**Selected examples of NIHR Bioresource approved studies, based on participant recall, samples and data, or data only.**

**T Barrett Oct 2020**

The link to the full list of approved studies is here: <https://bioresource.nihr.ac.uk/studies/>

**Defining the mechanisms and control of human regulatory T cell function in autoimmunity**

**Study code**
NBR08

**Lead researcher**
Prof. Graham Lord

**Study type**
Participant re-contact

**Institution or company**
King’s College London

**Speciality area**
Infection, Metabolic and Endocrine Disorders, Gastroenterology

**Summary**

We still lack a detailed understanding of how the immune system is regulated in the healthy human, and how dysregulation contributes to disease. Specifically, we need to understand how regulatory T cells (Tregs) control other immune pathways, how and where Tregs act and interact with other immune and inflammatory components, and how this understanding might be harnessed to treat autoimmune disease. This research will help move us forward in this field.

We have a strong commitment to translational research with ongoing clinical research into the immunology of transplantation, inflammatory bowel disease and sepsis. This includes projects investigating both novel biomarkers in these diseases and cutting-edge therapies, including cellular therapy.

**Whole Genome Sequencing and Analysis to identify new isease genes for hypertrophic cardiomyopathy**

**Study code**
DAA014

**Lead researcher**
Ashley Pritchard

**Study type**
Data only

**Institution or company**
Oxford University Hospitals NHS Foundation Trust

**Speciality area**
Cardiovascular Disease, Genomics and Rare Diseases

**Summary**

NA

**Primary Immunodeficieny**

**Study code**
DAA009

**Lead researcher**
Paul Lyons

**Study type**
Data only

**Institution or company**
University of Cambridge

**Speciality area**
Genomics and Rare Diseases

**Summary**

Primary immunodeficiency (PID) is characterised by recurrent and often life-threatening infections, autoimmunity and cancer, and it presents major diagnostic and therapeutic challenges. Although the most severe forms present in early childhood, the majority of patients present in adulthood, typically with no apparent family history and a variable clinical phenotype of widespread immune dysregulation. Consequently, in sporadic PID genetic diagnosis is difficult and the role of genetics is not well defined. We have addressed this by performing whole genome sequencing of a large cohort of PID patients. This analysis has identified new genes contributing to PID and deepened our understanding of the key pathways determining variation in human immune  responsiveness.

# Contribution of polygenic scores to hematological traits and diseases

**Study code**
DAA008

**Lead researcher**
Dragana Vuckovic

**Study type**
Data only

**Institution or company**
Wellcome Sanger Institute

**Speciality area**
Genomics and Rare Diseases, Haematology

## Summary

We have recently performed strongly statistically powered genotype-phenotype association studies and identified thousands of genetic variants involved in blood cell production. These variants together can explain a large amount of variability in blood cell composition among healthy individuals. However, it is unknown if and how they contribute to blood related diseases. We would like to use data from participants from the NIHR BioResource project for whom full blood count data are available to investigate whether a genetic predisposition to high or low blood cell counts may predict disease status in patients for whom no causal variants have been reported. Furthermore, we curated a list of new candidate variants that show statistic evidence of potential pathogenicity. We would like to check for the presence of these variants in the above patients, in order to validate the findings.

**LATTICE – Safety & efficacy of BMS-986165 in participants with moderate-to-severe Crohn’s Disease**

**Study code**
NBR52

**Lead researcher**
Dr Tim Raine

**Study type**
Participant re-contact

**Institution or company**
University of Cambridge/BMS

**Speciality area**
Gastroenterology

**Summary**

This is an investigational study, also known as LATTICE, of the experimental medication BMS-986165 in patients with moderate to severe Crohn's Disease, a chronic bowel disease that causes severe inflammation of the digestive tract. MS-986165 is an investigational oral, selective tyrosine kinase 2 (TYK2) inhibitor, which has been studied in a phase 2 trial of patients with moderate to severe plaque psoriasis (https://news.bms.com/pressrelease/bristolmyers/bristol-myers-squibbs-novel-oral-selective-tyk2-inhibitor-delivered-signi). The study is a phase 2 randomized, double-blind, placebo-controlled study of the safety and efficacy of BMS986165.

**GENBIO-SWAP70 – Identifying the cell type-specific roles of the coronary artery disease risk gene SWAP70**

**Study code**
NBR50

**Lead researcher**
Dr Dirk Paul

**Study type**
Participant re-contact

**Institution or company**
University of Cambridge

**Speciality area**
Cardiovascular Disease

**Summary**

This is a research study looking at cardiovascular disease (e.g. heart attacks, stroke) and immune-related diseases (e.g. type I diabetes). The purpose of this study is to identify and characterise the complex biological pathways that drive the development of these diseases.

