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Behaviour of Single Transmembrane Peptides During In Meso Crystallization from the Contrast-Matched Lipidic Cubic Phase of Monoolein

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In meso membrane protein crystallization within a lipidic mesophase has revolutionized the structural biology of integral membrane proteins (IMPs). High-resolution structures of these proteins are crucial to understanding fundamental cellular processes at a molecular level, and can lead to new and improved treatments for a wide range of diseases via rational drug design. However, overall success rates of the promising in meso crystallization technique remain low because of a fundamental lack of understanding about factors that promote crystal growth. In particular, to date, two decades from invention of the method, the protein-eye-view of the in meso crystallization mechanism had not been solved. We have investigated this for the first time using small-angle neutron scattering (SANS).
Contrast-matching between the scattering of the lipid membrane formed by MO and the aqueous solution was used to isolate and track the scattering of single-transmembrane peptides during the growth of protein crystals in meso. No peptide enrichment was observed at the flat points of the diamond cubic QIID phase of MO in contrast to suggestions in several modeling studies. During in meso crystallization of the DAP12 peptide a decrease in form factor and a transient fluid lamellar Lα phase could be observed providing direct evidence for the proposed crystallization mechanism. Synthesis of fully deuterated MO was required for this purpose and scattering of this new material in various solvents and under a range of conditions will be described, specifically regarding the effect of the relative scattering length densities (SLD) of the headgroup, acyl chain and solvent, which can advance the use of neutron scattering with other self-assembly materials.

Topic

Biology

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