Ion pumping by calcium ATPase of sarcoplasmic reticulum : a structural perspective

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Ca^{2+}-ATPase of skeletal muscle sarcoplasmic reticulum (SERCA1a) is an integral membrane protein of 110K and the best characterised member of the P-type (or E1/E2-type) ion translocating ATPases. It consists of 10 transmembrane helices, 3 cytoplasmic domains (A, actuator; N, nucleotide binding; P, phosphorylation) and small lumenal loops. In E1, transmembrane Ca^{2+}-binding sites have high affinity and face the cytoplasm; in E2, the binding sites have low affinity and face the lumen of sarcoplasmic reticulum (extracellular side). Actual transfer of bound Ca^{2+} is thought to take place between two phosphorylated intermediates, E1P and E2P. We have determined the crystal structures of this ATPase in 5 different states that cover the whole reaction cycle, and also carried out all atom molecular dynamics simulations for native structures and some mutants. These analyses show that ion pumps use large rearrangements of cytoplasmic domains to move transmembrane gates of ion pathway, and that ATP, phosphate, Ca^{2+} and Mg^{2+} are the principal modifiers of the domain interfaces. In this presentation, structural basis of ion pumping by Ca^{2+}-ATPase is overviewed briefly with particular emphasis on the transmembrane Ca^{2+}-binding sites.

Movies showing the structural changes in the reaction cycle can be downloaded from the authors' home page (http://www.iam.u-tokyo.ac.jp/StrBiol/).