Contribution ID : **23** Type : **Oral**

Protein-Eye View of the in Meso Crystallization Mechanism

Tuesday, 3 December 2019 11:15 (15)

Understanding the behavior of the protein within the nanostructured lipid mesophase is crucial for evolving biological and biomedical applications of hybrid protein-lipid materials. After more than two decades since the invention of the *in meso* crystallization method for membrane proteins, a protein-eye view of its mechanism is still lacking. Structural studies have suggested that integral membrane proteins partition at localized flat points on the bilayer surface of the cubic phase and that crystal growth occurs from a local fluid lamellar phase conduit. However, studies to date have focused on structural transitions occurring in the lipid mesophase. Here, it was shown using small-angle neutron scattering that the lipid bilayer of monoolein (the most commonly used lipid for biological and biomedical applications) can be contrast-matched using deuteration, allowing isolation of scattering from encapsulated peptides during the crystal growth process for the first time. During *in meso* crystallization, a clear decrease in form factor scattering intensity of the peptides was observed and directly correlated with crystal growth. A transient fluid lamellar phase was observed, providing direct evidence for the proposed mechanism for this technique. This suggests that the peptide passes through a transition from the cubic phase, via a fluid lamellar phase to the lamellar crystalline phase with similar layered spacing. When high protein loading was possible, the lamellar crystalline phase of the peptide in the single crystals was observed. These findings show the mechanism of *in meso* crystallization for the first time from the perspective of integral membrane proteins. The used time-of-flight (BILBY) SANS method with contrast-matching opens up the possibility to study hybrid protein-lipid materials for pharmaceutical, food and biological applications.

Reference: Leonie van 't Hag, Liliana de Campo, Nhiem Tran, Anna Sokolova, Raphael Trenker, Matthew E. Call, Melissa J. Call, Christopher J. Garvey, Anna E. Leung, Tamim A. Darwish, Anwen Krause-Heuer, Robert Knott, Thomas G. Meikle, Calum J. Drummond, Raffaele Mezzenga, and Charlotte E. Conn, Langmuir, 2019, 35(25), 8344-8356.

Speakers Gender

Female

Travel Funding

No

Level of Expertise

Early Career <5 Years since PdD

Do yo wish to take part in the poster slam

No

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Session Classification : Session 14

Track Classification : Structural biology and biological systems