

Seminar Series of the
CIHR Training Grant in
**Protein Folding and
Interaction Dynamics**

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**Allosteric Regulation of the
Sarcoplasmic Reticulum Ca²⁺-
ATPase by Phospholamban
and Sarcolipin using Solid-
State NMR Spectroscopy**

The membrane protein complexes between the sarcoplasmic reticulum Ca²⁺-ATPase (SERCA) and phospholamban (PLN) or sarcolipin (SLN) control Ca²⁺ transport in cardiomyocytes, thereby modulating cardiac muscle contractility. Both PLN and SLN are phosphorylated upon β -adrenergic-stimulated phosphorylation and up-regulate the ATPase via an unknown mechanism. Using solid-state NMR spectroscopy, we mapped the interactions between SERCA and both PLN and SLN in membrane bilayers. We found that the allosteric regulation of the ATPase depends on the conformational equilibria of these two endogenous regulators that maintain SERCA's apparent Ca²⁺ affinity within a physiological window. Here, we present new regulatory models for both SLN and PLN that represent a paradigm-shift in our understanding of SERCA function. Our data suggests new strategies for designing innovative therapeutic approaches to enhance cardiac muscle contractility.

Host: Dr. Scott Prosser

Thursday, March 27, 2014 - 12:00pm
Medical Sciences Building, Rm. 4279
University of Toronto