Application number/Title: 29755 - The contribution of PAR1 and PAR2 on the sex chromosomes to disease

Applicant PI: Professor Maciej Tomaszewski

Applicant institution: University of Manchester, Institute of Cardiovascular Sciences, Room 5.014, AV Hill Building, Oxford Raod, Manchester M13 9PL, United Kingdom

Lead Collaborators: 1) Professor Fadi Charchar

Collaborating Institutions and Addresses:
1) Federation University Australia, School of Applied and Biomedical Sciences, University Drive, Mt. Helen, Ballarat VIC 3350, Australia

Funding body:
British Heart Foundation grant PG/16/149/32176

Keywords provided by the Applicant PI to describe the research project:

Cardiovascular, genetics, sex

Application Lay Summary:

1a: The human sex chromosomes remain a fairly unexplored part of the human genome in terms of their role in complex disease as they have been excluded from genome wide association studies. The pseudoautosomal regions, PAR1 and PAR2 are homologous sequences of nucleotides on the X and Y chromosomes where recombination takes place between both sex chromosomes. The aim of this project is to examine whether genetic variation between PAR1 and PAR2 is associated with complex polygenic disorders and physiological traits.

1b: Understanding the biological mechanisms underlying many common disorders is one of the major goals of UK Biobank. In particular, the resource was established to facilitate research into better understanding of why certain individuals are more predisposed to common disorders than the others. To this end, we wish to examine common variants on the pseudoautosomal regions of the sex chromosomes associate with the risk of common diseases.

The data from this project will help to improve understanding of the role of the sex chromosomes in susceptibility to common disorders with a potential to develop stratified approaches to prediction and therapy.

1c: We will examine association between 1400 markers within the PAR1 and PAR2 (on the Biobank Axiom® Array) and the risk of coronary artery disease, inflammation-immunity related disorders (asthma, rheumatoid arthritis, type 1 diabetes and inflammatory bowel disease), hypertension, type II diabetes, obesity and chronic kidney disease and/or related physiological traits.

1d: We intend to use the full cohort with genotyping data.

Project extension: We are also interested in exploring the association between the PAR region and heritable phenotypes identified from the paper "Phoenome-wide heritibilty analysis of the UK Biobank". Therefore, I would be grateful if you could progress this request for access to additonal phenotype data in our PAR project.