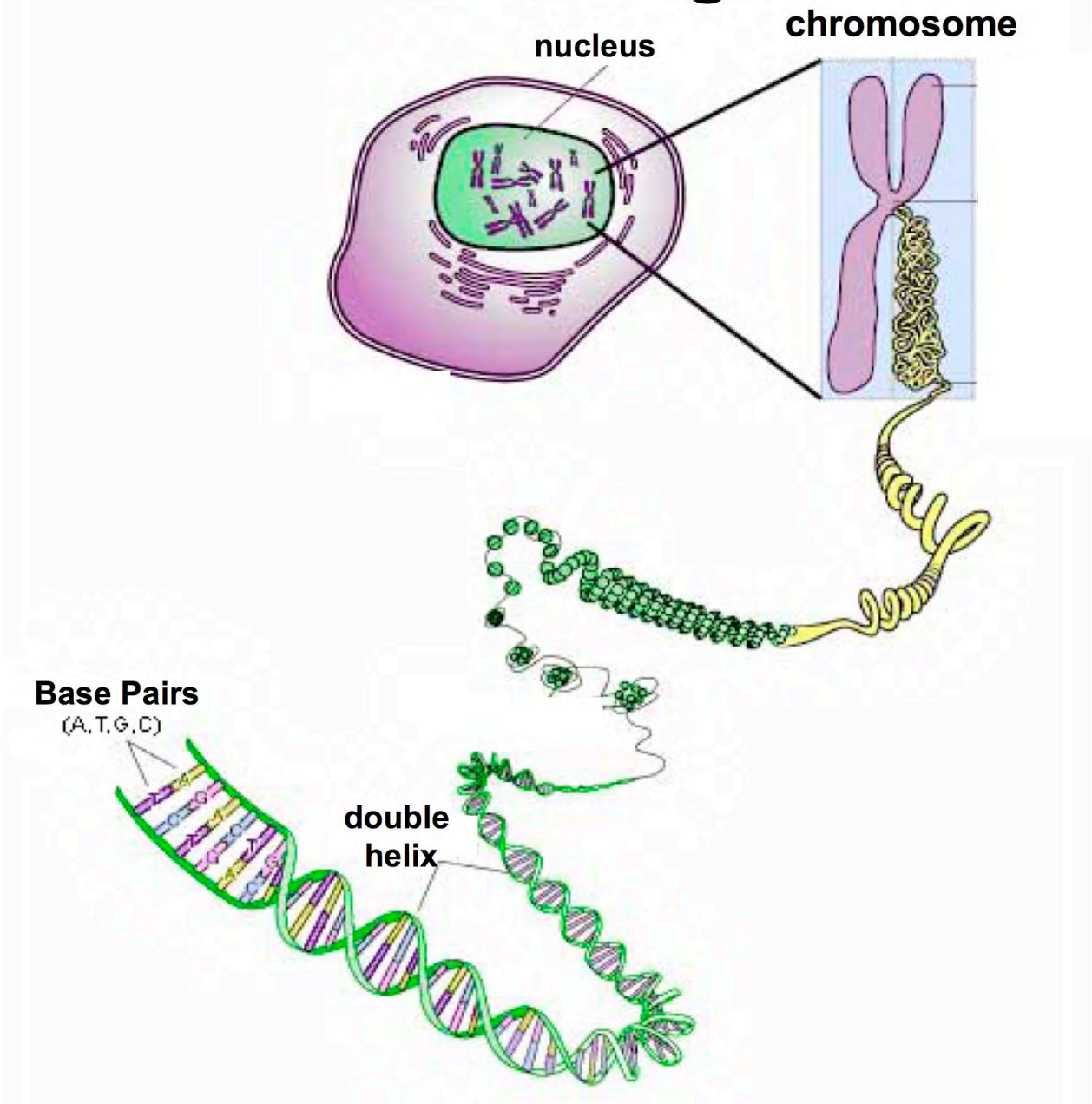


From a cell not dividing
UNPACKED



From a just divided cell
PACKED

Chromosomes are Single Pieces of DNA



How do genes provide instructions for building proteins?

From DNA sequence to Protein overview

http://www-class.unl.edu/biochem/gp2/m_biology/animation/gene/gene_a1.html

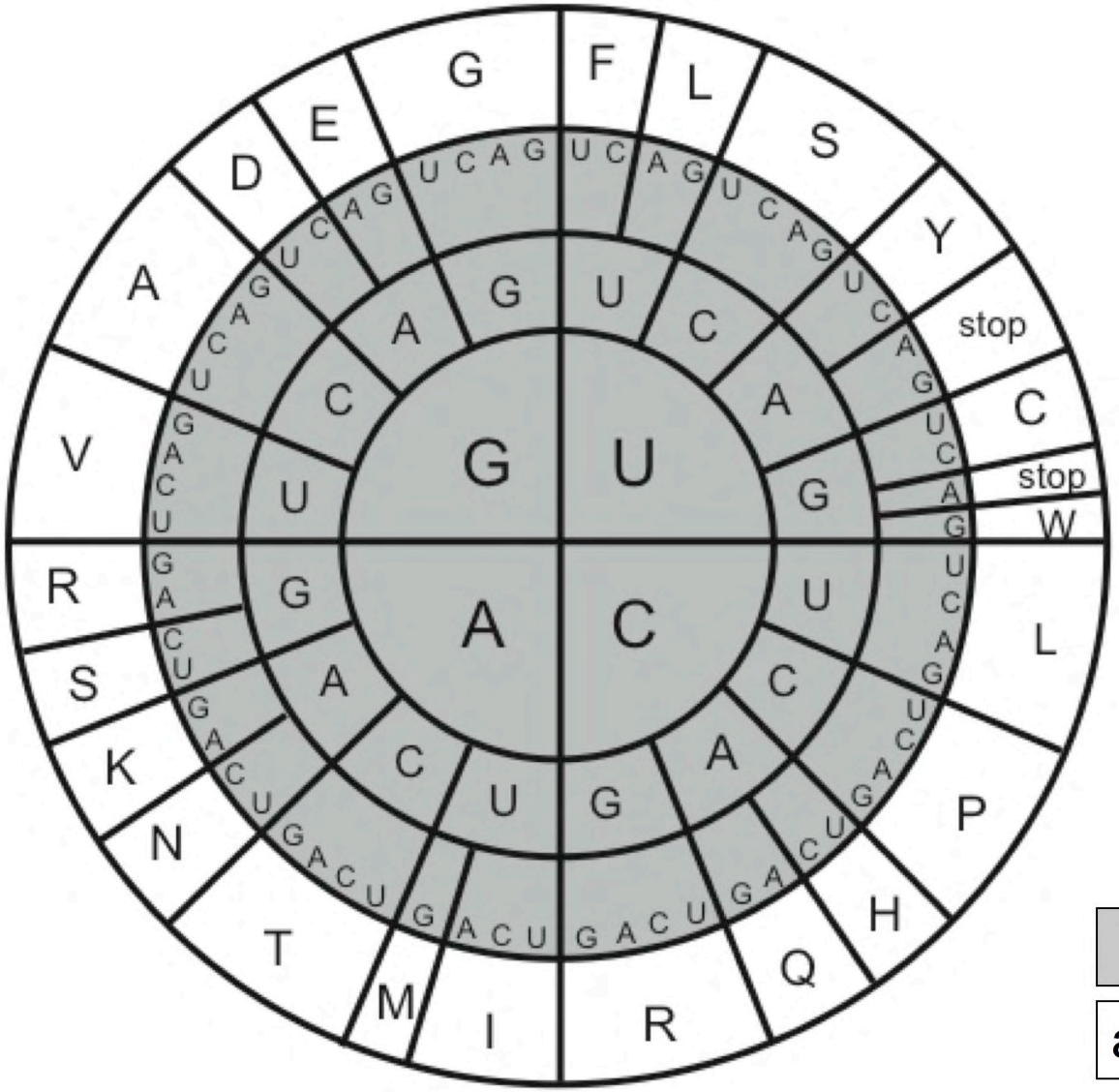
From DNA to RNA - more detail

http://www-class.unl.edu/biochem/gp2/m_biology/animation/gene/gene_a2.html

From RNA sequence to protein - more detail

http://www-class.unl.edu/biochem/gp2/m_biology/animation/gene/gene_a3.html

Coding Amino Acids



RNA

amino acid

Key to Toobers

Blue=positive charge (+)

K, R, H

Red=negative charge (-)

