

Kirsten Nowlan

Project title: The Role of Inflammatory Triggers in the Manifestation of Thymic Abnormalities that Leads to Autoimmunity.

Short Bio	6 months
Home Institution	University of Helsinki, Finland
Host institution	The Francis Crick Institute, London, UK
Project description	Thymic epithelial cells (TEC) play a crucial role in T cell tolerance and their dysfunction is associated with thymic abnormalities and autoimmune diseases like Myasthenia Gravis (MG). We propose that in genetically susceptible individuals, inflammatory triggers induce transcriptional changes in TECs, leading to chronic proinflammation. This impairs TECs' ability to regulate T cell differentiation, resulting in increased escape from negative selection. Additionally, inflammation may initiate ectopic germinal center (eGC) formation, promoting interaction between miseducated T cells and B cells, leading to production of autoantibodies. Through viral sequencing of MG thymic tissue, we aim to correlate specific viral pathogens with eGC presence. Utilising unsupervised NGS and scRNAseq, we investigate TEC phenotypic and transcriptional signatures to elucidate MG's pathogenic mechanisms. Finally, we will validate our findings using in vitro thymus organ culture to model inflammatory processes that ultimately lead to the thymic pathologies observed in MG, with external triggers.
Personal statement	<i>This fellowship has proven to be an invaluable opportunity for my career, offering extensive networking possibilities, exposure to various methodologies and techniques that I have seamlessly integrated into my own PhD projects. Working alongside accomplished scientists in the host group has been incredibly motivating and enhanced my overall experience. Moreover, the change of scenery has sparked my interest in previously unexplored areas of science, providing me with a fresh perspective on my own project and my career in science.</i>