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The 2.0 Å Structure of a Bacterial Cytochrome c Oxidase: Evidence for the Conservation of Lipid Binding Sites. Ling Qin[1], Carrie Hiser[1], Xi Zhang[1], Anne Mulichak[2], R. Michael Garavito[1], Shelagh Ferguson-Miller[1], [1]Dept. of Biochemistry, Michigan State Univ., East Lansing, MI, USA; [2]IMCA-CAT, APS, Argonne National Laboratory, Argonne, IL, USA

Crystals of the two subunit catalytic core of cytochrome *c* oxidase (C*c*O) from *Rhodobacter sphaeroides* were obtained with isotropic x-ray diffraction to 2.0 Å resolution, by using an expression construct designed to eliminate molecular inhomogeneity and an optimized purification protocol. Interesting features of this structure include identification of a Cd^{2+} inhibitory site, confirmation of an unusual covalent linkage between sidechain rings of a tyrosine and histidine close to the active site, and resolution of many waters, including the distinctive chain in the D-proton uptake pathway similar to that found in the four subunit holoenzyme. A number of alkyl chains of membrane lipids or detergents are observed in the structure, some with well-defined maltoside head groups. Comparison of C*c*O crystal structures from different sources reveals that alkyl chain positions of membrane lipids and detergent substitutes are conserved, indicating the mode and unexpected specificity of lipid binding sites on membrane proteins, as well as the ability of certain detergent molecules to mimic lipid binding. (supported by NIH GM26916; HFSP RG315/2000-M; MTTC-CSB-CTA 085P1000817; NIH P01GM57323)