## Research Theme
Infection and Immunity

## Research Project Title
Investigating Distinct Inflammatory Drivers of Severe Asthma in Singapore

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## Project Description
Asthma is a chronic immune and inflammatory disorder of the airways which affects 10-12% of the adult population in Europe. The majority of the high (£20.65 billion) annual costs of asthma in Europe are due to the 5% patients with severe asthma or therapy-resistant asthma that do not respond well to inhaled or oral corticosteroids (ICS and OCS). The high health and societal burden of severe asthma is also seen in Korea and is likely to be similar in Singapore. Severe asthma is heterogeneous and this PhD will examine whether the drivers of subsets of severe asthma in Europe and Singapore are distinct. In this study we will make use of the extensive results obtained through U-BIOPRED to determine whether the genetics and transcriptomics determined by eQTL analysis and the sputum microbiome can reveal similarities and differences between the European and Singapore severe asthma cohorts that indicate distinct mechanisms that could be used for targeted therapies in the future. Preliminary data indicate at least 5 subsets of severe asthma associated with distinct patterns of gene and protein expression which are associated with several clinical variables. This project will initially use signatures derived from U-BIOPRED that define severe asthma subsets to analyse the gene expression profiles in sputum from patients in Singapore using a focussed approach and to determine whether the same gene patterns are present. This will be extended to examine how Single Nucleotide Polymorphisms (SNPs) are associated with gene and/or protein expression (eQTL or pQTL). Part of the project is based on the hypothesis that mechanistic drivers of severe asthma subtypes are linked to perturbations in inflammation and the microbiome in stable disease causing the observed changes in innate immune function. We will compare the microbiome from severe asthmatics in Singapore with those in Europe and examine whether the increased incidence of NTM in Singapore patients has an effect on macrophage function in in vitro experiments. This PhD project will focus on studying the similarities and differences in severe asthma drivers in Singapore patients with the intention of stratifying these subjects into patients who will respond optimally to the new expensive therapies being developed. The four components of this work will be as follows;
a) To Investigate the expression of specific gene expression profiles that characterise severe asthma subsets in severe asthma subjects in Singapore
b) Use eQTL analysis to examine the contribution of genetics to gene expression profiles in patients with severe asthma in Singapore
c) To Describe the differences in bacterial microbiome in severe asthmatics from Europe and Singapore, and
d) To Assess the effect of NTM on macrophage functions including phagocytosis, inflammation and steroid responsiveness.

**Contact Us**

If you have questions regarding this project, please email the Principal Investigator.

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