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CryoEM of membrane protein complexes

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The arrival of direct electron detectors and new image processing software for cryoEM has made a wide range of macromolecular assemblies accessible for high-resolution structure determination that were previously out of reach. Our main interest is the structure and function of mitochondrial membrane protein complexes. By single-particle cryoEM we discovered an unexpected functional asymmetry in the bovine respirasome (Sousa et al, 2016) and a pair of long, membrane-intrinsic helices in subunit a of mitochondrial ATP synthase dimer that appear to play a key role in proton translocation (Allegretti et al, 2015). The structure of a yeast ATP synthase (Figure 1; Hahn et al, 2016) revealed how the complexes interact to form dimers that shape and compartmentalize the inner mitochondrial membrane. By electron cryo-tomography of mitochondria from a wide range of organisms (Davies et al, 2012; Mühleip et al, 2016; 2017) we found that rows of ATP synthase dimers along cristae ridges are a conserved, universal feature of mitochondrial membrane organization. Interestingly, ATP synthase dimers are absent from chloroplast membranes, suggesting that the dimer rows are required for harnessing the shallow pH gradient across the inner mitochondrial membrane for efficient ATP synthesis. In addition, we unravelled the membrane insertion mechanism of pneumolysin, the pore-forming toxin of the human pathogen Streptococcus pneumoniae, by a combination of cryo-EM and x-ray crystallography (van Pee et al, 2017), opening an avenue for the development of new antibiotics.

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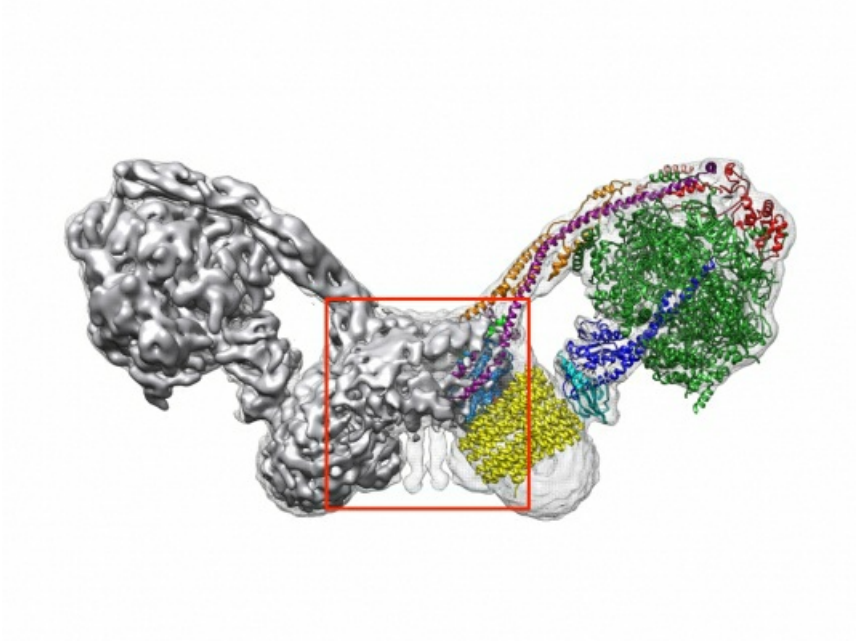

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