D, E

Yellow=hydrophobic

A, V, L, I, P, M, F, W

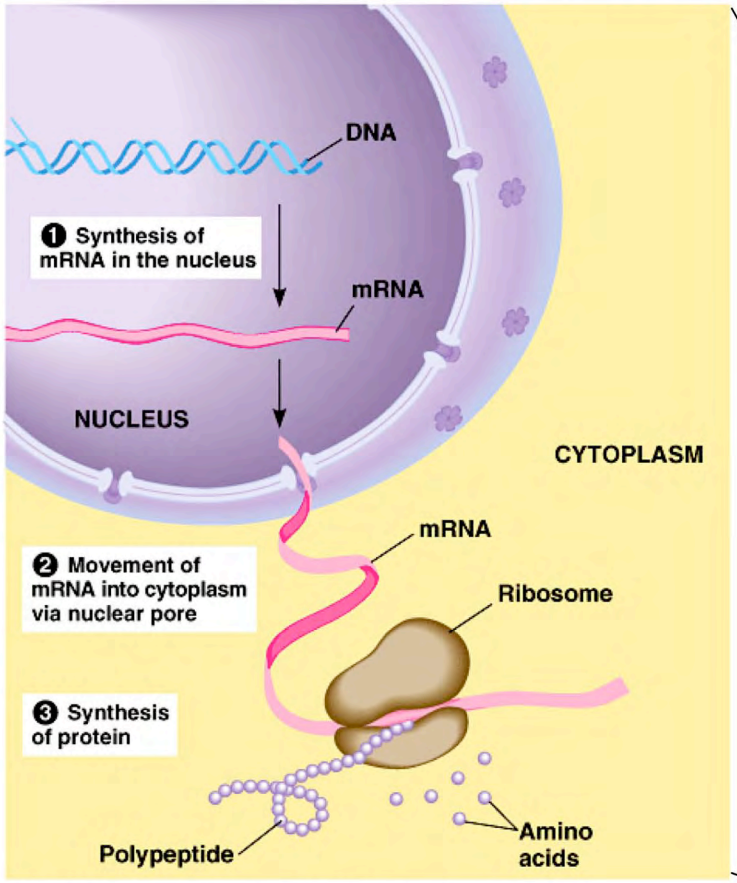
Green=hydrophilic

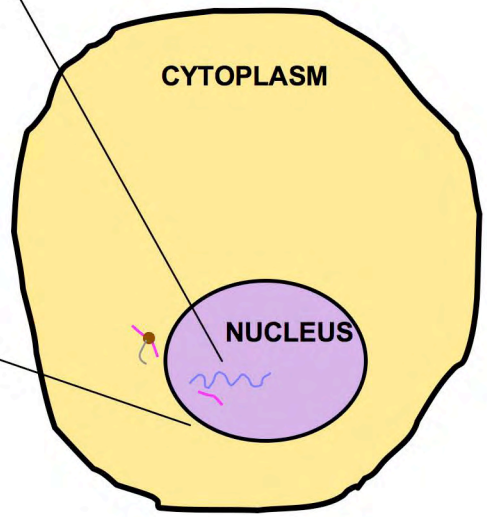
G, S, T, N, Q, Y

White = cysteine

C

Summary: DNA to protein





From Cells to DNA movie

View slide to play movie

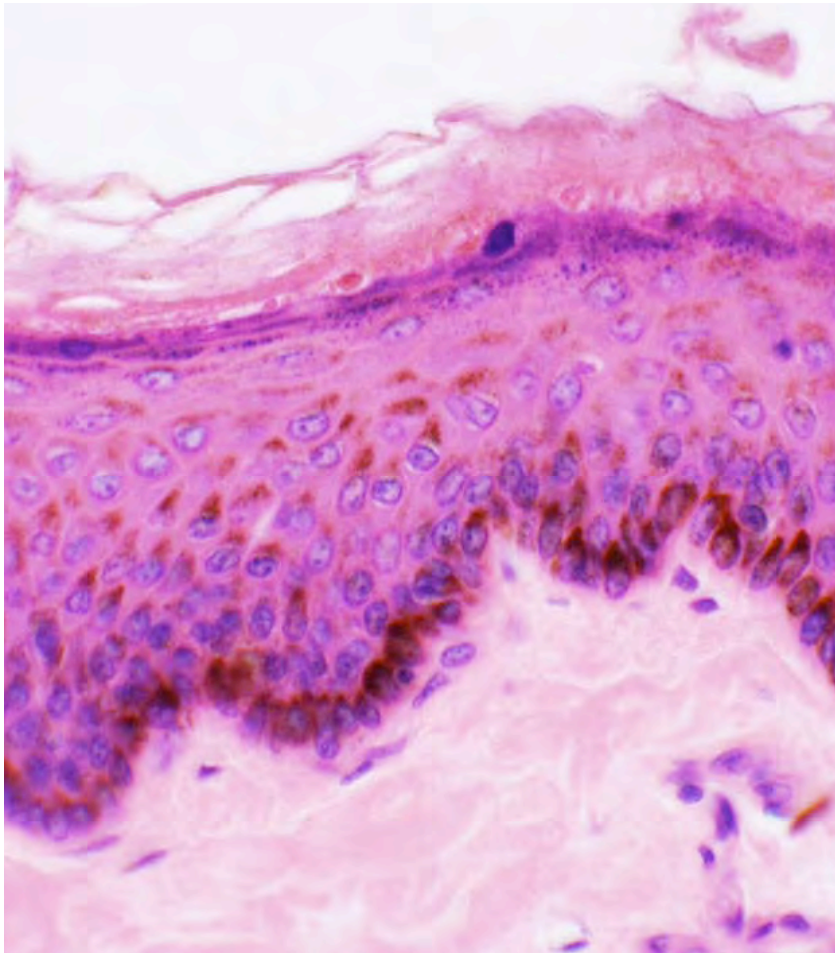
Click for another representation of DNA

From Cells to DNA movie

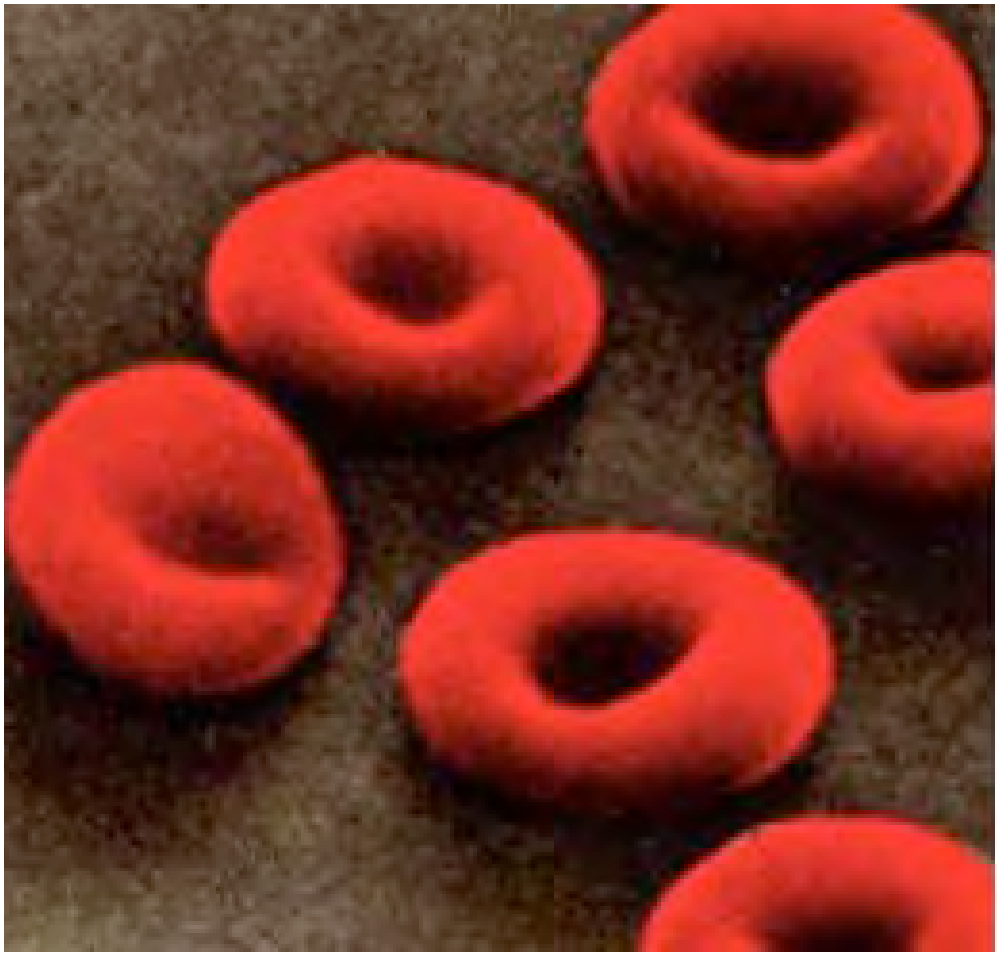
View slide to play movie

Click for another representation of DNA

How similar or different are cells?



Skin cells



Blood cells

1) Prepare gel

Holes for samples to be tested

gel

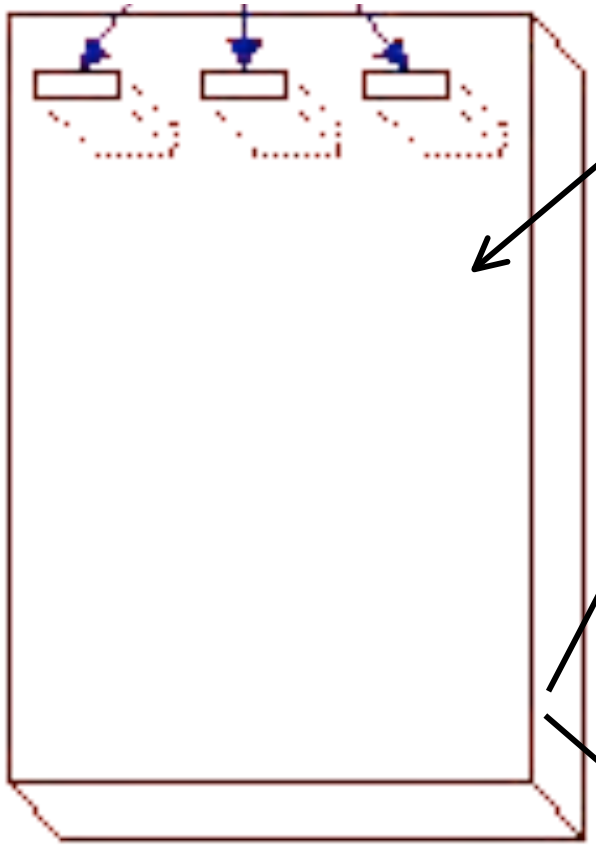
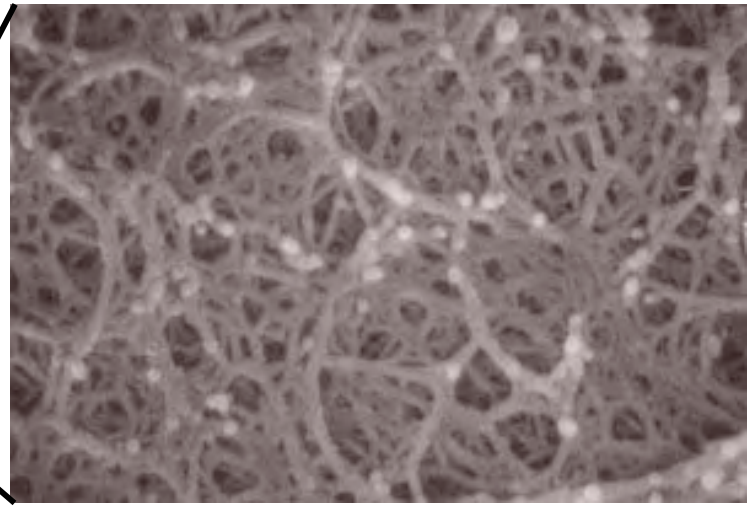
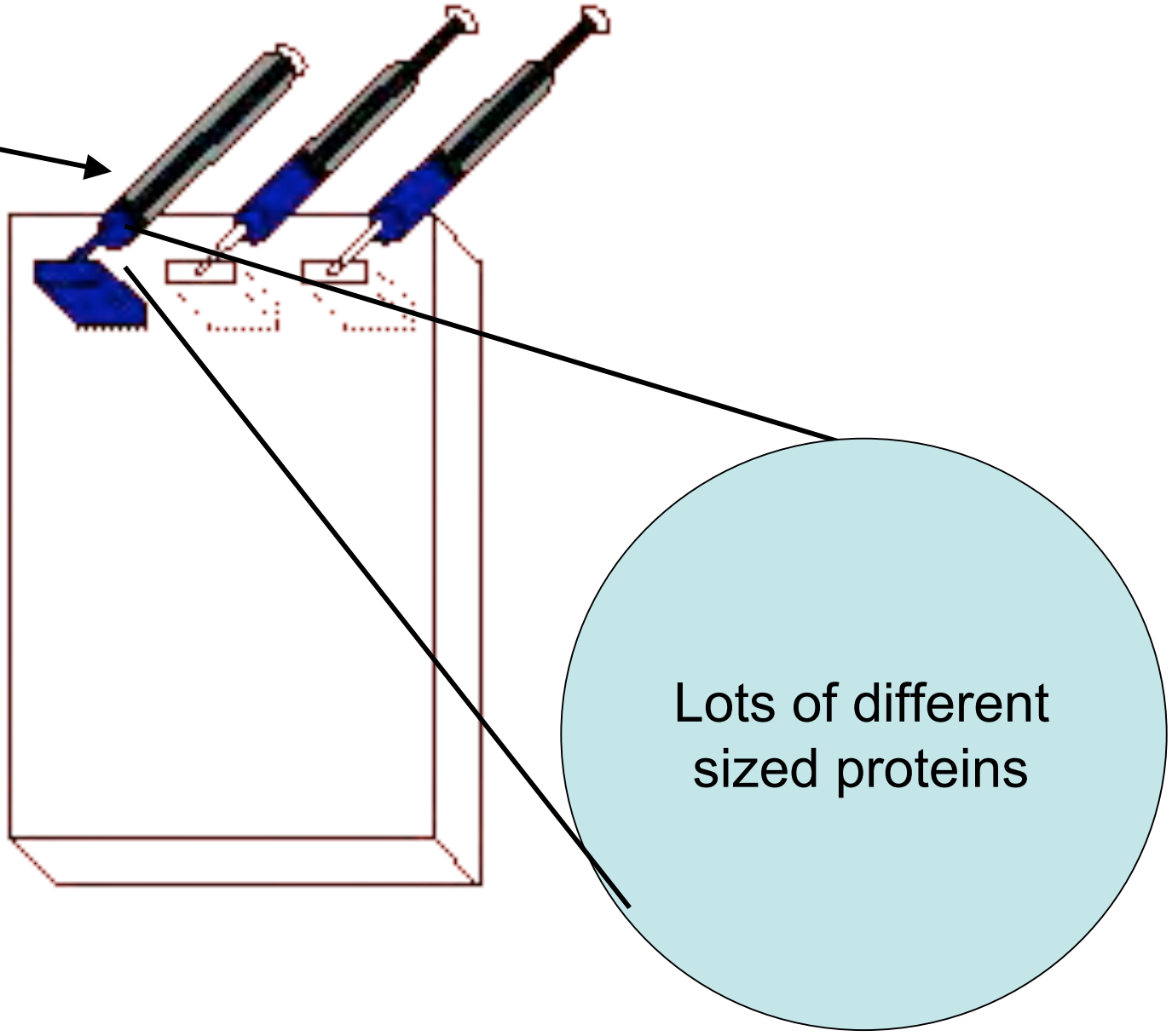


