

Ex vivo culture of neutrophils to examine neutrophil cell biology and enhance functionality

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Abstract

Due to their short life span native Poly-Morphonuclear Neutrophils (PMNs) are difficult to genetically manipulate. We have developed an optimal culture protocol for the ex vivo production of neutrophils from CD34+ stem cells isolated from peripheral blood. This protocol produces a 70% population of mature neutrophils with over 500-fold cell expansion. The resulting neutrophils display similar nuclear morphology and cell-surface marker expression profiles as native PMNs, while mass spectrometry analysis indicates that cultured neutrophils possess a highly similar proteome to PMNs. Additionally, stem cell-derived neutrophils also display an activatable respiratory burst and can produce Neutrophil Extracellular Traps (NETs). We are currently further characterizing stem cell-derived neutrophils, assessing the efficiency at which they phagocytose pathogens, degranulate and kill bacteria. Although numerous studies have produced neutrophils from CD34+ stem cells, as far as we are aware, this will be the first-time stem cell-derived neutrophils have been fully characterised. We plan to utilise this culturing system, along with the expertise the Toye lab has in genetic manipulation of early haematopoietic progenitors using lentivirus, to examine numerous aspects of neutrophil cell biology. In close collaboration with Dr Borko Amulic, we plan to focus on aspects that are difficult to study using neutrophil like cell lines, including NET formation and degranulation, as well as neutrophil disorders and differentiation defects.

Biography:

Ted Roberts is a PhD Student in Dynamic Molecular Cell Biology at University of Bristol. He has completed his Master of Philosophy - MPhil from the University of Cambridge.



[European Congress on Immunology](#) | Edinburgh, Scotland | March 04-05, 2020

Citation: Ted Roberts, Ex vivo culture of neutrophils to examine neutrophil cell biology and enhance functionality, Euro Immunology 2020, European Congress on Immunology, Edinburgh, Scotland, March 4 -5 , 2020, 14