Principal Investigator
Professor John Danesh

Applicant Institution University of Cambridge, Public Health and Primary Care, Cardiovascular Epidemiology Unit, Strangeways Research Lab, Cambridge

Application Number / Title
11193 - "Relevance of genetic determinants of major lipids to health and disease" - The Lipids Working Group of the UK Biobank Cardio-metabolic Consortium

Lead Collaborators:

1) Professor Naveed Sattar
2) Dr David Preiss
3) Dr Eleftheria Zeggini
4) Professor Panos Deloukas
5) Dr Paul O'Reilly
6) Dr Manuel Rivas

Collaborating Institutions and Addresses:

1) University of Glasgow, Cardiovascular and Medical Sciences, 126 University Place, Glasgow G12 8TA, United Kingdom
2) University of Oxford, Clinical Trial Service Unit, Clinical Trial Service Unit, Old Road Campus, Oxford OX3 7LF, United Kingdom
3) Wellcome Trust Sanger Institute, Human Genetics, Wellcome Trust Genome Campus, Hinxton, Cambridge CB10 1HH, United Kingdom
4) Queen Mary University of London, William Harvey Research Institute, Charterhouse Square, London EC1M 6BQ, United Kingdom
5) King’s College London, MRC SGDP Centre, Psychiatry, Psychology and Neuroscience, DeCrespigny Park, Denmark Hill, London SE5 8AF, United Kingdom
Keywords

Lipids, lipoproteins, cardiovascular, genetics, interactions, causality.

Application Lay Summary:

1a: Major lipids and lipoproteins are well-known risk factors for cardiovascular disease, the UK’s leading cause of mortality. Previous studies have identified genetic variation influencing lipid levels, but much of the genetic architecture remains unexplained. This application, made by the lipids working group of the UK-Biobank Cardio-Metabolic Consortium, proposes to:
(1) correlate genetic data with lipid levels to identify novel genetic determinants;
(2) conduct fine-mapping analyses to pinpoint causative variants/genes and assess pleiotropy;
(3) identify potential pathways to target to reduce disease risk;
(4) identify lifestyle factors that interact with genetic variation to affect lipid levels.

1b: This project will use the power, detailed phenotypic information, and prospective nature of UK Biobank to improve our understanding of the genetic determinants of major lipids and lipoproteins contributing to the characterization of cardiovascular disease aetiology. Furthermore, it will empower the discovery of new drug targets informing medicines development for prevention of cardiovascular outcomes, thereby improving population health.

1c: Our analysis will involve correlating genetic changes found in the UKB participants with their blood lipid levels (e.g., “good” and “bad” cholesterol) to identify important genetic factors. We will then combine our findings with publicly available information (e.g., gene expression in liver) to identify causal genes involved. The wealth of information in UKB (and external sources) on multiple phenotypes will allow us to investigate the consequences of modifying lipid-related pathways in many different human diseases.

1d: The full cohort will be required.