Image from powerful microscope

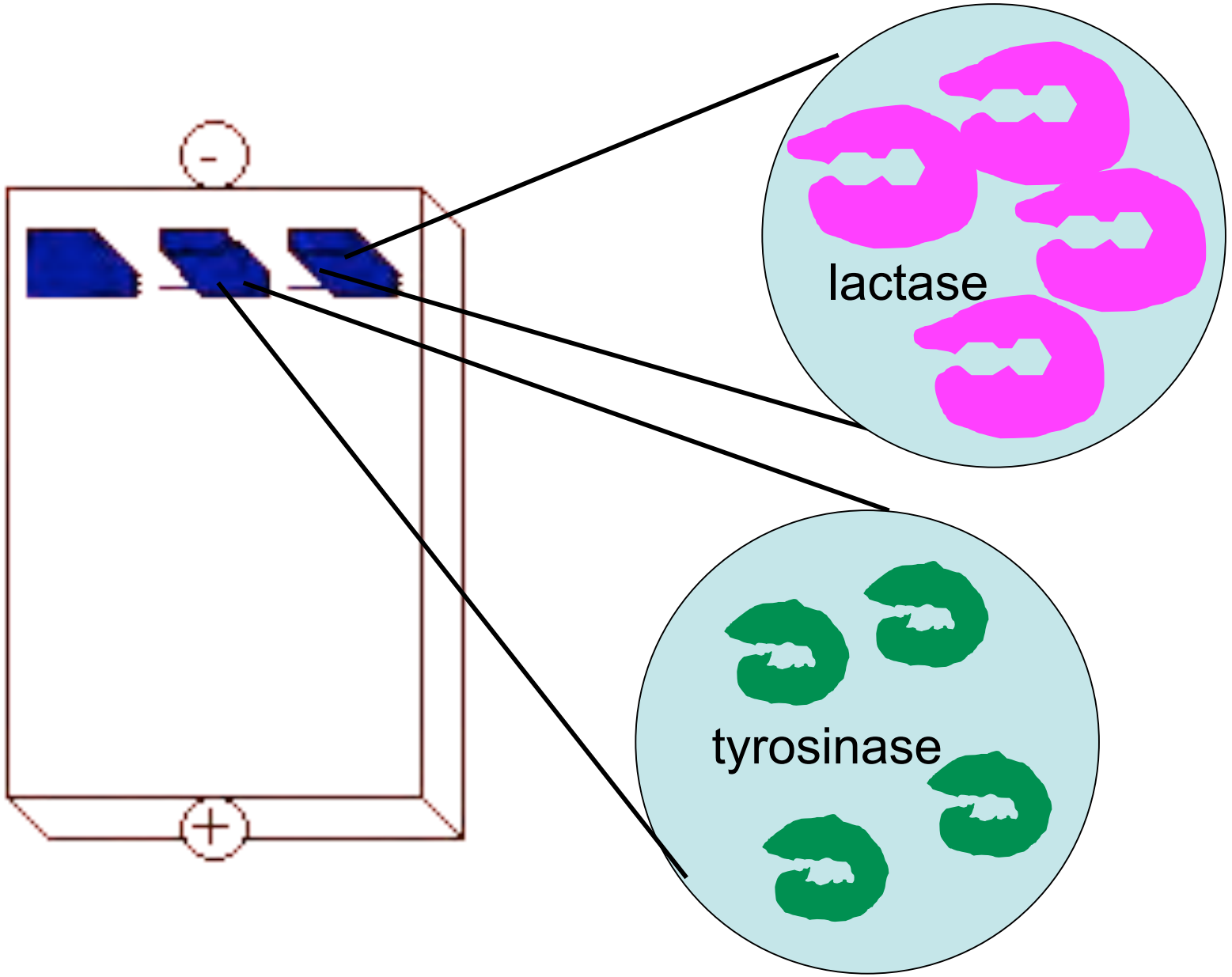


2) Put protein sample in hole

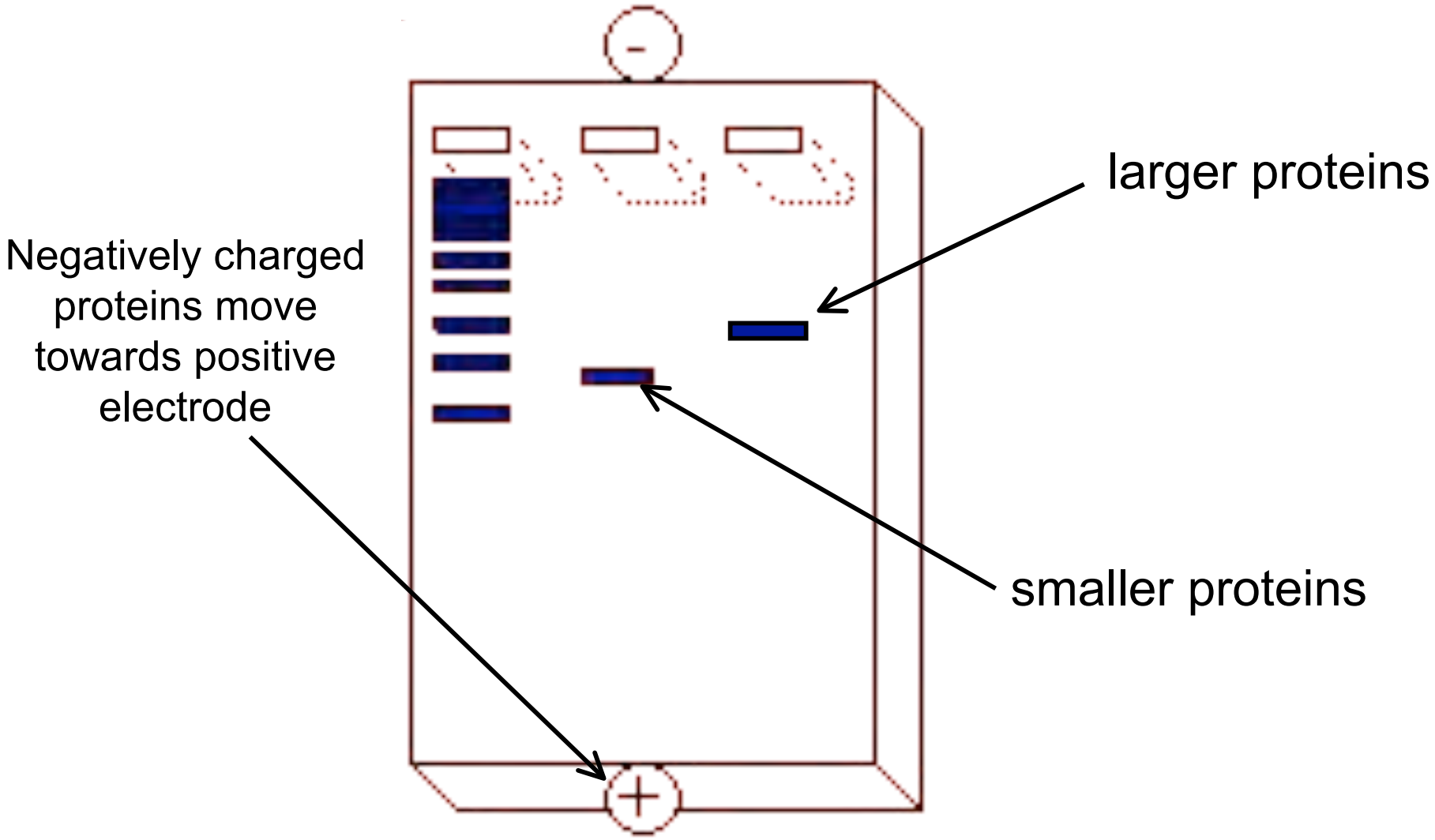
Pipet with solution of proteins



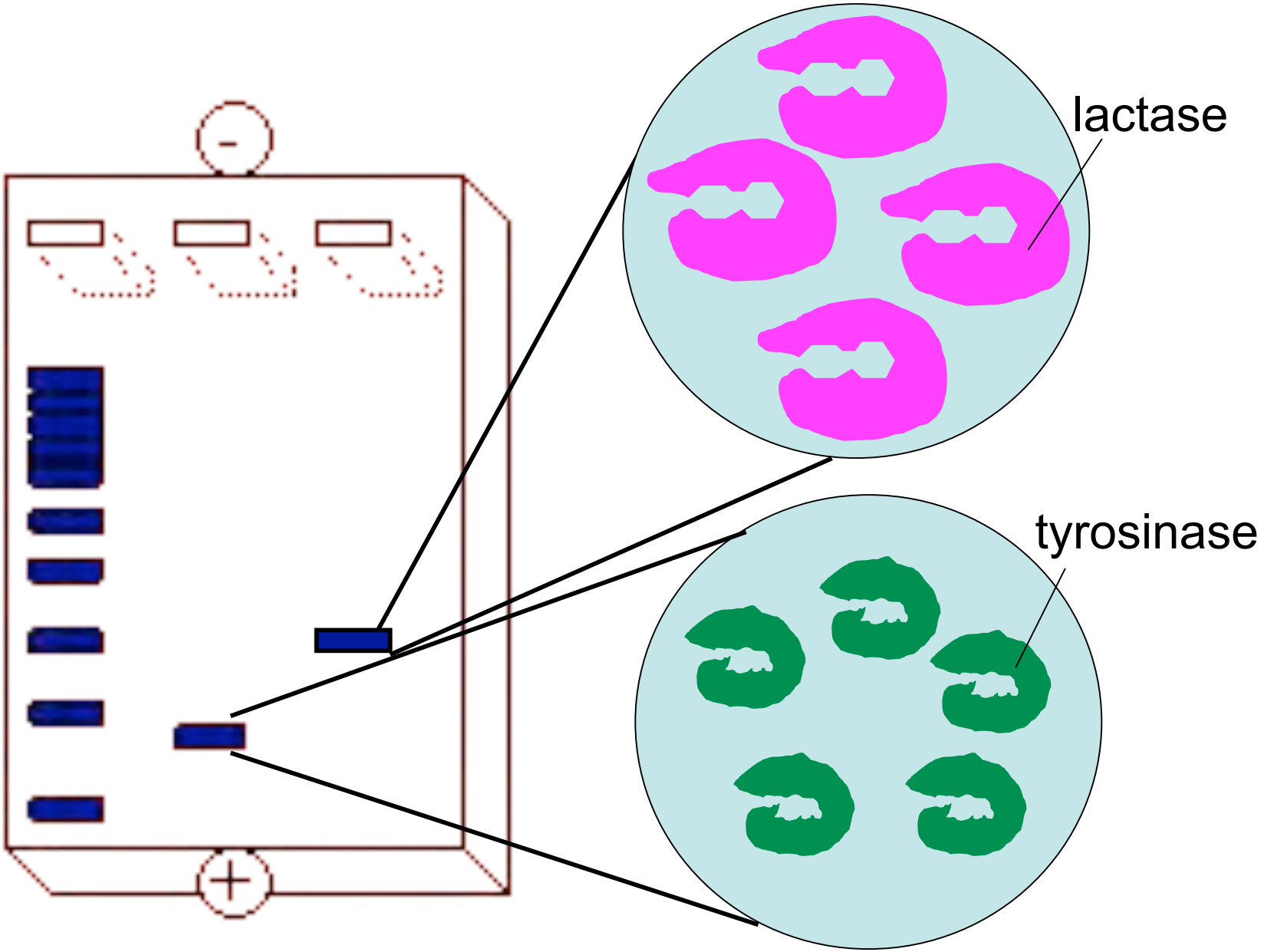
3) Include all the samples you want to test



