Chemical & Physical Sciences
UNIVERSITY OF TORONTO
MISSISSAUGA

**Colloquium Seminar Series**
**Wednesday, October 31, 2018**
**3:10pm in CC2150**

# Dr. Michael Overduin

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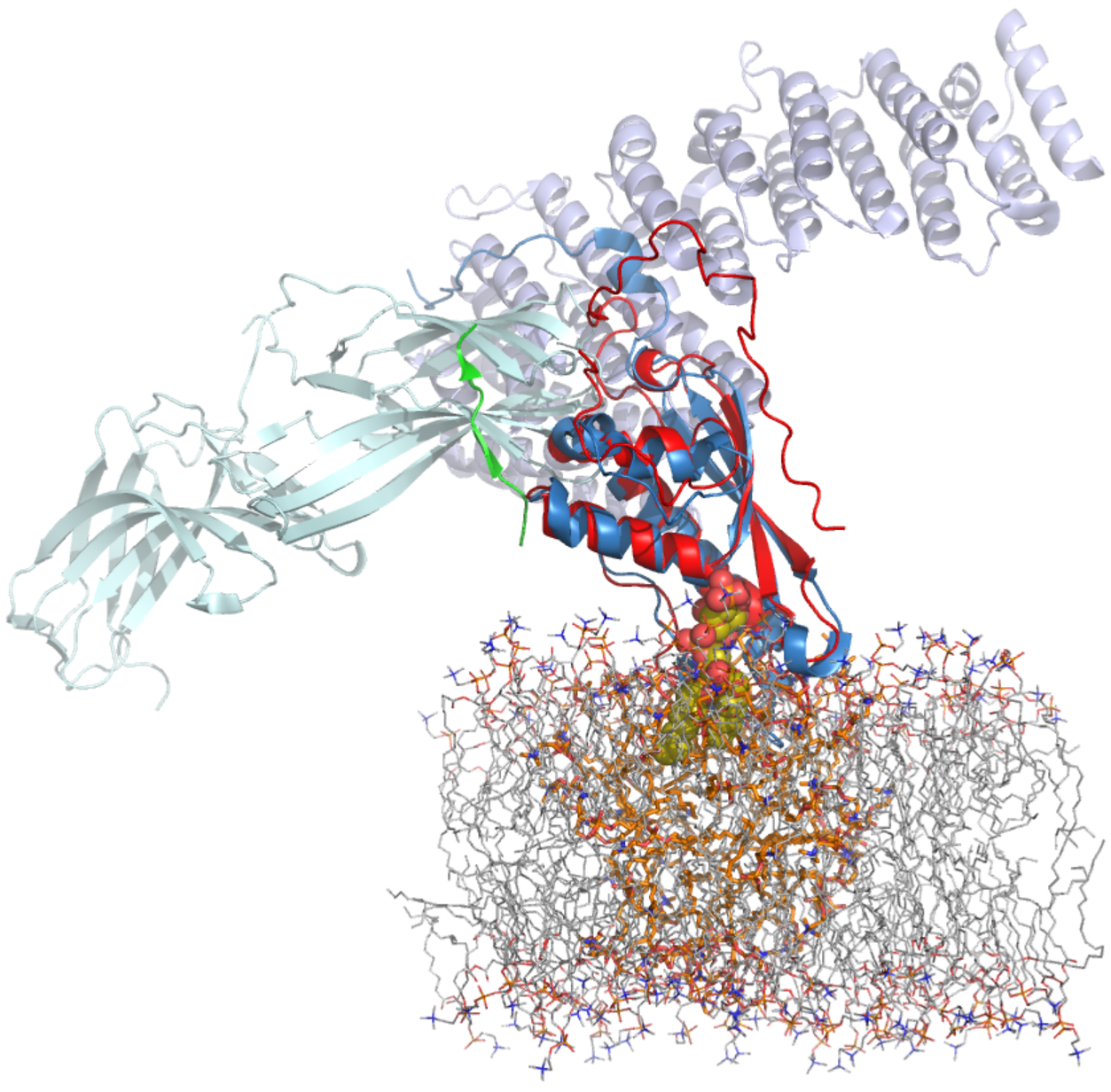
# Structural biology of bacterial, prion and human proteins in membranes



The overall aim of the Overduin lab is to determine how proteins recognize and organize lipids in biological membranes. We are elucidating the mechanism of an E. coli protein called YraP, which is found in Gram negative bacteria. The relatives of YraP includes hemolysins, mechanosensitive channels, the membrane-pore forming protein Secretin, and a variety of eukaryotic proteins. We propose that they share a common function based on lipid recognition, and are elucidating the cellular function, molecular interactions and 3D structures. We are determining how this lipoprotein engages the phospholipids found in the membrane that surrounds Gram negative bacteria.

Our approach is to use nuclear magnetic resonance spectroscopy to solve membrane protein structures, measure their interactions with lipid molecules, and then validate the lipid ligands and binding determinants in cell-based assays. Software tools are also being developed to discover novel protein:lipid interactions, including a computational tool (MODA) that rapidly and accurately predicts membrane optimal docking areas on any protein structure. We have also pioneered polymer-based nanodiscs for native lipid-protein complex solubilization, and are using these to study the composition of infectious prions. Finally, drug-like ligands for therapeutic targets including kinases are being discovered by drug fragment screening. Hybrid structures being solved by NMR, X-ray crystallography and small angle X-ray scattering are revealing the mechanisms of oncogenic states that drive cancer progression.