Sepsis is a clinically complex syndrome defined as the host’s systemic response to infection. Sepsis, if left unchecked can develop into severe sepsis (Sepsis with organ dysfunction) and septic shock (severe sepsis with acute circulatory failure) and eventually death. 46% of Intensive care unit (ICU) bed days a year are attributed to severe sepsis. Hence, sepsis is a major burden on the NHS, costing an estimated £2-3 billion a year (Board Technology Strategy, 2011).

We postulated that histone modifications might be causally or consequentially related to the development and severity of sepsis. We have used mass spectrometry to probe the histone modifications associated with sepsis using in-vitro models of both the adaptive and innate immune system. One of these models uses Lipopolysaccharide (LPS) tolerisation of human primary monocyte derived macrophages to model the phenotypically altered macrophages seen in septic patients. Using this model, mass spectrometry was used to identify and characterise a wide range of histone post-translational modifications present on the core histones H3 and H4. In addition, we have used quantitative mass spectrometry approaches to examine changes in relative abundance of a wide range of histone modifications upon initial exposure to LPS. These results further demonstrate the complex role that histone modifications play in sepsis. The understanding of which may lead to new therapeutic pathways to treat sepsis or the identification of a biomarker for the progression of sepsis.