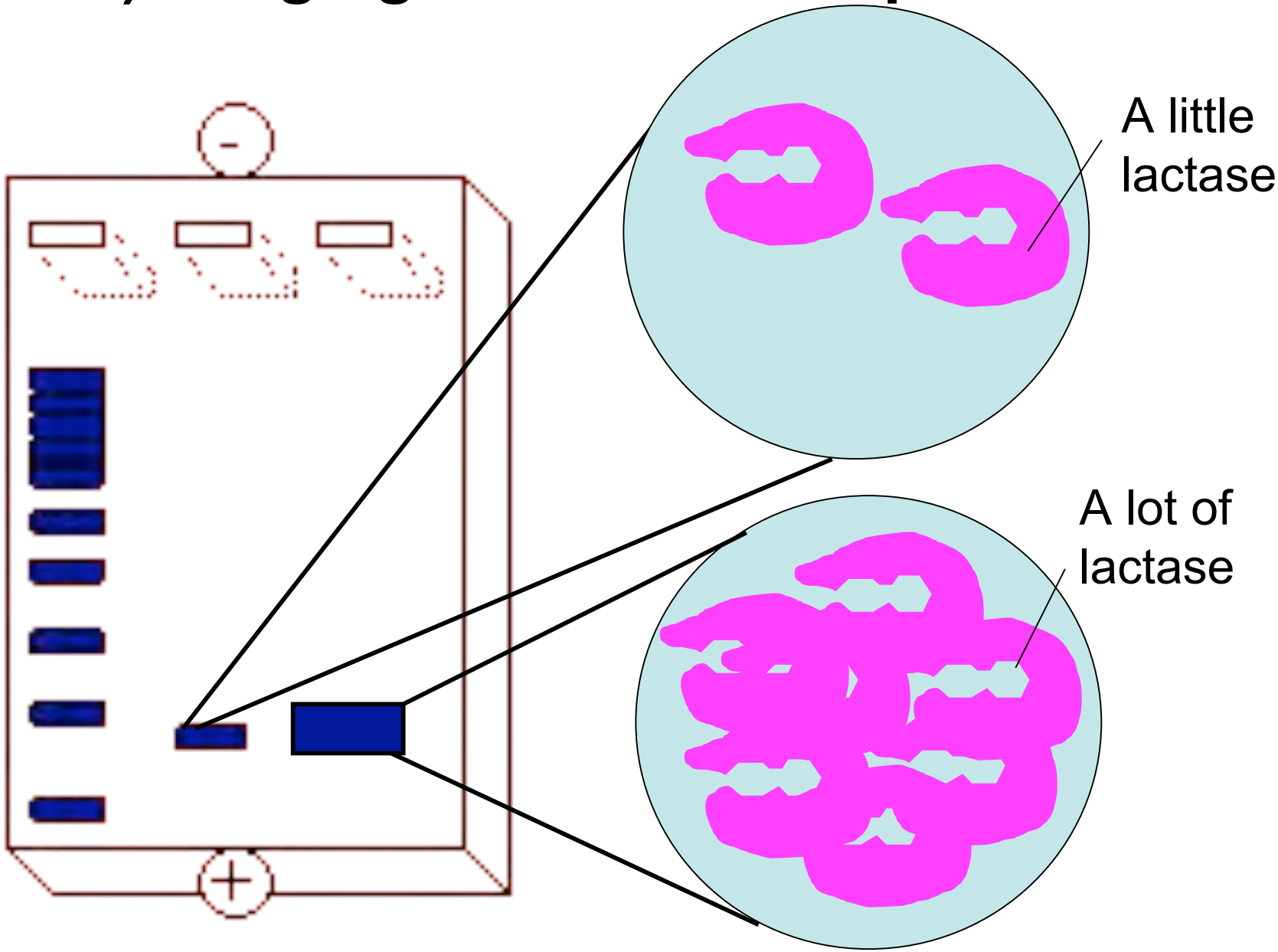
4) Provide power to the electrodes



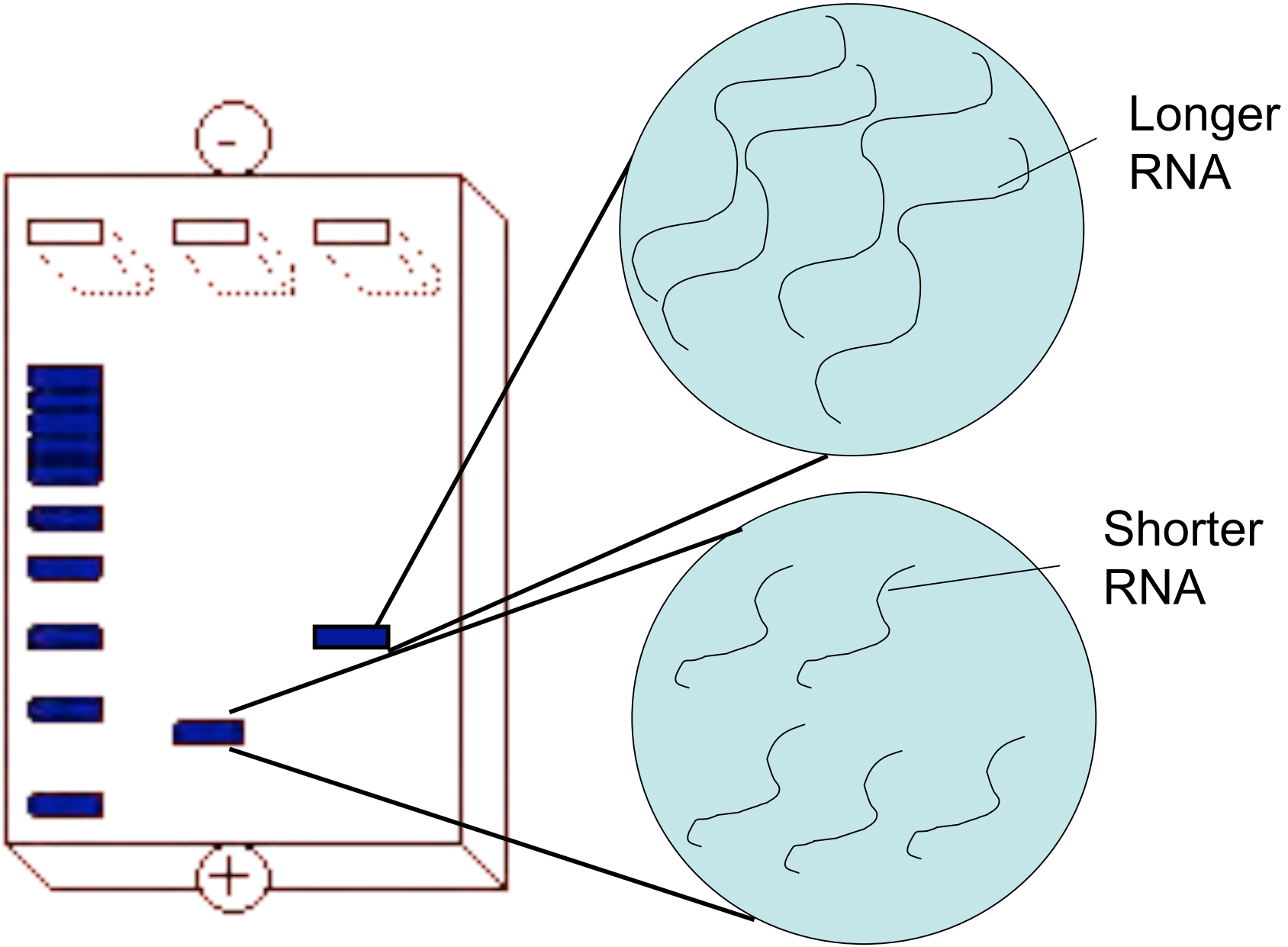
5a) Proteins separate based on size



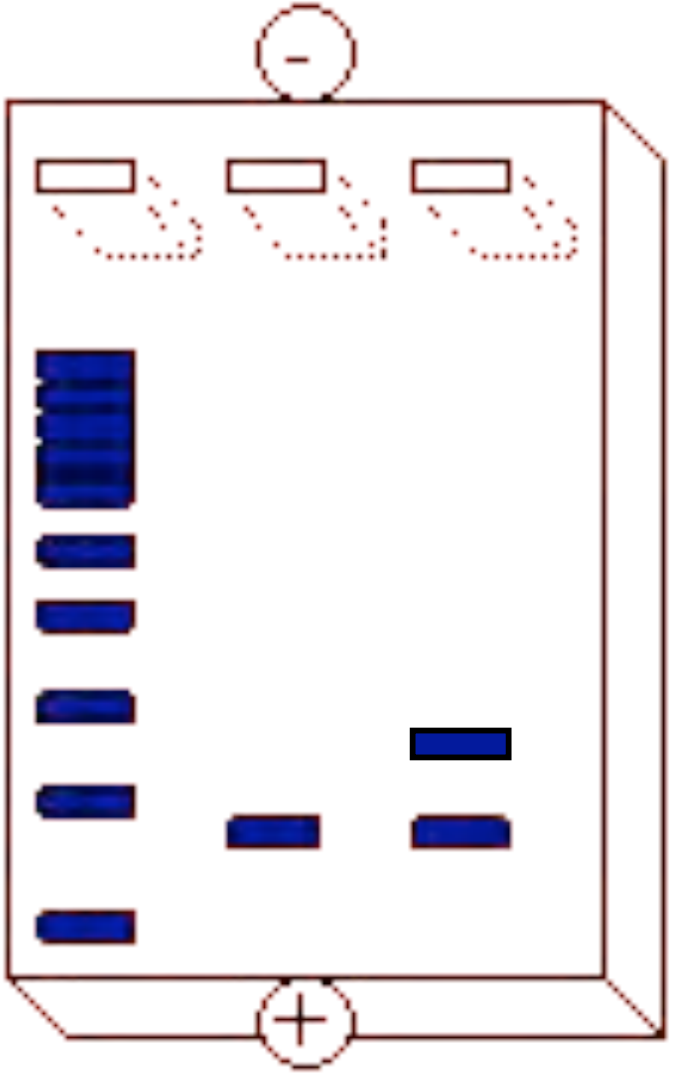
5b) Judging the amount of protein

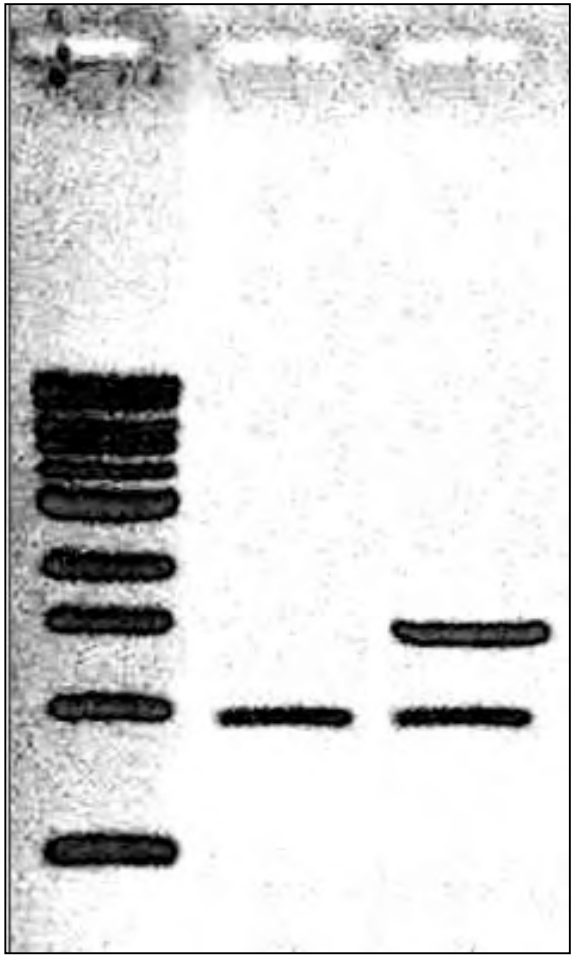


5c) Analyzing RNA



6) Take a picture to record your work





Lactose intolerance in Jason's family

Lactose intolerance:

