WPC2025 ABSTRACT TEMPLATE

Cryo-EM structure of the four-subunit *Rhodobacter sphaeroides* cytochrome bc_1 complex in styrene maleic acid nanodiscs

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Cytochrome bc_1 complexes are ubiquinol:cytochrome *c* oxidoreductases, and as such, they are centrally important components of respiratory and photosynthetic electron transfer chains in many species of bacteria and in mitochondria. The minimal complex has three catalytic components, which are cytochrome *b*, cytochrome c_1, and the Rieske iron–sulfur subunit, but the function of mitochondrial cytochrome bc_1 complexes is modified by up to eight supernumerary subunits. The cytochrome bc_1 complex from the purple phototrophic bacterium *Rhodobacter sphaeroides* has a single supernumerary subunit called subunit IV, which is absent from current structures of the complex. In this work we use the styrene–maleic acid copolymer to purify the *R. sphaeroides* cytochrome bc_1 complex in native lipid nanodiscs, which retains the labile subunit IV, annular lipids, and natively bound quinones. The catalytic activity of the four-subunit cytochrome bc1 complex is threefold higher than that of the complex lacking subunit IV. To understand the role of subunit IV, we determined the structure of the four-subunit complex at 2.9 Å using single-particle cryogenic electron microscopy. The structure shows the position of the transmembrane domain of subunit IV, which lies across the transmembrane helices of the Rieske and cytochrome c_1 subunits. We observe a quinone at the Q_o quinone-binding site and show that occupancy of this site is linked to conformational changes in the Rieske head domain during catalysis. Twelve lipids were structurally resolved, making contacts with the Rieske and cytochrome *b* subunits, with some spanning both of the two monomers that make up the dimeric complex. (Text in Calibri, 9 pt, Full justification, auto-hyphenation, <350 words)