Principal Investigator

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Summary of research

blood, myeloid:lymphoid, pleiotropy, mendelian randomisation

Application Lay Summary:

1a: Peripheral blood consists of numerous subsets of white blood cells that can be classified as myeloid or lymphoid in origin and nature. Recent evidence suggests that the ratio of myeloid:lymphoid (My:Ly) subsets is a robust predictor of a wide variety of diseases including heart disease, cancer and infection and of survival. Here we aim to use a reverse-regression approach to identify the set of diseases in which the My:Ly ratio is of prognostic value. We then propose to explicitly model pleiotropy, and use Mendelian randomisation to test whether the My:Ly ratio is causatively associated with these diseases.

1b: This work aims to understand the pathophysiologic significance of an easily measured blood parameter in survival and provide a robust estimate of which diseases the My:Ly ratio is of practical value. By describing the genetic underpinnings and then using this understanding to test causal associations, this

work aims to enhance our understanding of human health by testing a tool to predict health and identifying causal pathways for health.

1c: Using data on blood cell subsets (platelets, neutrophils, monocytes, lymphocytes, basophils and eosinophils) we will first test whether a range of phenotypes including early death, cardiovascular events, cancer diagnoses and infectious disease diagnoses are associated with the ratio of myeloid:lymphoid subsets or individual counts. This will be performed in the individuals who do not have genotype data available as yet. Then using the subset of the cohort with genotype data we will perform a GWAS of the subset counts, to identify non-pleiotropic genetic correlates that will be used as instrumental variables in a Mendelian randomisation study.

1d: Full cohort.