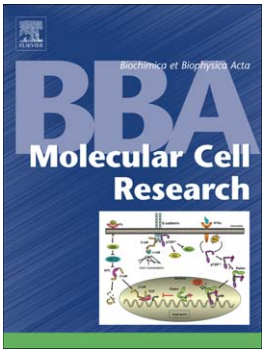

The transport mechanism of the mitochondrial ADP/ATP carrier

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Abstract

The mitochondrial ADP/ATP carrier imports ADP from the cytosol and exports ATP from the mitochondrial matrix, which are key transport steps allowing oxidative phosphorylation in eukaryotic organisms. The transport protein belongs to the mitochondrial carrier family, a large transporter family in the inner membrane of mitochondria. It is one of the best studied members of the family and serves as a paradigm for the molecular mechanism of mitochondrial carriers. Structurally, the carrier consists of three homologous domains, each composed of two transmembrane α-helices linked with a loop and short α-helix on the matrix side. The transporter cycles between a cytoplasmic and matrix state in which a central substrate binding site is alternately accessible to these compartments for binding of ADP or ATP. On both the cytoplasmic and matrix side of the carrier are networks consisting of three salt bridges each. In the cytoplasmic state, the matrix salt bridge network is formed and the cytoplasmic network is disrupted, opening the central substrate binding site to the intermembrane space and cytosol, whereas the converse occurs in the matrix state. In the transport cycle, tighter substrate binding in the intermediate states allows the interconversion of conformations by lowering the energy barrier for disruption and formation of these networks, opening and closing the carrier to either side of the membrane in an alternating way. Conversion between cytoplasmic and matrix states might require the simultaneous rotation of