

About the metal specificity of P1-type ATPases

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P1-type ATPases are responsible for active transport of soft metal ions across membranes. Using ATP hydrolysis as energy source, they accumulate the transported ion on one side of the membrane. In prokaryotes, P1-type ATPases represent one of the detoxification systems allowing the cell to extrude toxic ions out of the cytoplasm. Should the opposite occur and the cell be in a metal deprived environment, P1-type ATPases will fight against metal leaking out of the cell. In eukaryotes also, those that are addressed to the vacuole or to the plasma membrane can achieve detoxification. Finally, in some organisms such as yeast and mammals or photosynthetic bacteria, the P1-type ATPases are addressed to the Golgi network or to the thylakoid membrane and participate to a more sophisticated function that ensures copper homeostasis.

Up to now, two main ionic specificities have been observed among the soft-metal ATPases which have been actually studied. In one group, the ATPases transport Cu^+ or Ag^+ , in the other one, Cd^{2+} , Zn^{2+} , Pb^{2+} , Hg^{2+} or Co^{2+} . According to their sequence and presumed structure, two types of metal binding sites are found in P1-type ATPases. One type is the membrane site which is thought to include the CPC/H motif - one of the P1-type ATPases signatures - and allows the metal ion to cross the membrane, thanks to a tight coupling with ATP hydrolysis. The other type is at the soluble N-terminus of the protein and comprises the CxxC motif - another P1-type ATPases signature. The role of the N-terminus is still not clearly understood, since some P1-type ATPases have been shown to be active, even in the absence of their N-terminus. The importance of each type of site in determining the protein specificity will be discussed from *in vitro* and *in vivo* studies, with special attention to the fact that *in vivo*, the specificity can also depend on expression regulating factors or on partner proteins.