1) No (Mom)

2) Yes (Jason)

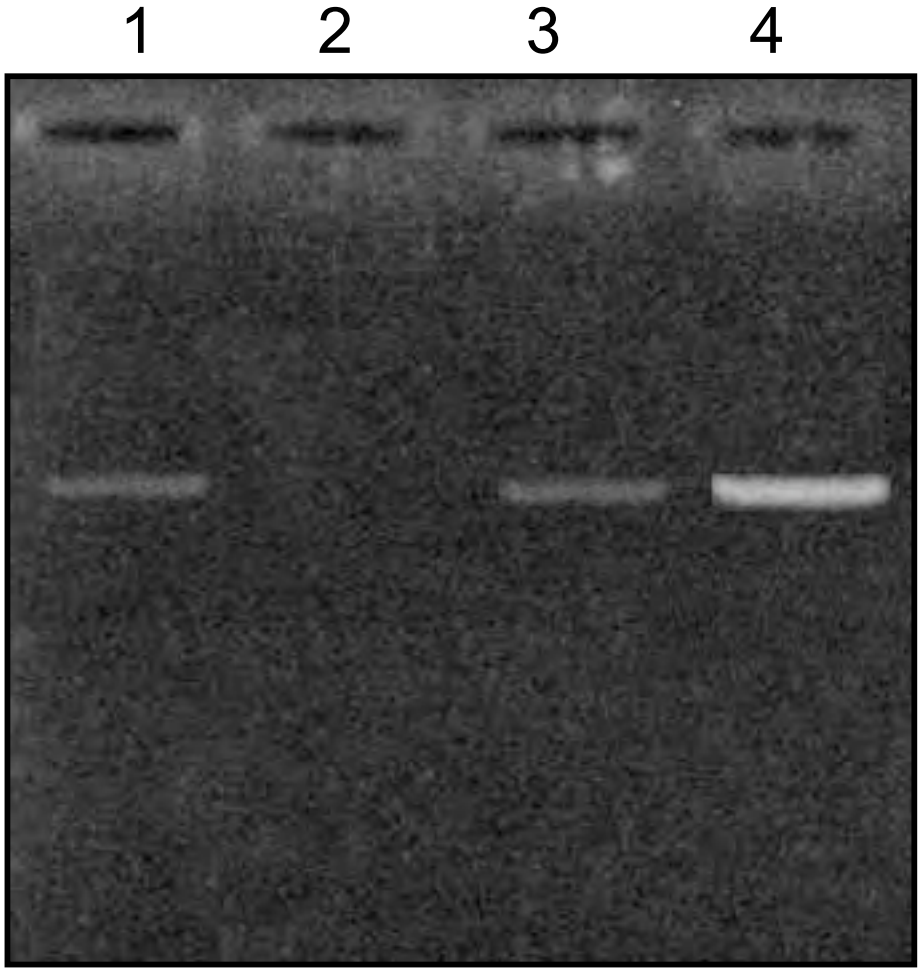
3) No (Chelsea)

4) No (Maya)

Results: DNA sequence analysis of lactase gene:

Mom:	no mutations in lactase genes
Jason:	no mutations in lactase genes
Chelsea:	no mutations in lactase genes
Maya:	no mutations in lactase genes

Results: RNA analysis of lactase gene



Lactose intolerance:

1) No (Mom)
2) Yes (Jason)
3) No (Chelsea)
4) No (Maya)

Gel electrophoresis: Lactase samples from 4 people

Lactose intolerance:

1) No (Mom)
2) Yes (Jason)
3) No (Chelsea)
4) No (Maya)

Why does Jason have no protein?
Why Mom and Chelsea have less protein?

Results: DNA sequence of area near the lactase gene

Mom: ATTTGC |||||| TAAACG ATCTGC |||||| TAGACG	Jason: ATCTGC |||||| TAGACG ATCTGC |||||| TAGACG
Chelsea: ATCTGC |||||| TAGACG ATTTGC |||||| TAAACG	Maya: ATTTGC |||||| TAAACG ATTTGC |||||| TAAACG

Erythropoietin (EPO)

Lots of oxygen

O-O O-O O-O O-O O-O O-O O-O O-O O-O

environment

Small amount of oxygen

O-O O-O O-O

gene

AGCTTCCCGGGATGAGGGCCC
TCGAAGGGCCCTACTCCCGGG

gene “on” **some** of the time

AGCTTCCCGGGATGAGGGCCC
TCGAAGGGCCCTACTCCCGGG

gene “on” **most** of the time

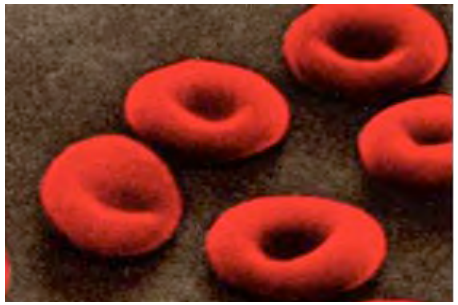
protein

some protein

lots of protein

some cells

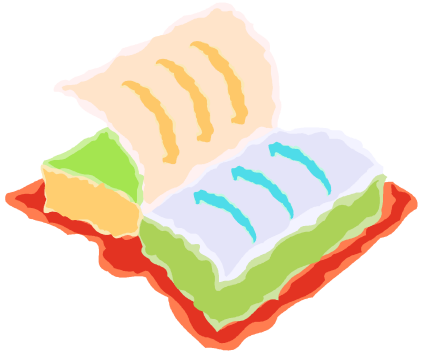
cells



lots of cells

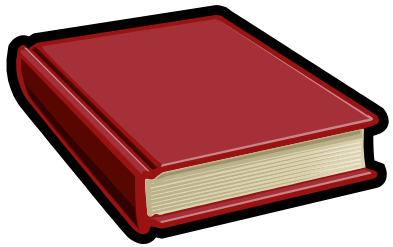
Gene organization

gene



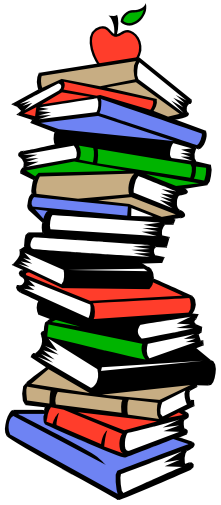
1 set of instructions for how to make 1 protein

chromosome



Thousands of sets of instructions for how to make thousands of proteins (1 book)

