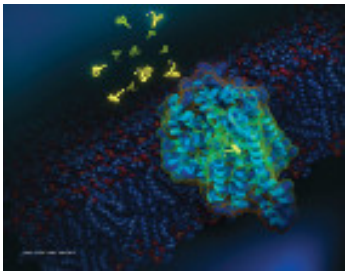

Contribution ID: **52** Type: **not specified**

Lipid & Cholesterol's Impact on the Functional Structure of Membrane Proteins: Insights from Solid-State NMR

Membrane curvature generation and membrane remodeling underlie many biological processes such as virus entry into cells and virus budding. How proteins mediate this curvature generation is a fundamental question that is still poorly understood. I will present our recent structural studies, using solid-state NMR spectroscopy, of three membrane proteins that give insights into the mechanisms of virus-cell membrane fusion and virus budding. 1) We have investigated the structure of the membrane-interacting domains of the fusion proteins of the parainfluenza virus 5 (PIV5) and human immunodeficiency virus (HIV). For the PIV5 fusion protein, the fusion peptide (FP) and the transmembrane domain (TMD) show striking membrane-dependent conformations. The β-sheet conformation causes negative Gaussian curvature and membrane dehydration, which are required for membrane merger, while the α-helical conformation resides in low-curvature lamellar membranes and forms three-helix bundles. Therefore, the local lipid composition of the membrane is a key regulator of the site of virus-cell fusion. 2) For the HIV fusion protein gp41, we have determined the oligomeric structure of the membrane-proximal external region (MPER) and the TMD. We find that this domain is trimerized in the lipid membrane with a helix-turn-helix conformation, suggesting that this domain stabilizes the trimer structure of gp41 and promotes membrane curvature during the fusion process. 3) The influenza virus buds from host cells in a cholesterol-dependent manner using the matrix protein M2. To understand how cholesterol interacts with M2 to generate membrane curvature, we have determined the cholesterol-binding site of M2 by measuring protein-cholesterol distances and cholesterol orientation in the membrane. The data represent the first direct determination of the cholesterol-binding structure of a membrane protein in lipid bilayers, and moreover indicate a specific mechanism by which cholesterol concentration gradients in the membrane drive the M2 protein to the neck of the budding virus to conduct membrane scission.

Author: Prof. HONG, Mei (MIT, Boston, MA, USA)

Presenter: Prof. HONG, Mei (MIT, Boston, MA, USA)