**Sym1 forms a channel in the inner mitochondrial membrane**

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The mitochondrial DNA depletion syndrome (MDS) is characterized by a rapidly progressing liver failure and neurological defects. Patients carry autosomal recessive mutations in the gene *MPV17/SYM1,* which causes loss of mtDNA and defects in the respiratory chain. Here we report on the yeast protein Mpv17/Sym1, which localizes to mitochondria, where it is integrated in the inner mitochondrial membrane.BN-PAGE of solubilised mitochondrial membranes revealed that Mpv17/Sym1 isorganized into at least two high molecular weight complexes of 120 and 220 kDa. Using import studies of *in vitro* translated protein into isolated mitochondria we dissected the import pathway of the yeast protein and structural requirements necessary for its proper assembly. Mpv17/Sym1 is homologous to a highly abundant protein in the peroxisomal membranes, which was shown to form a channel. In order to discover a similar function, yeast Mpv17/Sym1 was affinity purified from isolated mitochondria, reconstituted in lipid bilayers and electrophysiological measurements were performed. We are able to show that yeast Mpv17/Sym1 has a channel forming activity. For a biochemical analysis, mutants in the yeast gene were generated, which reflect those found in patients. We studied stably expressing mutant forms of the protein and investigated their ability to form complexes in BN-PAGE and analyzed their assembly into complexes using import assays.