Abstract
Modern medicine has developed by classifying disease into defined diagnostic categories, and recently genetics and genomics has largely been occupied trying to uncover the genetic variants that drive their development. Even within a specific diagnostic category, however, the clinical course a disease takes can vary greatly between individuals. Thus to a patient with immune-mediated disease, for example, long-term outcome can be far more important than the specific diagnosis they are given.

To investigate what controlled long term patient outcome we recruited patients with Crohn’s disease, ulcerative colitis, ANCA-associated vasculitis and SLE, at diagnosis. We then performed a comprehensive RNA expression analysis of separated leucocyte subsets and correlated this with prospective clinical follow-up data over a median of 6 years. We found a CD8 T cell transcription signature that predicts outcome, but is not associated with diagnosis, in these important immune-mediated diseases. A candidate gene study based on pathways identified by this signature in Crohn’s disease revealed a novel pathway driven by FOXO3 that regulates inflammation and is associated with long-term outcome, but not diagnosis, in a number of conditions. This lack of association between the genetics of susceptibility and outcome was then confirmed at genome-wide level.

This presentation will explore new data extending this work that defines a clinically useful prognostic biomarker in IBD, but also addresses the specific immunological mechanisms driving long-term outcome in immune-mediated disease and infection, and the genetics that underpins this. Evidence will be presented suggesting that the biology underlying long-term disease outcome, or prognosis, is distinct from that driving specific diagnosis, and represent an under-investigated but clinically relevant aspect of disease pathogenesis.

Recommended Reading