This study is organised by Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care and is situated at University of Cambridge

**AdipO2 – Body fat distribution and diabetes risk: the role of adipose tissue oxygen metabolism**

**Study code**
NBR37

**Lead researcher**
Dr Konstantinos Manolopoulos

**Study type**
Samples and data

**Institution or company**
University of Birmingham

**Speciality area**
Metabolic and Endocrine Disorders

**Summary**

Fat tissue plays an important role in human metabolism as it stores energy derived from meals. However, fat accumulation as seen in obesity is associated with cardiovascular disease and the development of diabetes, and is also linked to inflammation. In this research project, we will study the relationship between fat tissue oxygen metabolism  (an  important  metabolic  factor)  and  inflammation  in  lean  and  obese  subjects.  We  wish  to  explore the mechanisms  by which oxygen  affects  abdominal and  thigh  fat  function  including  nutrient  handling  and  the production of inflammatory factors, since a deeper understanding of these mechanisms could pave the way for future treatments of obesity complications. We will conduct an in vivo physiology study in healthy lean and obese postmenopausal female volunteers that will allow us to study fat tissue function under near-normal conditions. The in vivo study involves taking blood samples from veins specifically draining fat tissue before and after a standardised high-fat meal, alongside measurements of fat tissue blood flow. These measurements are supplemented with extensive lab-based characterisation of fat tissue from biopsies taken during the in vivo study.

# Generation of pluripotent stem cell lines to test novel compounds for the treatment of disease

**Study code**
NBR25

**Lead researcher**
Dr David Bunton

**Study type**
Participant re-contact

**Institution or company**
REPROCELL Europe Ltd

**Speciality area**
Ophthalmology

## Summary

iPSCs are somatic cells (non-reproductive cells) that are manually reprogrammed in the laboratory to become pluripotent, that is they have an ability to become different cell types.

With this study, we plan to generate an induced pluripotent stem cell (iPSC) line from each donor.  The iPSCs can then be used as a research tool in studies investigating the disease, drug discovery and pre-clinical evaluation of potential new treatments.

This reprogramming technology offers several advantages for researchers which include:

* the ability to generate several different cell types from one iPSC culture,
* the potential to study many different diseases (common and rare) and their treatment,
* tissue regeneration capabilities,
* and it is an ethically non-controversial strategy to generate patient-specific stem cell lines.

This research will further our understanding of the biology of the retinal disease and may lead to the development of potential treatments for the major causes of blindness.

# Investigation of genetic susceptibility markers to arthritic conditions and how they contribute to disease

**Study code**
NBR24

**Lead researcher**
Dr Annie Yarwood

**Study type**
Participant re-contact

**Institution or company**
University of Manchester

**Speciality area**
Musculoskeletal Disorders

## Summary

Over the last 10 years significant progress has been made identifying variants in DNA which predispose people to arthritic diseases including rheumatoid arthritis, juvenile idiopathic arthritis and psoriatic arthritis.  The challenge now is to determine how these genetic changes contribute to disease, alter treatment response or determine disease outcome. This study will investigate how possessing an ‘at risk’ genotype could influence disease in terms of DNA structure, gene regulation, protein expression and cellular function in healthy volunteers. This will provide a better understanding of the important molecules, pathways and cells which are altered by genetic susceptibility variants and how they may result in disease. This study has the potential to identify novel targets for therapy which could lead to drug repositioning or novel therapies being developed.

# Discovery of metabolite biomarkers in rare diseases

**Study code**
NBR14

**Lead researcher**
Dr Leonardo Bottolo

**Study type**
Data only

**Institution or company**
University of Cambridge

**Speciality area**
Genomics and Rare Diseases

## Summary

Metabolites are the end-products of gene expression, which are closely related to protein and enzymatic reactions. With the advent of metabolomics as a powerful tool for both biomarker discovery and understanding functional consequences, the identification of specific differences between complex metabolite profiles is becoming an important step in the data analysis pipeline. So far metabonomic profiles have provided potential biomarkers for screening complex disorders such as cardiovascular diseases, kidney disorders, type 2 diabetes, etc. and they enhance accuracy of diagnosis of hyperlipidemia and atherosclerosis. However little is known about the discriminatory power of metabonomic profiles for differential diagnosis of several rare diseases.

We are investigating if metabonomic profiles can be used as a discovery tool for precision medicine to test whether it can increase the diagnostic yield significantly.

This in turn could lead to better treatment choice for patients, and the selected metabolites can serve as biomarkers to improve diagnosis and therapeutic intervention.

We hope to reveal new metabolic pathways by a fully data-driven network representation, and investigate network differences that allow the identification of “common” and “specific” metabolites footprints across rare diseases.

# Functional consequences of disease susceptibility genes in lupus (SLE)

**Study code**
NBR02 / CBR135

**Lead researcher**
Prof. Tim Vyse

**Study type**
Participant re-contact

**Institution or company**
Kings College London

**Speciality area**
Haematology

## Summary

We have previously shown that variation in several genes increases the risk of SLE. In order to understand how differences in genes affect the risk of developing SLE we need to take blood samples from volunteers who do not have lupus so that we can understand how these genes influence ‘healthy’ body responses in comparison to the responses of people who have lupus.