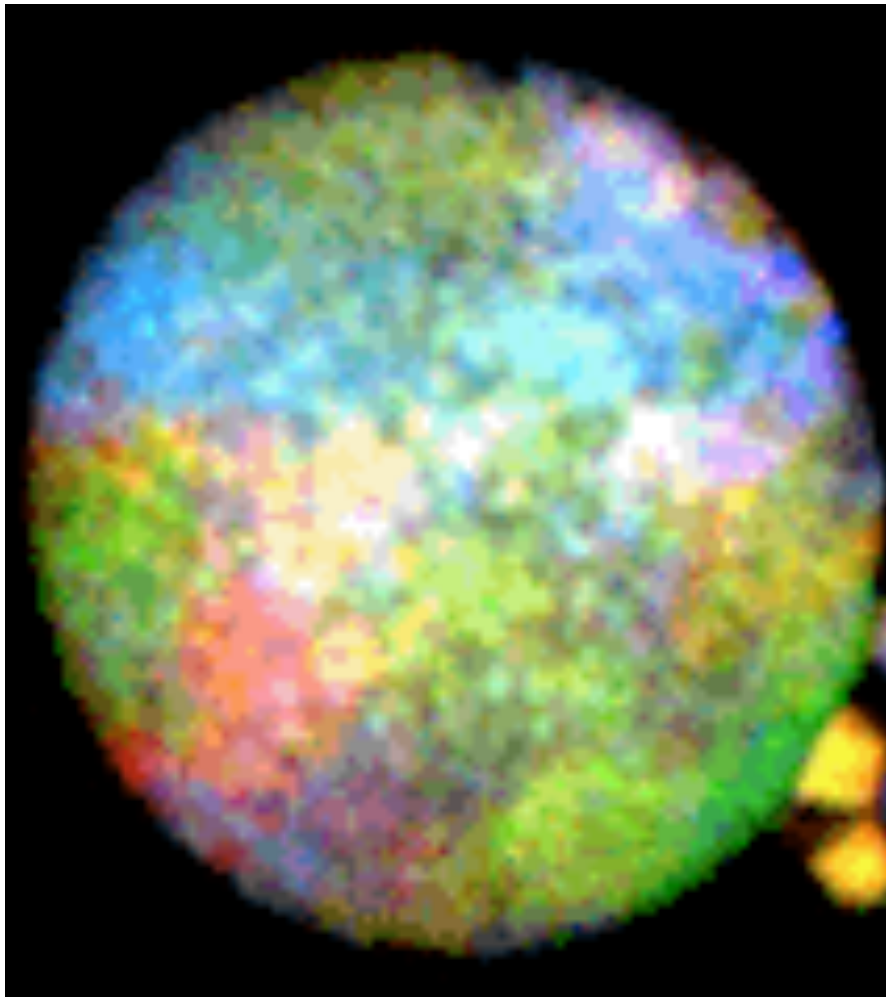
genome



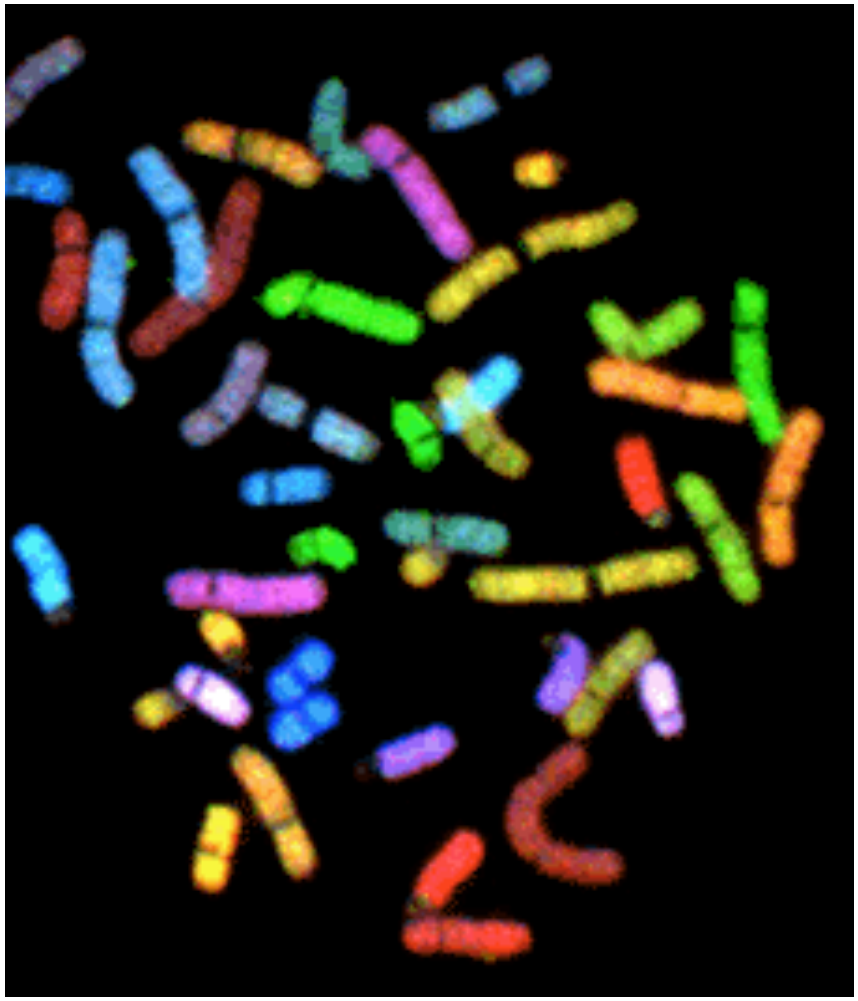
All the sets of instructions for how to make all the proteins we need (23 “books” x 2)

