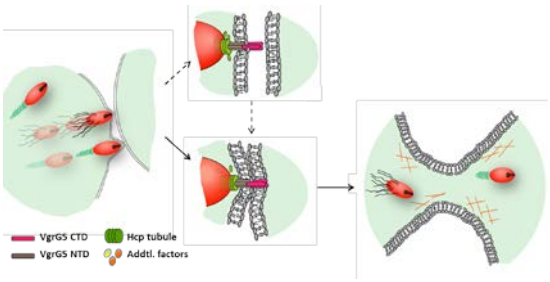
GUEST SPEAKER SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

Virulence from the rhizosphere: membrane fusion and the *Burkholderia* intercellular life cycle



Burkholderia pseudomallei is a Tier 1 Select Agent that causes the often fatal human disease melioidosis*. B. pseudomallei* and related species invade a variety of cell types, replicate in the cytoplasm, and efficiently spread to adjacent cells. Using genetic dissection and photothermal nanoblade delivery, which allows the efficient placement of bacterium-sized cargo into the cytoplasm of mammalian cells, we have investigated temporal and spatial requirements for virulence determinants in the *Burkholderia* intracellular life cycle. The Bsa type III secretion system is essential for escape from primary endosomes, and by nanoblade delivery we demonstrate that cell-cell spread is dependent on the activity of a type VI secretion system that functions downstream from T3SS-mediated endosome escape. A remarkable feature of *Burkholderia* is their ability to induce the formation of multinucleated cells (MNCs) in diverse cell types. By infection and nanoblade delivery, we observe a remarkable correspondence between mutant phenotypes in assays for cell fusion and plaque formation, and time-course studies show that plaque formation represents MNC death. Our data show that the primary means for intercellular spread by *B. pseudomallei* and related species involves T6SS-mediated membrane fusion, and we propose a model in which a unique activity at the C terminus of VgrG5, which is positioned at the tip of the T6SS apparatus, is responsible for fusion following injection across the membranes of adjacent cells.

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Host: Dr. Alex Ensminger and Dr. William Navarre

Date: Monday December 8th, 2014
Time: 4PM
Place: Fitzgerald Building, 150 College Street, Room 103