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Structural basis of [2Fe-2S] Cluster Export by Mitochondrial Atm1

Content

In eukaryotes, iron-sulfur clusters are essential cofactors for numerous physiological processes, but these clusters are primarily biosynthesized in mitochondria. Previous studies suggest mitochondrial ABCB7-type exporters are involved in maturation of cytosolic iron-sulfur proteins. However, the molecular mechanism for how the clusters are translocated from mitochondria remains elusive. Here, we report a series of cryo-electron microscopy structures of a eukaryotic homolog of human ABCB7, CtAtm1, determined at average resolutions ranging from 2.8 - 3.2 Å, complemented by functional characterization and molecular docking in silico. We demonstrate that CtAtm1 accepts delivery from glutathione-complexed iron-sulfur clusters. A partially occluded state links cargo-binding to residues at the mitochondrial matrix interface that line the end of a positively-charged cavity. The binding region becomes internalized and is partially divided in the fully occluded state, compatible with transport of a cluster intermediate. Collectively, our findings offer fundamentally new insights into the transport mechanism of eukaryotic ABCB7-type proteins.

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