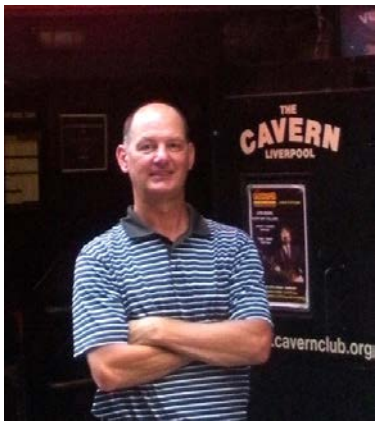
GUEST SPEAKER SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

How Phosphorylation Controls Ubiquitination by Parkin, a Key E3 Ligase in Early-Onset Parkinson's Disease



Mutations in the E3 ligase Parkin (park2) are a central cause for early-onset Parkinson's disease. Under oxidative stress conditions this enzyme functions with the E2 conjugating enzyme UbcH7 to ubiquitinate and degrade the outer mitochondrial membrane substrates Miro-1 and mitofusin-1 to maintain cellular health. Parkin is a complex 465-residue E3 ubiquitin ligase comprising an N-terminal "ubiquitin-like" (Ubl) domain and a C-terminal catalytic region, consisting of a RING0, BRcat (Benign Required for Catalysis), RING1 and Rcat (Required for Catalysis) domains. In its resting state parkin in essentially inactive, maintained through its auto-inhibitory Ubl domain that blocks ubiquitin catalysis. Essential steps required to activate parkin include phosphorylation of the Ubl domain in conjunction with recruitment of phospho-ubiquitin. Our lab has examined how these phosphorylation steps alter the structure of parkin and how early-onset mutations modulate these pathways

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Date: Thursday July 27th, 2017
Time: 2PM
Place: Donnelly Centre, 160 College St
Red Seminar Room