ISRCTN12295348 https://doi.org/10.1186/ISRCTN12295348

Retinal organoids for the study of inherited retinal diseases

Submission date
08/03/2022

Recruitment status
No longer recruiting

Registration date
21/03/2022

Overall study status
Completed

Last Edited
07/06/2022

Condition category
Eye Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The retina is the light-sensitive nerve layer that lines the inside of the back of the eye and converts light into electrical signals that are transmitted to the brain through the optic nerve. Inherited retinal diseases (IRDs) are characterised by retinal degeneration associated with genetic mutations. IRDs can affect individuals at any age and progress at different rates with worsening sight or blindness over time. The blinding nature of IRDs, lack of treatment, and complex heterogeneity (diversity) associated with these conditions highlight the need for research and new treatments. Two main challenges in developing effective treatments for IRDs relate to the absence of suitable experimental models that replicate the human disease, and the lack of understanding of the mechanisms underlying retinal degeneration which may be unique to primates. The aim of this study is to examine the disease mechanisms and assess the effectiveness of targeted genetic treatments using retinal organoids (tissue cultures derived from stem cells) as a model. Eventually, the study findings will greatly aid the translation of new treatments to the clinic.

Who can participate?
Patients aged 18 years or over with clinical and genetic diagnosis of inherited retinal disease.

What does the study involve?
The researchers will generate retinal cells and organoids from peripheral blood samples taken from patients with diagnosed IRDs. This would require first turning the blood cells into induced pluripotent stem cells (iPSCs) using established laboratory techniques. The iPSCs could be maintained in culture and differentiated into retinal cell types or retinal organoids. The researchers will use the retinal organoids/cells as a model to study their anatomical, functional and molecular characteristics with a view to assessing potential clinical treatments in a research setting. This might include, for instance, gene therapy, cell therapy, immunology, transplantation and/or gene-editing technologies.

What are the possible benefits and risks of participating?
The study findings will not directly benefit the participant, but may potentially benefit the many

people with retinal degenerations that lead to blindness. This study involves minimal intervention in the form of providing a blood sample, so the study poses very little (almost no) risk to the participants.

Where is the study run from?
This study is run from the Nuffield Department of Clinical Neurosciences (University of Oxford) jointly with the Oxford Eye Hospital (John Radcliffe Hospital, OUH Foundation Trust, NHS) (UK)

When is the study starting and how long is it expected to run for?
December 2021 to March 2025

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Prof. Robert E MacLaren
maclaren@eye.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Cristina Martinez Fernandez de la Camara

ORCID ID
https://orcid.org/0000-0002-6612-6162

Contact details
Nuffield Department of Clinical Neurosciences
Level 5&6, West Wing
John Radcliffe Hospital
Oxford
United Kingdom
OX3 9DU
+44 (0)1865223701
maclaren@eye.ox.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
301603

Central Portfolio Management System (CPMS)
51617

Study information

Scientific Title

Modelling and rescue of inherited retinal diseases using induced pluripotent stem cell (iPSC)-derived retinal cells and organoids

Study objectives
An experimental clinical laboratory study to investigate the pathophysiology of inherited retinal diseases and the effects of genetic therapies to prevent retinal degeneration using retinal cells or organoids derived from induced pluripotent stem cells generated from patients' blood samples.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/02/2022, London - Westminster Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 (0)207 104 8066, +44 (0)207 1048236; westminster.rec@hra.nhs.uk), REC ref: 21/PR/1761

Primary study design
Observational

Study design
Clinical laboratory research study

Study type(s)
Other

Health condition(s) or problem(s) studied
Inherited retinal degenerations

Interventions
Once informed written consent has been obtained and all the questions answered, a blood sample will be taken from the participants by either a clinician or a research nurse in the Oxford Eye Hospital. As soon as the blood sample is taken, it will be processed in the laboratory to isolate the white cells (called peripheral blood mononuclear cells [PBMC]). These PBMCs will be used to generate retinal organoids and/or retinal cells for laboratory experiments.

Intervention Type
Other

Primary outcome(s)
Expression level and function of the disease-causing proteins in retinal organoids or retinal cell types derived from patients' iPSC, measured using western blot analysis, immunohistochemistry, proximity ligation assay or electrophysiology at a single timepoint

Key secondary outcome(s)
Expression and functional assays of the target gene for genetic or cell therapies in retinal organoids or retinal cell types derived from patients' iPSC, measured using western blot analysis, immunohistochemistry, proximity ligation assay or electrophysiology at a single timepoint

Completion date
31/03/2025

Eligibility

Key inclusion criteria
1. Participant is willing and able to give informed consent for participation in the study
2. Male or female, aged 18 years or over
3. A clinical diagnosis of inherited retinal disease with a genetically confirmed mutation
4. All volunteers should be in good health apart from any specific ocular disease

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. The participant may not enter the study if they have an active infectious disease or if they have impaired wound healing (tested as part of the routine care)
2. Pregnant women

Date of first enrolment
15/06/2022

Date of final enrolment
30/03/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford University Hospitals
John Radcliffe Hospital
Headley Way
Headington
Oxford

United Kingdom
OX3 9DU

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research, Ref. NIHR201338

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No