Membrane Protein Structure-Function Studies With Lipid Mesophases

M. Caffrey
Trinity College Dublin, School of Medicine and School of Biochemistry and Immunology, Trinity Biomedical Sciences Institute, Dublin, Ireland martin.caffrey@tcd.ie

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Abstract

One of the primary impasses on the route that eventually leads to membrane protein structure through to activity and function is found at the crystal production stage. Diffraction quality crystals, with which structure is determined, are particularly difficult to prepare currently when a membrane source is used. The reason for this is our limited ability to manipulate proteins with hydrophobic/amphipathic surfaces that are usually enveloped with membrane lipid. More often than not, the protein gets trapped as an intractable aggregate in its watery course from membrane to crystal. As a result, access to the structure and thus function of tens of thousands of membrane proteins is limited. In contrast, a veritable cornucopia of soluble proteins have offered up their structure and valuable insight into function, reflecting the relative ease with which they are crystallized. There exists therefore an enormous need for new ways of producing crystals of membrane proteins. One such approach makes use of lipid liquid crystalline phases (mesophases). I will describe the method, our progress in understanding how it works and recent community-wide advances in applying the method for membrane protein structure determination. The use of bicontinuous mesophases for the functional characterization of membrane proteins and for serial femtosecond crystallography using an X-ray free electron laser will also be described.