Circulating blood cells generate immunoactive phospholipids that promote haemostasis, and regulate vascular inflammation.

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In recent years it has become appreciated that blood cells that participate in acute response to injury generate large numbers of lipids that comprise bioactive eicosanoids attached to phospholipids. The lipids are formed during early activation by pathophysiological agonists and are termed enzymatically-oxidised phospholipids (eoxPL). In this talk, I will summarise work of the last 10 yrs, showing how we applied mass spectrometry to identify and characterize a large array of eoxPL formed in platelets, neutrophils, monocytes and eosinophils. These lipids are generated in ng amounts and remain cell-associated where they change membrane electronegativity. They promote blood clotting and changes to immune behavior of leukocytes. Mice lacking eoxPL (*ALOX12*$^{-/-}$ or *ALOX15*$^{-/-}$) bleed longer on challenge and generate smaller thrombi. They are protected against atherosclerosis and abdominal aortic aneurysm when back-crossed onto the ApoE$^{-/-}$ background. We have found eoxPL to be significantly elevated and immunogenic in human venous thrombotic disease. The most abundant eoxPL are either phosphatidylethanolamines or phosphatidylcholines, however we recently found phosphatidylinositol forms, suggesting crosstalk between eicosanoid and phosphoinositide signalling in human platelets. How these lipids contribute to human and murine physiological response to injury and vascular inflammation will be discussed.