All are written in the same alphabet - DNA

Chromosomes: Interphase vs. metaphase

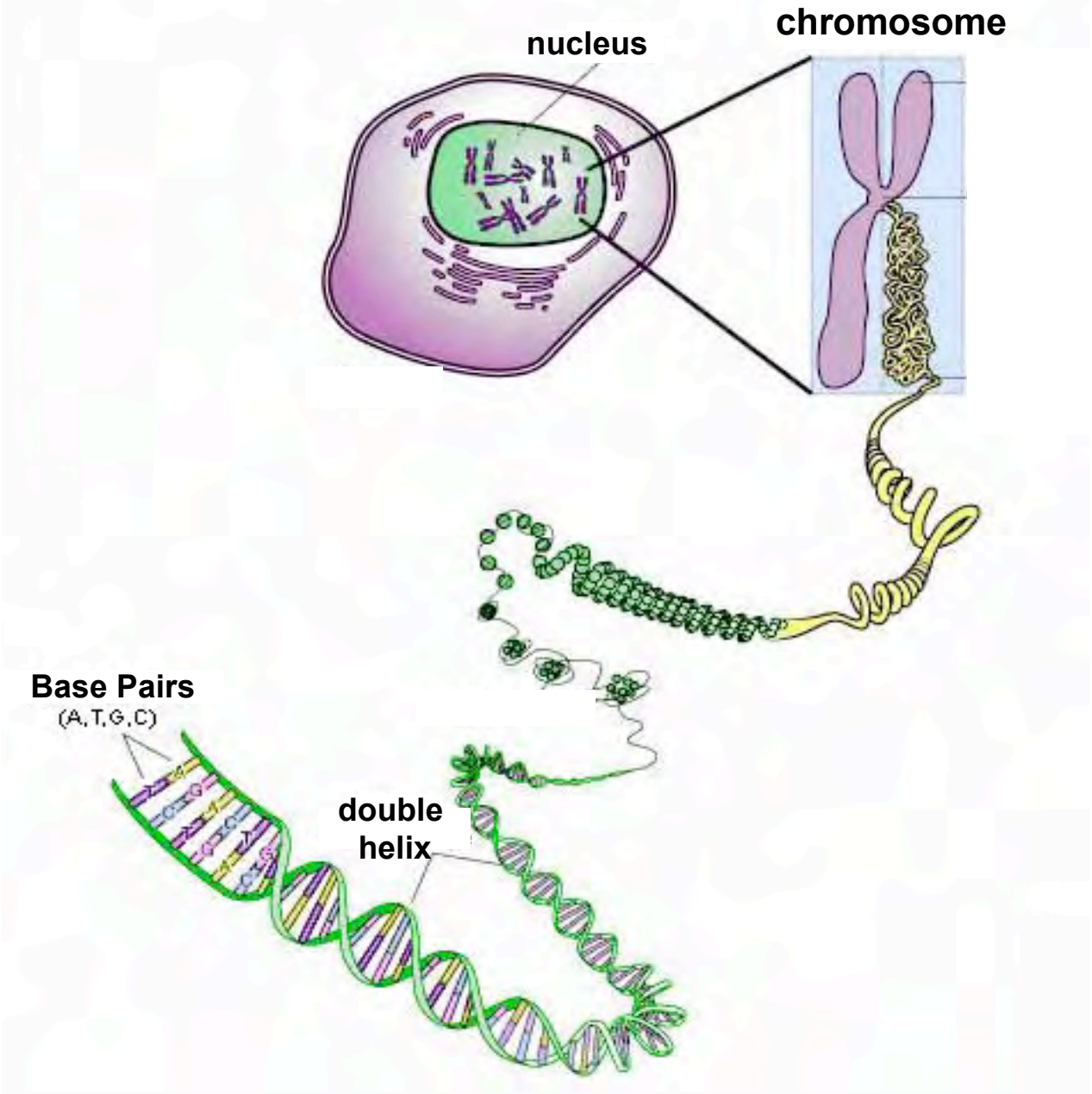


Interphase chromosomes
UNPACKED

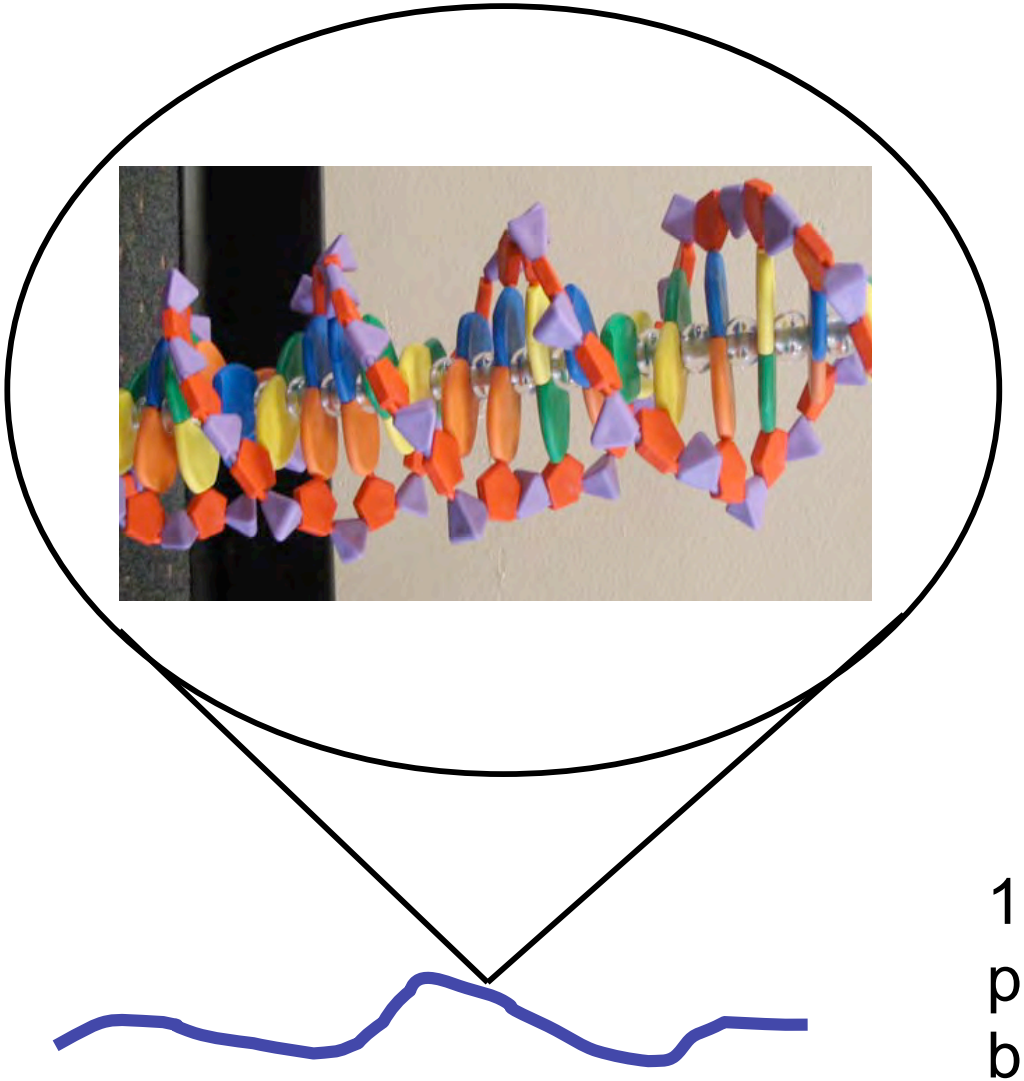


Metaphase Chromosome
PACKED

Chromosomes are single strands of DNA



Size of DNA



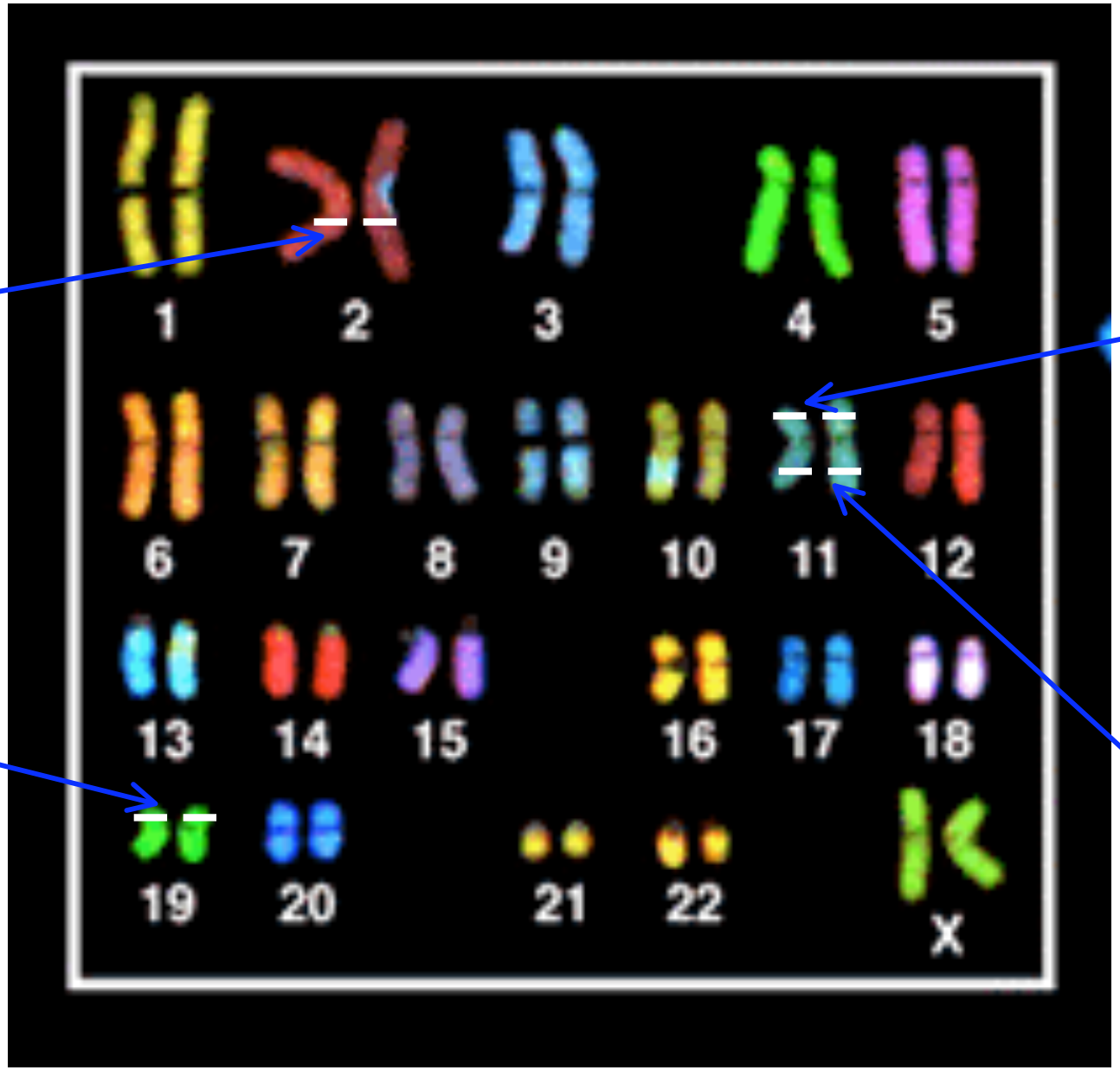
Small piece of DNA

14 pairs of DNA bases = 0.0000035 millimeters

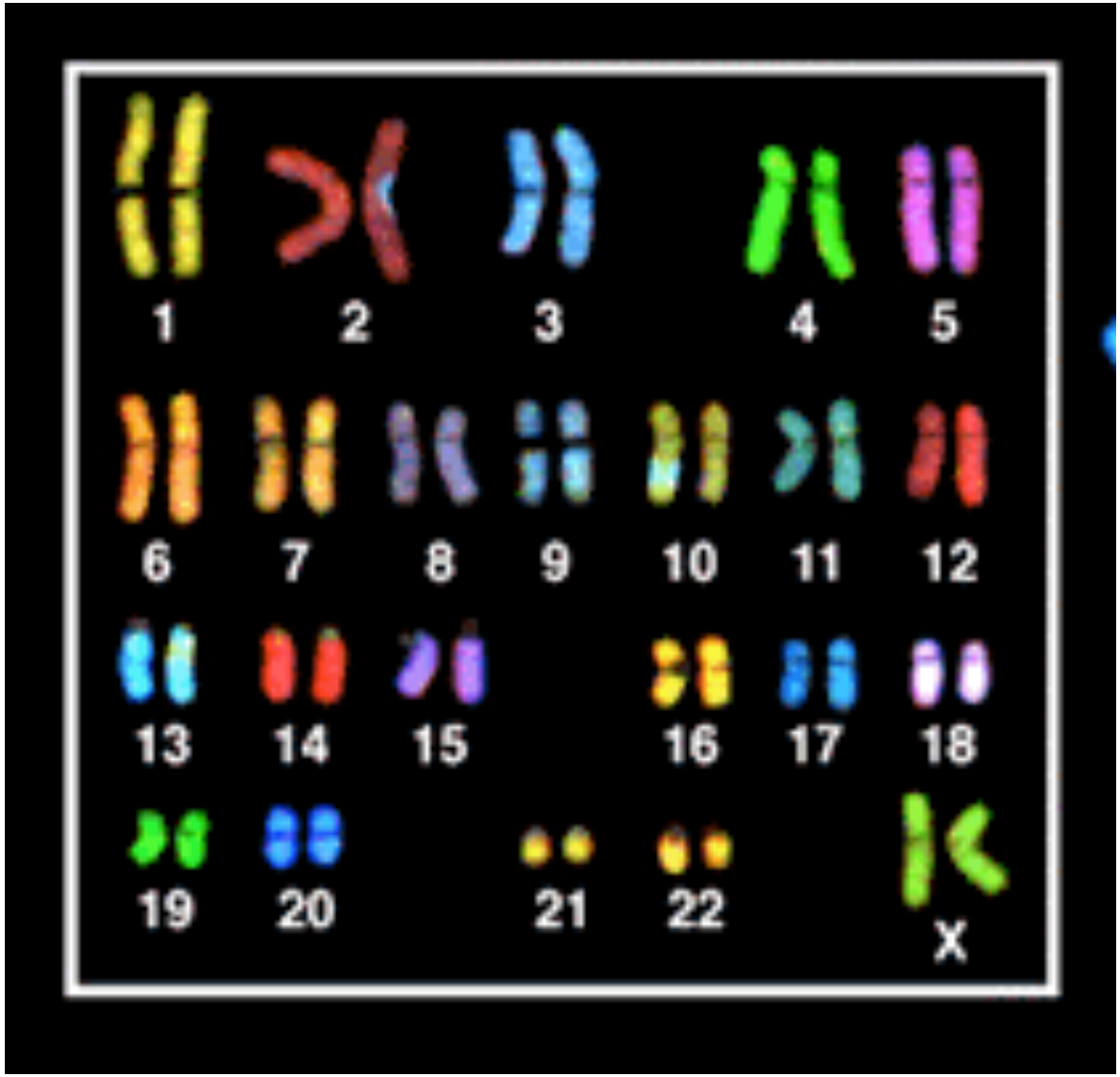
Chromosome 11

135,000,000 pairs of DNA bases = 41 millimeters

Genes in Chromosomes



Human Chromosomes: 23 pairs (one from mom, one from dad)



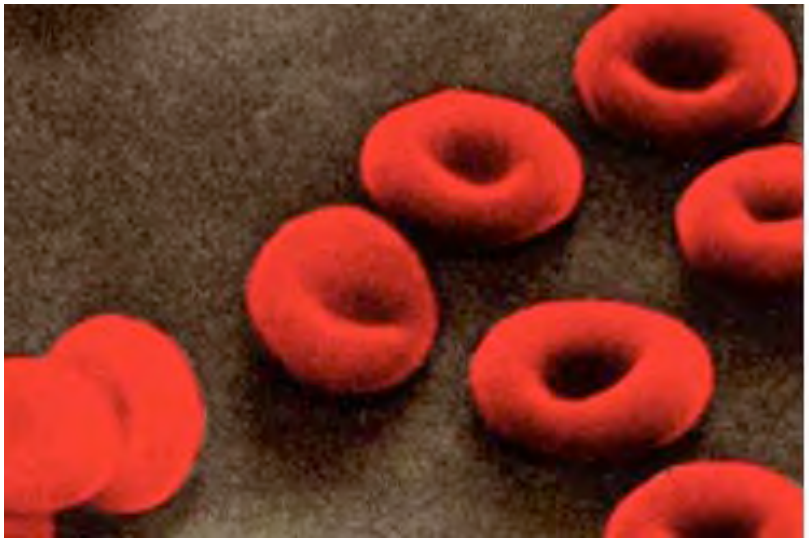
How similar are two DNA sequences?

Example of comparing DNA sequences

Human DNA sequence: ATATTCCAAA
Chimp DNA sequence: ATATTAAAAA
* * * * * * * *

8/10 identical = 80% identical

Sickle Cell Disease

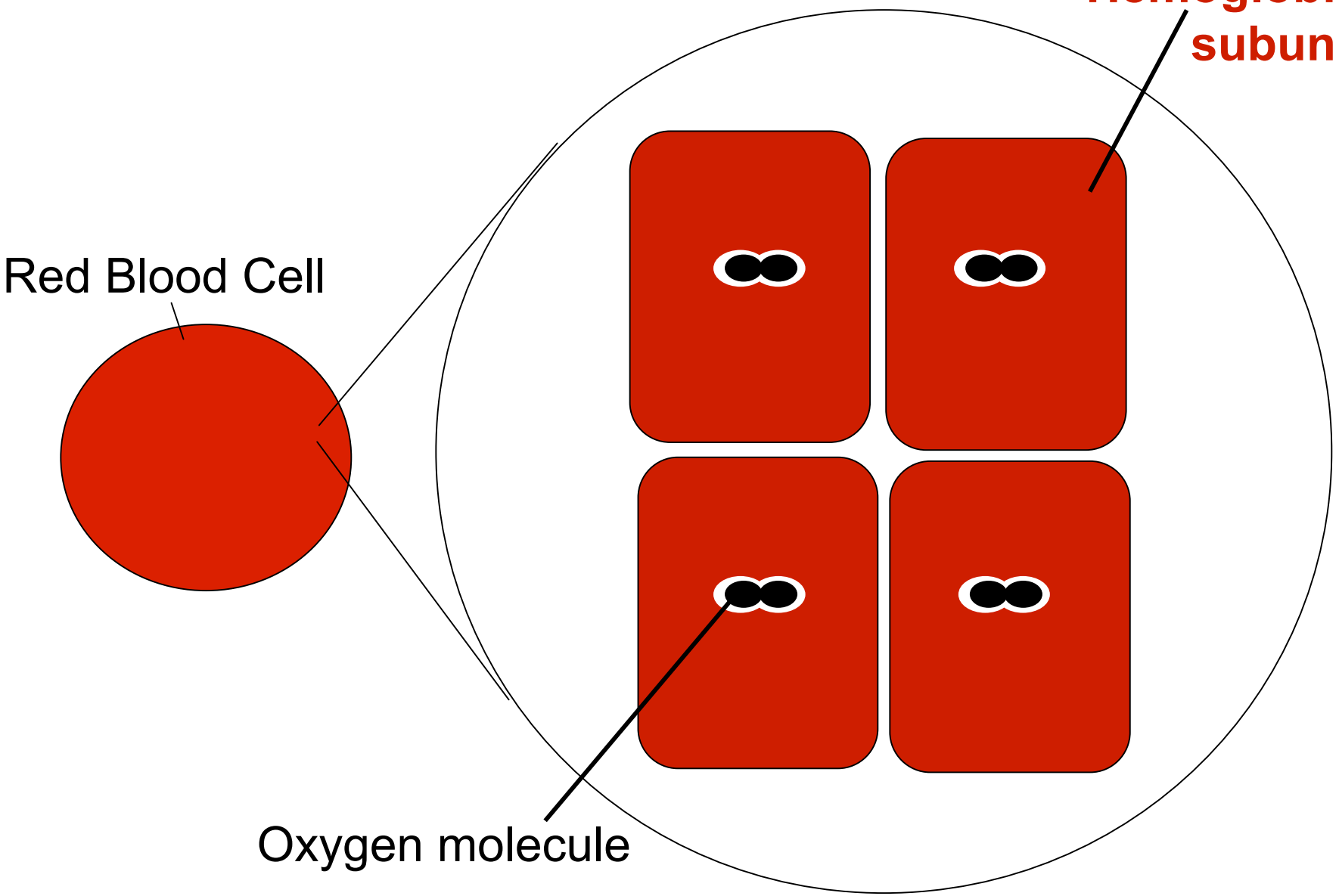


normal red blood cells

sickled red blood cells

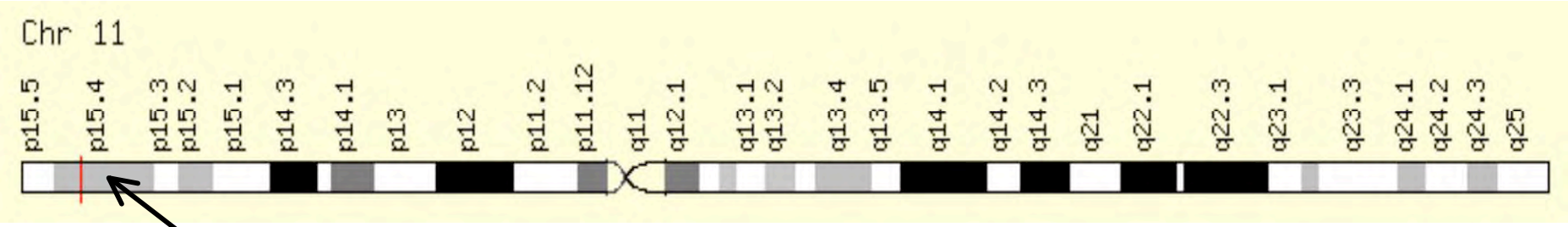
Interview with sickle cell patient: pain

