Chemical & Physical Sciences
UNIVERSITY OF TORONTO
MISSISSAUGA

COLLOQUIUM

TUESDAY, JANUARY 22ND, 2013
12:00 P.M. (SHARP) – 1:00 P.M.
IB270

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"Synergies and snags in balancing folding and function of natural and designed beta-trefoil proteins"

The beta-trefoil clan of protein superfamilies includes a great number of binding proteins that share a common internally symmetric tertiary structure but have extremely diverse primary sequences and functions. We have studied the folding and function of representative beta-trefoil proteins: Hisactophilin, a myristoylated, histidine-rich, pH-dependent, actin- and membrane- binding protein; and ThreeFoil, a designed 3-fold symmetric carbohydrate binding protein. A combination of experiment and modelling reveals trade-offs and synergies in the folding and function of Hisactophilin, arising from the wild-type protein sequence characteristics, in particular the high histidine content, and the effects of the common covalent fatty acyl modification which plays a central role in regulated signalling functionality. Bioinformatics, computer modelling, consensus and rational design approaches produced the intended symmetric structure for ThreeFoil with multivalent carbohydrate binding functionality and unexpectedly high kinetic but apparently low thermodynamic stability. The results for these proteins reveal general molecular mechanisms underlying folding, misfolding, and function.