ABSTRACT FORM

Division of Medicine Research Retreat, Thursday 30th June 2022

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Position:	Research Fellow		
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Presentation Title:	Reduced Levels of 12,13-DiHOME Correlate with Increased Levels of Immature Neutrophils in an Acute Inflammatory Response		
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Presentation preference:	Poster;		

ABSTRACT: (please keep your abstract within this page maximum 300 words)

The soluble lipid mediators, epoxy-oxylipins, exhibit anti-inflammatory/pro-resolution characteristics in numerous in vitro and animal studies. However, these observations are yet to be translated into a human setting. The aim of this study was to understand the influences of epoxy-oxylipins in the human resolving inflammatory response by targeting the first step in their metabolism i.e. blocking the conversion of 12,13-EpOME to 12,13-DiHOME by the soluble epoxide hydrolase (sEH) enzyme. As a result, an alternate therapeutic route to the current approach of targeting the pathways involved in the initiation of inflammation may be validated.

Epoxy-oxylipin levels were raised by pharmacologically inhibiting sEH with GSK2256294 (15 mg taken orally). Two hours post dosing, inflammation was induced by intradermal injection of UV-killed E. coli in each forearm. Peripheral blood was sampled at baseline and 2h post dosing as well as 24h and 48h post induction of inflammation. Negative pressure suction blisters were raised at 4h and 24h post infection. Cell numbers/phenotypes and lipid levels, in both sample types, were analysed by polychromatic flow cytometry and mass spectrophotometry, respectively.

In peripheral blood, GSK2256294 significantly increased the levels of 12,13-EpOME whilst decreasing the levels of 12,13-DiHOME. This was associated with a greater number of 'immature' neutrophils. At the site of inflammation, the clearance of UV-killed E. coli was reduced significantly.

These data suggest a novel pathway by which epoxy-oxylipins regulate immature neutrophil release during infection and indicate these newly released neutrophils have a lower capacity to carry out bacterial phagocytosis.