Chemical & Physical Sciences
UNIVERSITY OF TORONTO
MISSISSAUGA

COLLOQUIUM
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KN132

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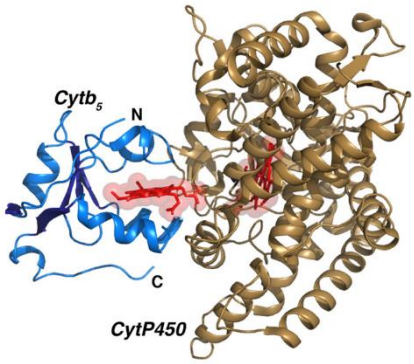
Probing Molecular Dances in the Cell Membrane by NMR Spectroscopy



Membrane proteins are an exciting class of biomacromolecules and play important roles in a variety of biological processes that are directly linked to major diseases including cancer, aging-related diseases, and infectious diseases. A complete understanding of their function can only be accomplished using high-resolution structures. In spite of recent developments in structural biology, membrane proteins continue to pose tremendous challenges to most biophysical techniques. A major area of research in my group is focused on the development of NMR techniques to study the dynamic structures of membrane bound proteins such as cytochrome b5, cytochrome P450 and cytochrome P450-reductase. In the first-half of my talk, I will present strategies to study the structure and dynamics of these challenging systems and also on the electron transfer mechanism that enables the enzymatic function of P450. The accumulation of misfolded proteins is a hallmark feature in numerous human disorders such as blood diseases like sickle cell anemia, neurodegenerative diseases like Alzheimer's disease and Parkinson's disease, and metabolic diseases such as type II diabetes. Misfolded protein aggregates may deposit in tissues, can be intracellular, extracellular, or both. The conformational changes accompanying misfolding can result in disruption of the regular function of the protein or may result in a gain of function that is often associated with toxicity. Amyloid peptides represent a subset of misfolded proteins whose misfolded state shares unique characteristics. Our research group has been investigating the high-resolution structures of early amyloid intermediates, amyloid-membrane interaction and membrane disruption, and the interaction of polyphenols with amyloid proteins. In the second-half of my presentation, NMR structures of early intermediates of amyloid peptides, mechanisms of amyloid-induced membrane disruption, and amyloid inhibition by polyphenolic compounds will be discussed. Solid-state NMR results on the interaction of amyloid fibers with lipid bilayers, and novel NMR approaches to investigate amyloid formation will also be presented.