Seminar Series of the CIHR Training Grant in

Protein Folding and Interaction Dynamics

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Ligand-gated ion channel architecture and mechanism

My laboratory is interested in the structural underpinnings of neurotransmitter-gated ion channel function. We are currently investigating the family of pentameric ligand-gated channels that includes the nicotinic acetylcholine receptors, 5-HT3, GABAA and glycine receptors as well as several receptors found in invertebrates. All of these receptors share a conserved 3D architecture, but there is limited atomic-resolution structural information for those found in eukaryotes. There are a number of poorly understood but fundamental receptor mechanisms that we aim to resolve through structure determination and careful biophysical analysis. We are fascinated by how binding of a small chemical transmitter to an extracellular domain of the receptor achieves opening of a gate in the membrane >50 Å away, on a sub-millisecond timescale. We are also interested to understand the structural basis of the diverse selectivities for ions (charge and valence), mechanism(s) of desensitization and principles of ligand selectivity and allosteric modulation. We are now beginning work on heteromeric receptors, which provide an additional level of complexity and would yield insights into what defines the assembly of the limited number of subunit combinations found in the nervous system. I will review recent progress in the field, describe the methods we are using to study these oligomeric membrane proteins and present structural studies on an invertebrate glutamate-gated chloride channel.

Host: Dr. Scott Prosser

Thursday, February 19, 2015 - 12:00pm
Medical Sciences Building, Rm. 4171
University of Toronto