About mitochondrial importWhile the mitochondrial genome encodes a handful of proteins, most of the hundreds of proteins that reside in the mitochondrion are encoded by nuclear genes, translated in the cytoplasm, and imported into mitochondria via a series of complex molecular machines. Many of the proteins imported into mitochondria are involved in respiration, which is not an essential process: S. cerevisiae is able to carry out either fermentative growth on carbon sources such as glucose, or respiratory growth on nonfermentable carbon sources such as glycerol and ethanol. However, since maintenance of the mitochondrial compartment is essential to life, mutations that completely disrupt mitochondrial import are lethal.About the TIM23 complexThe Translocase of the Inner Mitochondrial membranereceives proteins from the Translocase of the Outer Mitochondrial membraneand either directs them into the mitochondrial matrix or facilitates their integration into the mitochondrial inner membrane. The membrane-embedded core of the complex is composed of three essential proteins: Tim23p, Tim17p, and Tim50p. Tim23p and Tim17p, which share sequence similarity, comprise the twin-pore structure through which precursor proteins translocate. Tim23p alone has the ability to form a voltage-sensitive channel, but Tim17p is required in vivo for maintenance of the twin-pore architecture and for normal function of the pore. Tim17p also has a role in sorting incoming proteins to the mitochondrial matrix or the inner membrane. Tim50p interacts with precursor proteins and with Tim23p to guide precursors from the TOM complex to the TIM23 complex. Two additional non-essential components, Tim21p and Pam17p, interact with the core of the TIM23 complex and may modulate its activity.Proteins destined for the mitochondrial matrix require the action of a sub-complex of the TIM23 complex, known as the import motor or presequence translocase-associated motorcomplex. Its catalytic component is Ssc1p, a member of the heat shock 70 protein family commonly referred to as mtHsp70, which undergoes cycles of binding and release of the precursor, hydrolyzing ATP and changing conformation in the process. The nucleotide release factor Mge1p promotes this cycle by facilitating the dissociation of ADP from Ssc1p. Other components include Tim44p, an essential subunit that mediates the association of the core TIM23 complex with the PAM complex; Pam18p, a J-protein cochaperone that stimulates the ATPase activity of Ssc1p; and Pam16p, a J-like protein that binds to Pam18p and regulates its activity. Pam17p mediates the association between Pam16p and Pam18p. Once imported proteins reach the mitochondrial matrix, their correct folding is facilitated by a soluble complex consisting of Ssc1p and its cochaperones Mdj1p and Mge1p.A subset of proteins destined for insertion into the mitochondrial inner membrane is translocated via the TIM23 complex but then inserted laterally into the inner membrane rather than entering the mitochondrial matrix. This mechanism is currently not understood in detail. The TIM23 complex adopts different conformations during the two kinds of import, but it is unclear whether this inner membrane import is accomplished by the core complex alone, or by the entire TIM23 complex including the import motor subunits.About MGE1 MGE1 encodes an essential protein of the mitochondrial matrix that is a sequence and functional homolog of E. coli GrpE. Mge1p and related proteins act as nucleotide release factors for chaperones of the Hsp70 family: after ATP hydrolysis by the chaperone, the nucleotide release factor promotes the dissociation of ADP, allowing the binding and hydrolysis of another ATP molecule. Mge1p promotes ADP release from Ssc1p in the import motor complex, allowing the cycle of ATP-dependent protein translocation to proceed. Certain conditional mge1 mutations affect its function in import. Mge1p also acts in a soluble complex in the mitochondrial matrix, with Ssc1p and the J-protein Mdj1p, that re-folds denatured proteins. In addition, Mge1p functions as a nucleotide release factor for the Hsp70 family chaperone Ssq1p, which facilitates the folding of proteins containing iron-sulfur clusters.