Donnelly Centre
for Cellular + Biomolecular Research
UNIVERSITY OF TORONTO

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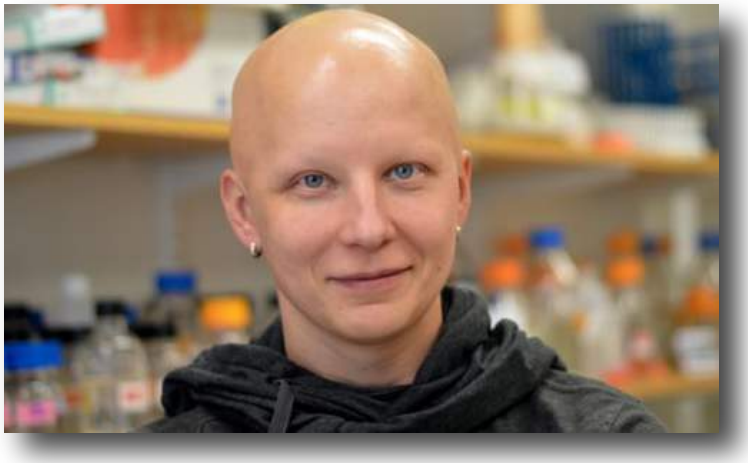
"High-throughput profiling of protein/protein and drug/target interactions in human cells"



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March 10, 2014 | 11:00 a.m.
Donnelly James Friesen | Cecil Yip
Red Seminar Room

Abstract:

Hsp90 is an abundant cellular protein that promotes the folding and function of its substrate proteins (clients). In vivo, Hsp90 also associates with a large and diverse set of co-factors (co-chaperones) that regulate its specificity and function. We have systematically characterized the client specificities of Hsp90 and its co-chaperones by affinity purification coupled to mass spectrometry (AP-MS) and by a quantitative pairwise interaction assay (LUMIER). We uncover hundreds of novel chaperone clients, delineate their participation in specific co-chaperone complexes, and establish a surprisingly distinct network of protein/protein interactions for co-chaperones. Focusing on kinases, a large and well-established client class, we show that Hsp90 recognizes its clients in acombinatorial fashion: kinase-specific co-chaperone Cdc37 provides recognition of the kinase family, whereas thermodynamic parameters determine client binding within the family. Finally, we demonstrate that the sensitivity of chaperones to subtle conformational changes in their client proteins can be exploited to profile drug/target interactions in human cells.

Host: Charlie Boone