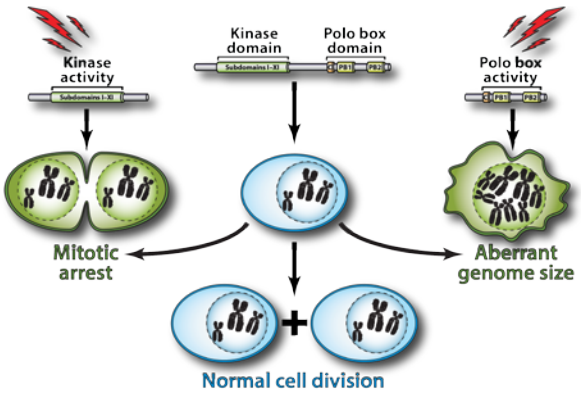
GUEST SPEAKER SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

When genome integrity and cell cycle decisions collide: roles of polo kinases in cellular adaptation to DNA damage



The drive to proliferate and the need to maintain genome integrity are two of the most powerful forces acting on biological systems. When these forces enter in conflict, such as in the case of cells experiencing DNA damage, feedback mechanisms are activated to ensure that cellular proliferation is stopped and no further damage is introduced while cells repair their chromosomal lesions. Interestingly, the drive to proliferate can under specific conditions overcome the DNA damage response and lead to a reactivation of the proliferative program in checkpoint-arrested cells. This phenomenon is known as adaptation to DNA damage and is observed in all eukaryotic species where the process has been studied. The molecular mechanisms underlying this biological phenomenon are currently not understood. Taking advantage of unique separation-of-function mutants, we show that the Polo-like kinase (PLK) Cdc5 uses a phosphopriming-based interaction mechanism to suppress G2/M checkpoint arrest by targeting polo kinase activity to centrosomes. We also show that key subunits of the evolutionarily conserved RSC complex are critical downstream effectors of Cdc5 activity in checkpoint suppression. Importantly, the lethality and checkpoint defects associated with loss of Cdc5 phosphopriming activity can be fully rescued by artificially anchoring Cdc5 kinase domain to yeast centrosomes. Collectively, our results highlight a previously unappreciated role for centrosomes as key signaling centers for the suppression of cell cycle arrest induced by persistent or unrepairable DNA damage.

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Host: Dr. Laurence Pelletier

Date: Tuesday October 27th, 2015
Time: 10AM
Place: Donnelly Centre
160 College Street
Red Seminar Room