

Native Cell Membrane Nanoparticles System for Membrane Proteins

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We devised a native cell membrane nanoparticles system, which we applied in a single-particle cryo-EM study of the multidrug exporter AcrB. Lipid-AcrB nanoparticles were prepared directly from membranes without any use of detergents. A 3D reconstruction in C1 symmetry achieved a final density map at 3.2 Å resolution, an atomic model of quasi-C3-symmetric AcrB was fitted to this map, and the residual density revealed many ordered lipid molecules. Most remarkably, a central cavity between the three transmembrane domains contains a 24-lipid patch of well-ordered bilayer structure. Inner leaflet lipid chains pack in a hexagonal array like that in phosphatidylethanolamine crystal structures, whereas the outer leaflet has highly irregular packing. Protein side chains interact with both leaflets and participate in the hexagonal pattern. The AcrB export mechanism requires reorganization of the lipid bilayer structure. This system should be broadly applicable for membrane protein structural biology and structure-based drug discovery and development.

Biography:

Youzhong Guo was born in Xiangcheng, Henan, China, in 1974. He received the B.S. degree in biology from Henan Normal University, Xinxiang, Henan, China, in 1997. He received the Ph.D. degree in pharmacy/structural biology from the University of Texas at Austin, Austin, TX, U.S.A., in 2010. From 2010 to 2016, he worked with Dr. Wayne A. Hendrickson as a postdoc in Columbia University, New York, NY, U.S.A. In 2016, he joined the Department of Medicinal Chemistry, Virginia Commonwealth University, Richmond, VA, U.S.A. as an Assistant Professor. His current research interests include membrane protein structural biology and structure-based drug discovery.