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Crystal structures of a UbiA superfamily prenyltransferase

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UBIAD1 is a eukaryotic member of the UbiA superfamily prenyltranferases that catalyze a key synthetic step of ubiquinones, menaquinones, chlorophylls, hemes, and vitamin E. These lipophilic aromatic compounds are released into membranes to serve as electron and proton carriers for cellular respiration and photosynthesis and as antioxidants to reduce cell damage. Here we report the first crystal structures from the superfamily that capture an archaealUbiA in its apo and substrate-bound states.The structures reveal nine transmembrane helices and an extra-membrane cap domain that surround a large central cavity containing the active site. To facilitate the catalysis inside membranes, UbiA has evolved a unique active site that opens laterally to the lipid bilayer. The UbiA structures provide a framework to understand disease-related mutations inUBIAD1.

Biography

Weikai Li received his graduate training of structural biology at Yale in the laboratory of Tom Steitz. As a postdoctoral fellow in Tom Rapoport's Lab at Harvard Medical School, Li learned structural and biochemical techniques to study membrane proteins. Li is currently an assistant professor at Washington University in St. Louis, and his research program focuses on intramembrane enzymes related to hematology. His lab has determined crystal structures of vitamin K epoxide reductase (VKOR), which is a key enzyme that supports blood coagulation and disulfide-bond formation. VKOR is the target of warfarin; the most commonly used oral anticoagulant. More recently, the Li lab has solved the first structure in the UbiA superfamily, which synthesizes lipophilic aromatic compounds (e.g. ubiquinones) that play essential roles in biological membranes.

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