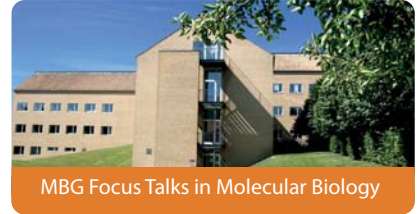


MBG FOCUS TALK

hosted by Section for Structural Biology



Monday 25th June 2018 from 9:15-10:00

MBG conference room (3130-303), Gustav Wieds Vej 10C, 8000 Aarhus C

By Matthew L Wohlever, Ph.D.

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Quality Control of Mitochondrial Tail Anchored Proteins

Mislocalized tail-anchored (TA) proteins of the outer mitochondrial membrane are cleared by a newly identified quality control pathway involving the conserved eukaryotic protein Msp1 (ATAD1 in humans). Msp1 is a transmembrane AAA-ATPase but its role in TA protein clearance is not known. Here, using purified components reconstituted into proteoliposomes we show that Msp1 is both necessary and sufficient to drive the ATP-dependent extraction of TA proteins from the membrane. A crystal structure of the Msp1 cytosolic region modeled into a ring hexamer suggests that active Msp1 contains a conserved membrane-facing surface adjacent to a central pore. Structure-guided mutagenesis shows that the axial pore loops, but not the N-domain, are critical for TA protein extraction in vitro and for functional complementation of Msp1 knockout yeast in vivo. Together these data provide a molecular framework for Msp1-dependent extraction of mislocalized TA proteins from the outer mitochondrial membrane.

Host: Professor Poul Nissen