



The Centre for Blood Research Seminar Series



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Wednesday, June 12th, 2013

LSC 3 - Life Sciences Centre

2350 Health Sciences Mall

12-1pm

“Granzymes: More than Just Killer Proteases”

Granzymes (Granule-secreted enzymes) are a family of serine proteases that were traditionally viewed as cytotoxic proteases released by lymphocytes to initiate target cell apoptosis. Although originally proposed to potentially have intracellular and extracellular functions, upon the discovery that the pore forming protein perforin could facilitate Granzyme B (GzmB) entry into cells and apoptosis, other potential functions for this protease were, for the most part, disregarded. As there are multiple granzymes in humans and mice, perforin knockout mice were, and still are, often used to rule out a role for granzymes in disease. However, clinical and biochemical evidence suggests that this approach overlooks critical perforin-independent, and other non-cytotoxic roles for these proteases in disease. Long known to be a pro-apoptotic protease expressed by cytotoxic lymphocytes and natural killer cells, it is now accepted that GzmB can be expressed by other cell types of immune and non-immune origin. Given GzmB retains its activity in the blood, bronchoalveolar lavage, wound fluid and synovial fluid, cleaves many extracellular proteins and cell surface receptors, and is markedly elevated in many age-related and chronic inflammatory diseases, this protease may contribute to pathogenesis. My laboratory has investigated the role of intracellular and extracellular GzmB in several models of skin and cardiovascular injury, inflammation and repair. The present talk will discuss our recent findings and novel roles for GzmB in pathophysiological processes.



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