DEPARTMENT OF
PHYSIOLOGY

Dr. F.C. MacIntosh Lectureship Seminar

Co-hosted by

Cystic Fibrosis Translational Research CENTRE

GUEST SPEAKER

Dr. Albert van der Vliet

Professor, Department of Pathology and Laboratory Medicine, Larner College of Medicine, University of Vermont

FRIDAY, DECEMBER 1, 2023
11:00AM

MCINTYRE MEDICAL SCIENCES BUILDING
ROOM 1034

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"THE NADPH OXIDASE DUOX1 IN REDOX-DEPENDENT EPITHELIAL HOMEOSTASIS, EXTRACELLULAR MATRIX REMODELING, AND FIBROTIC LUNG DISEASE"

NADPH oxidases (NOX) represent a family of dedicated oxidant-generating enzymes that serve widespread biological roles, ranging from host defense, cell proliferation or differentiation, to immune regulation. In the lung, the NOX isoform DUOX1 is expressed primarily within the respiratory epithelium, and our past studies have demonstrated its role in innate epithelial responses to various injurious triggers (including pathogens and asthma-inducing allergens), by mediating various wound responses via cellular redox signaling pathways involving tyrosine kinases such as SRC and EGFR. Among these DUOX1-mediated injury responses is the epithelial secretion of the alarmin IL-33, which serves to maintain epithelial integrity by activating type 2 immune responses. We also demonstrated that epithelial DUOX1 expression and activation is enhanced during allergic asthma, and contributes to type 2 inflammation and airway remodeling as major features of allergic airways disease. More recently, we also uncovered an apparent functional role for DUOX1 in macrophages, indicating its contributing roles in macrophage recruitment and profibrotic activation in models of allergic airway inflammation or pulmonary fibrosis. Lastly, based on previous studies linking DUOX1 to extracellular oxidative crosslinking processes in various organisms via activation of secreted heme peroxidases, we are currently exploring a link between DUOX1 and peroxidasin (PXDN), a recently identified heme peroxidase involved in collagen IV crosslinking within basement membranes (BM), and have obtained preliminary evidence for a concerted role of DUOX1 and PXDN in oxidative matrix remodeling that may promote lung stiffening in fibrotic lung disease. Curiously, these PXDN-mediated cross-linking mechanisms rely on the presence of bromide (Br-), and also give rise to alternative oxidative ECM modifications, including the formation of 3-bromo-tyrosine (Br-Y) in several BM proteins. The relevance and therapeutic implications of these various oxidative mechanisms for fibrotic lung disease will be discussed.