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Interaction of Prohibitin peptides with membrane models

Tuesday, 21 March 2023 16:00 (2 hours)

Prohibitins (PHB1 and PHB2) are highly conserved heterodimeric proteins arranging into a large multimeric ring at the inner mitochondrial membrane. They play a crucial role in premature cellular aging, tumor suppression, cell cycle regulation, apoptosis and mitochondrial homeostasis via their interaction with AAA-proteases. We set out to (i) characterize the interaction between the N-terminal helices of PHB (NT-PHB) with the membrane and establish a possible synergy of the two PHB homologues, and (ii) understand the role of cardiolipin in this interaction using interface and bulk neutron techniques.
NR and QCM-D experiments demonstrate that both peptides are able to remove lipid from the bilayer. In SANS, the addition of peptide disrupts the membrane, modifying its integrity by fusing membranes and removing lipids from the vesicles. The effect of the peptide on the membrane is concentration-dependent as well as dependent on the lipid membrane composition with CL and PE enhancing the effect of the peptides on the vesicles.
We propose that both PHB peptides act in synergism to remodel the inner mitochondrial membrane in order to create raft-like areas that allow the support of large protein complexes such as the hexameric AAA-proteases. Future studies will investigate how the interaction between PHB and AAA-proteases is realized at a molecular level in order to understand PHB's role in mitochondrial homeostasis.

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