CBR

The Centre for Blood Research Seminar Series

Wednesday, November 25, 2015

LSC 3 - Life Sciences Centre
2350 Health Sciences Mall
12-1pm

Dr. Jürgen Kast

Professor, *Department of Chemistry, UBC*

"Lysophosphatidic acid as a platelet agonist in atherosclerosis"

In various cardiovascular diseases, rupture of atherosclerotic plaques leads to life-threatening events due to subsequent thrombus formation. In addition to collagen and tissue factor, plaques contain a large variety of lipid species. Lysophosphatidic acid (LPA), a bioactive phospholipid, has been found to accumulate in plaques. LPA activates platelets in a subset of individuals, yet the underlying molecular mechanism and its relevance to atherosclerosis remain unclear. To address this issue, we decided to compare LPA to other platelet agonists regarding their impact on platelets and beyond. For this, we developed novel quantitative proteomics approaches that identify changes in small GTPase activation, protein secretion, glycoprotein expression, and cysteine oxidation, but also employed molecular and cellular assays as well as inhibitor studies. We found LPA to be a *bona fide* platelet agonist that shares some characteristics with other agonists, but also has unique features. Moreover, we gained new insights into platelets' involvement in plaque development via the activation of monocytes, the role of P-selectin and platelet-monocyte aggregates in this process, and the interplay between LPA and other plaque factors.

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