

Femtosecond crystallography of membrane proteins in the lipidic cubic phase (LCP)



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Weis' talk will cover his contributions to structure determination efforts using XFEL of membrane protein samples. An abstract of his webinar is attached. Hope to see everyone at the webinar.

"Despite recent technological advances in heterologous expression, stabilization and crystallization of membrane proteins (MPs), their structural studies remain difficult and require new transformative approaches. During the past two years, crystallization in lipidic cubic phase (LCP) has started gaining widespread acceptance, owing to the spectacular success in high-resolution structure determination of G protein-coupled receptors (GPCRs) and to the introduction of commercial instrumentation, tools and protocols. The recent appearance of X-ray free-electron lasers (XFELs) has further enabled structure determination from substantially smaller crystals than previously possible, offering exciting new opportunities in structural biology. The unique properties of LCP material have been exploited to develop special protocols and devices that have established a new method of serial femtosecond crystallography of MPs in LCP (LCP-SFX). In this method, microcrystals are generated in LCP and streamed continuously inside the same media across the intersection with a pulsed XFEL beam at a flow rate that can be adjusted to minimize sample consumption. Pioneering studies that yielded the first room temperature GPCR structures, using a few hundred micrograms of purified protein, validate the LCP-SFX approach and make it attractive for structure determination of difficult-to-crystallize MPs and their complexes with interacting partners. Together with the potential of femtosecond data acquisition to interrogate unstable intermediate functional states of MPs, LCP-SFX holds promise to advance our understanding of this biomedically important class of proteins. "