The Mechanistic Details of Arsenic Binding

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Metals play an essential role in many biological reactions. The metabolic pathways of both essential and toxic metals are still relatively unknown. Arsenic is a metal of great current concern. In countries such as Bangladesh, West Bengal, and India, arsenic levels are substantially higher than the 10 ppb limit recommended by the WHO, and chronic arsenic poisoning is often observed. The effects of chronic arsenic poisoning range from hyperkeratosis and skin lesions to cancer of the skin, lung, bladder and kidney. Bioaccumulation of arsenic has also been documented in seaweed and seaweed-eating sheep and is another example of the prevalence of arsenic contamination.

Arsenic toxicity has been well documented, however the mechanistic details of arsenic toxicity are still unknown. Based on the inorganic chemistry of arsenic, it is suspected that sulphur-ligands would be primary targets for arsenic binding. The cysteine in glutathione and the cysteines in metallothionein - a two domain sulphur-rich metal-binding protein that is known to bind to Group 11 and 12 metals in the form of metal-thiolate complexes - are therefore thought to interact with arsenic. Recent studies have shown that inorganic As^{3+} and its two trivalent methylation metabolites; monomethylarsonous acid and dimethylarsinous acid, will bind metallothionein.

We report the conditions under which As^{3+} binds to the individual domains of human metallothionein I, and to metallothionein from the seaweed *Fucus vesiculosus* using electrospray ionization time of flight mass spectroscopy (ESI-TOF-MS). *Fucus vesiculosus* is a brown algae known to accumulate toxic heavy metals. We report $5As^{3+}$ will bind to the 16 cysteines present in Fucus metallothionein[1]. Kinetic and mechanistic data on As^{3+} binding to metallothionein will also be presented. Understanding of the mechanism of metal binding *in vitro* may help to provide models for metal metabolism *in vivo*.

1. Merrifield, M.E., Ngu, T., Stillman, M.J. (2004) Arsenic binding to *Fucus vesiculosus* metallothionein. Biochemical and Biophysical Research Communications. 324: 127-132