Project Details	
Project Code	MRCPHS26Ex Frontini
Title	How common genetic variation determines protein abundance and its effect on disease.
Research Theme	PHS
Project Type	Dry lab
Summary	Proteins are the ultimate effector of the information encoded in the genome. Their effects are modulated by human genetic variation both qualitatively (changes in protein sequence) and quantitatively (changes in protein abundance). The candidate will use a large cohort of paired gene expression (RNA-seq) and proteomic (mass-spec) data from primary cells isolated from volunteers to determine how common genetic variation affects protein abundance and, through this mechanism, risk for human diseases.
Description	In the past two decades thousands of variants in the genome have been associated with quantitative traits, such as blood count or height, and common disease susceptibility using Genome Wide Association Studies (GWAS) Proteins are the building block of the cell and the ultimate effector of the information encoded in the genome. The levels of individual protein species affect the functioning of cells and could be the cause of diseases. Molecular quantitative trait loci (QTL) capture the association between genetic variation and intermediate phenotypes, such as gene expression (eQTL), transcriptional isoforms usage (isoQTL) and protein levels (pQTL). The aim of the project is to develop approaches for integrating and exploiting a novel dataset and apply these to understand the genetic architecture of protein abundance and its relationship with common diseases. In this project, the candidate will take advantage of the availability of paired multi omics data (genetic, gene expression, and protein quantification) in four cell types from the blood of 1000 individuals to identify eQTLs, isoQTL and pQTL. They will use statistical methods to determine which genetic variants affect protein levels, and whether this is mediated by effects on gene expression or transcriptional isoform usage (both linked to mRNA levels), or through other mechanisms, such as protein stability. Additionally, the candidate will integrate their data with GWAS summary statistics for human diseases and other traits to determine whether effects on protein abundance are likely to mediate genetic associations with these traits. The candidate will join a supervisory group with an extensive track record of using these approaches to study cardiovascular and psychiatric disorders. They will be part of a multi-disciplinary collaborative research environment that includes clinicians, biologists, statisticians and bioinformaticians. The candidate will take ownership of identifying relevant computational methods, their application, together with methodology development where necessary, to integrate the available data. They will lead the analyses and with the direction of the supervisory team, will coordinate the assembly of evidence to support the publication of their findings in peer-reviewed journals. While the project is focused on blood cell types derived data, the methodologies developed will be relevant to a broad range of disease areas.

Supervisory Team	
Lead Supervisor	
Name	Dr Mattia Frontini
Affiliation	Exeter
College/Faculty	Health and Life Sciences
Department/School	Department of Clinical and Biomedical Sciences
Email Address	m.frontini@exeter.ac.uk
Co-Supervisor 1	
Name	Professor Nicholas Bray
Affiliation	Cardiff
College/Faculty	Division of Psychological Medicine and Clinical Neurosciences
Department/School	Medical School
Co-Supervisor 2	
Name	Dr Kate Burley
Affiliation	Bristol
College/Faculty	School of Cellular and Molecular Medicine
Department/School	Haematology
Co-Supervisor 3	
Name	
Affiliation	
College/Faculty	
Department/School	