MRC/BJA Fellowship Abstract

An integrated metagenomic approach to understanding disease heterogeneity in severe sepsis due to community acquired pneumonia

Sepsis represents a major public health burden worldwide with significant associated morbidity and mortality. Evidence suggests that susceptibility to sepsis and clinical outcome is modulated by genetic factors. However, current research has been limited by a complex, heterogeneous disease phenotype.

Community acquired pneumonia is the commonest cause of sepsis. Its diverse microbial aetiology remains elusive in one-third of intensive care patients and evidence suggests we underestimate the role of viral and bacterial coinfection.

My proposal aims to advance our understanding of the aetiology and host response in severe sepsis due to community acquired pneumonia by building on an established cohort of patients recruited through the UK Genomic Advances in Sepsis (GAinS) study.

I will utilise next-generation sequencing techniques to analyse the nucleic acids of viral and bacterial species in patient plasma samples, enabling more accurate classification of disease aetiology. This metagenomic profiling will be used to inform and extend the genomic and transcriptomic analyses performed to date for the GAinS cohort, including analysis of gene expression signatures and integration with expression quantitative trait loci mapping and a genome-wide association study of sepsis survival. This integrated approach has the potential to enable clearer resolution of biological processes and define novel therapeutic targets in sepsis.

Dr Cyndi Goh