Hemoglobin



Chromosomal location of Hemoglobin

Chromosome 11

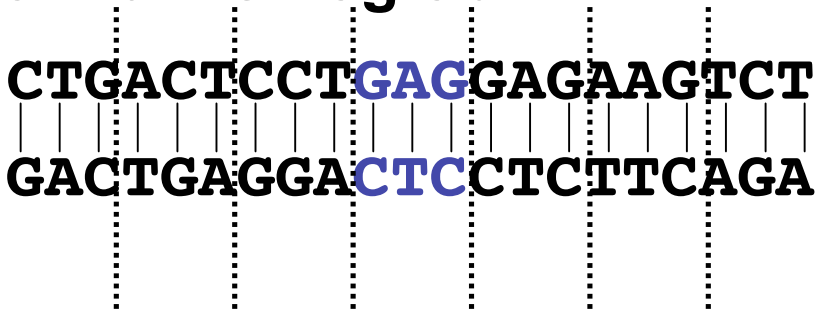


Hemoglobin gene

Mutation found in Hemoglobin

Sequence of normal hemoglobin

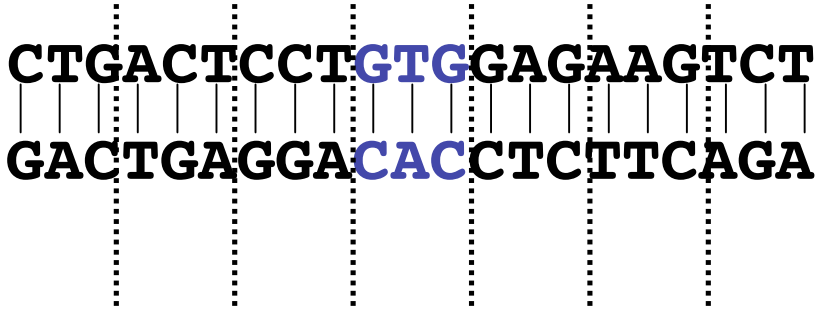
DNA:



Amino acids:

Sequence found in sickling hemoglobin

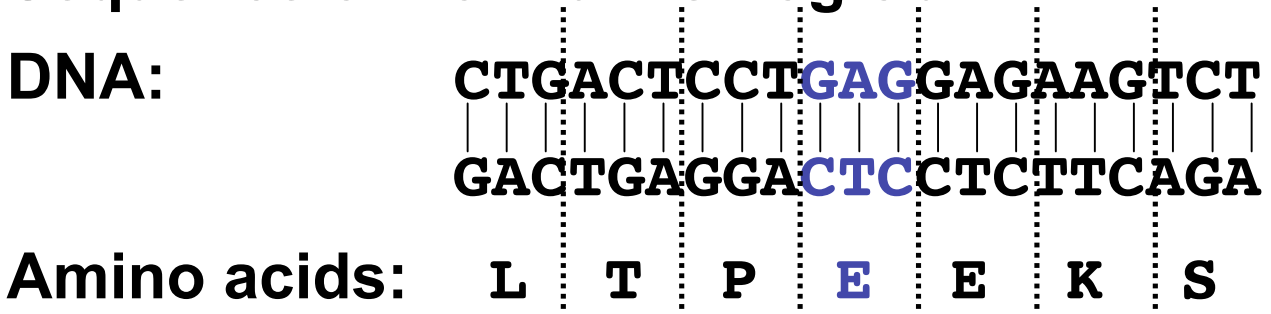
DNA:



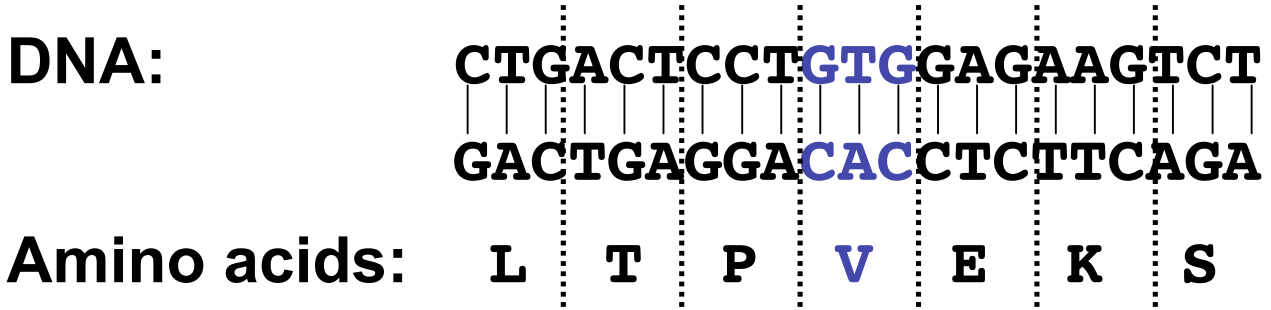
Amino acids:

Mutation found in Hemoglobin

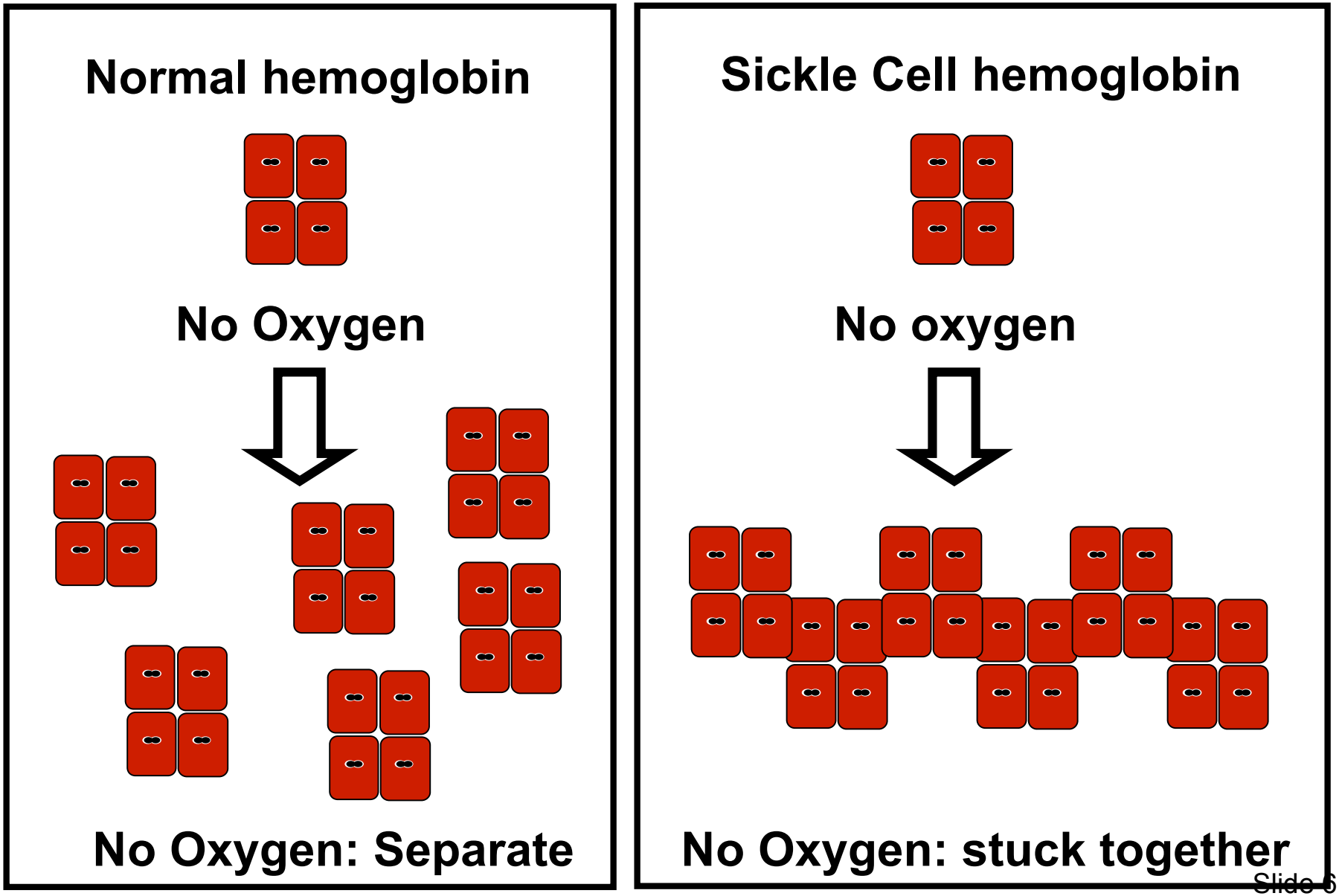
Sequence of normal hemoglobin



Sequence found in sickling hemoglobin



Sickle Cell Hemoglobins Stick Together



Effects of Sickle Cell Mutation

CTGACTCCTGAGGAGAAGTCT
GACTGAGGACTCCTCTTCAGA

CTGACTCCTGTGGAGAAGTCT
GACTGAGGACACCTCTTCAGA

DNA

↓

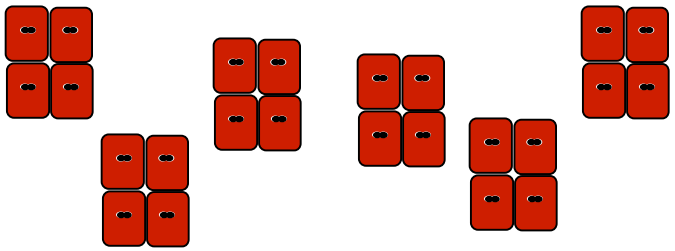
order of amino acids

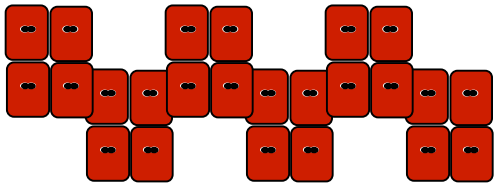
L T P E E K S

L T P V E K S

↓

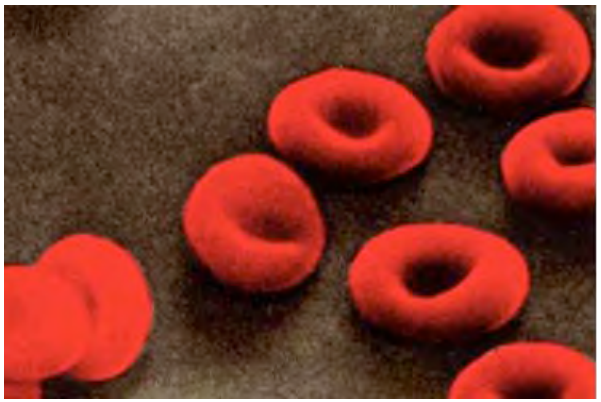
protein shape





↓

cell function



Frequency of Sickle Cell Causing Mutation vs. Frequency of Malaria Causing Microbe