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S16 Protein / Lipids Interaction

16L1

Membrane-bound respiratory nitrate reductase functioning: It takes two to tango

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The structural and functional integrity of biological membranes is vital to life. The interplay of lipids and membrane proteins is crucial to several fundamental processes ranging from respiration, photosynthesis, signal transduction, solute transport to motility. Evidence is accumulating that specific lipids play important roles in the structure, function and even localization of membrane proteins. X-ray structures of purified membrane proteins have revealed tight and specific binding of lipids [1]. For instance, cardiolipin, an anionic phospholipid, has been found associated to a number of bacterial and eukaryotic respiratory complexes, even though the functions associated to lipid binding often differ considerably [2–3]. However, a major question in general biochemistry still open is how lipids affect, at a molecular level, respiratory complex function.

In the bacterium *Escherichia coli*, the resolution of the structure of several respiratory complexes has revealed the presence of tightly bound phospholipids of yet unknown function [4–5]. Here, we investigate the consequences that lipids have on the structure and function of the nitrate reductase complex. Our results demonstrate that cardiolipin binds specifically in the vicinity of the quinol substrate site and that this binding activates this respiratory complex by tuning the interaction with the quinol substrate [6]. Hence, cardiolipin binding constitutes per se the final step of nitrate reductase biogenesis occurring after completion of folding and assembly of the entire complex, a process assisted by the dedicated chaperone NarJ. While our results provide the first molecular basis for the activation of a bacterial respiratory complex by cardiolipin, we can anticipate that this general trend is followed by other respiratory complexes.

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16L2

Lipid protein interaction in enzymes from the respiratory chain: An electrochemical and FTIR spectroscopic study on the role of integral lipids

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Biochemical studies have shown that phospholipids are essential for the catalytic activity of several membrane proteins. During the past years, a number of structures of integral membrane proteins at high resolution emerged, some of them showing protein-associated phospholipid molecules.

A key question is to determine what role the bound lipids can play. For example, in fatty acids the carboxylic acid is titratable with a pKa in solution near 4 (similar to that of the amino acids Asp or Glu). The phosphate group in any phospholipids can be titrated, as can the additional groups such as serine (PS) or choline (PC) or other groups that make up phospholipids. These charged and zwitterionic groups have their pKa changed when they are associated with proteins. In addition, the charge on these groups influences the pKa of surrounding residues and may change the redox potential (Em) of nearby cofactors as recently shown for the bc1 complex. The shift of the redox potentials is one element that may explain the inactivity of several membrane proteins in the absence of lipids.

The effect of the integral lipids on complexes of the respiratory chain was studied by an electrochemical approach. In order to understand on a molecular level the interaction with the protein, reaction induced FTIR difference spectroscopy was used. This technique allows monitoring the reorganization within a protein upon the induced reaction. It is thus possible to study the role of phospholipids, bound within the protein structure and, importantly, reorganizing during the redox reaction of the protein. Interestingly the reactivation of respiratory complex I and of the bc1 complex with lipids affects the spectral range characteristic of the CO vibration.

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