



The Centre for Blood Research Seminar Series

Wednesday, August 6th, 2014

LSC 3 - Life Sciences Centre

2350 Health Sciences Mall

12-1pm

Dr. Michael Hughes

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Biomedical Research Centre

UBC

“Leaky Pipes and Urine Trouble:

The role of podocalyxin in vascular and kidney barrier functions”

With over 1 million annual cases and 200, 000 deaths per year, sepsis is the leading cause of death in hospitalized patients (U.S. stats). Although methods to prevent infection can limit the number of cases, up to 40% of cases arise from sterile tissue injuries from ischemia-reperfusion or other non-infectious inflammation. Regardless of the primary cause, sepsis is increasingly recognized as a multifactorial syndrome resulting in the failure of tissue barriers that normally maintain separation of fluids and metabolites. Unfortunately, there are no effective treatments for sepsis and, instead, patients receive intensive non-specific support. Moreover, there are no known parameters to predict if a patient will become septic or if he/she will recover or succumb.

Podocalyxin is a CD34-family sialomucin that is required for the normal glomerular filtration function of kidney podocytes (a specialized epithelial cell). We have found that podocalyxin, a sialomucin expressed on vascular endothelial cells (vECs), has a role in maintaining barrier function in the lung and other organs under experimental conditions that mimic sepsis. When expressed on endothelial cells lining the blood vessels, podocalyxin maintains vascular barrier function in the lung and limits lipopolysaccharide (LPS)-induced edema. When exposed to LPS in combination with a selective protease-activated receptor 1 (PAR-1) agonist (to mimic thrombosis), podocalyxin-deficient mice experience a temporary loss of mobility (perhaps from loss of hemodynamic control). We have found that podocalyxin-deficient vECs have an adhesion defect and may lay down abnormal basement membranes. Therefore, we conclude that podocalyxin in vECs is required for the normal development and maintenance of vascular barrier functions.



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