Donnelly Centre
for Cellular + Biomolecular Research
UNIVERSITY OF TORONTO

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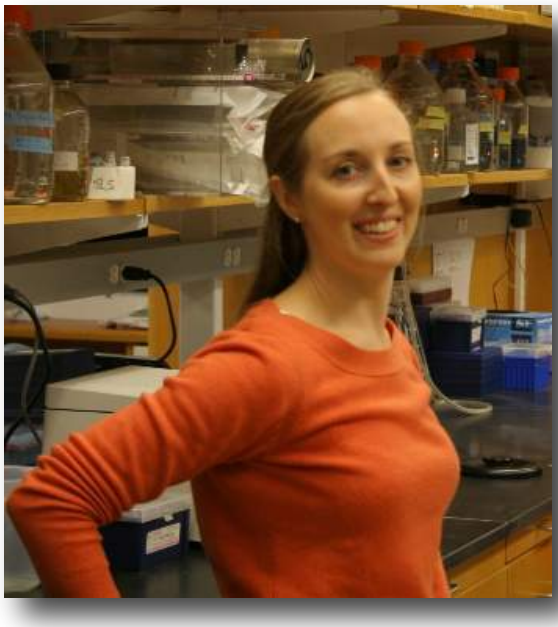
"Single cell dynamics of the proliferation-quiescence decision"



Sabrina Leigh Spencer

Postdoctoral Research Fellow
Chemical and Systems Biology
Stanford School of Medicine
Tobias Meyer's lab

Tuesday, March 4, 2014 | 4:00 pm
The Donnelly Centre
James Friesen | Cecil Yip Red Seminar Room

Abstract:

Cellular signaling pathways translate external cues into a change in cellular state. Studying these processes at the single cell level reveals remarkable cell-to-cell variability in response to stimuli, even among genetically identical cells in a uniform environment. During both my PhD and postdoc, I have used fluorescence time-lapse microscopy of single cells to link heterogeneity in upstream signaling events to a cell's ultimate fate. In the case of cells treated with death-inducing ligands, I observed that a subpopulation of cells always survived exposure to these ligands while the remainder died. Using a combination of sister-cell pedigree analysis, mathematical modeling, and fluorescence time-lapse microscopy, I showed that naturally occurring differences in the expression levels of proteins regulating ligand-induced apoptosis are a major cause of cell-to-cell variability in the timing and probability of death. In the case of cell cycle entry, I developed a sensor for CDK2 activity and discovered a bifurcation point at mitotic exit where cycling cells choose between two future fates. Some newly born cells immediately build up CDK2 activity and commit to the next cell cycle, while others lack CDK2 activity and enter a G0-like state. This bifurcation is directly controlled by the CDK inhibitor p21 and is regulated by mitogens during a 'restriction window' in G2/M of the previous cell cycle. Both the life-death and proliferation-quiescence decisions are quite variable from cell to cell, and therefore only a quantitative, dynamic, and single cell approach will enable a mechanistic understanding of these processes. With this understanding in hand, we can predict and possibly alter the fate of individual cells.

Host: Amy Caudy