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Protein engineering to design better enzyme replacement therapies for Fabry disease

Submission date
31/03/2026

Recruitment status
Recruiting

Registration date
28/04/2026

Overall study status
Ongoing

Last Edited
07/05/2026

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims:
Lysosomal storage disorders (LSDs) are rare, inherited metabolic disorders causing life-threatening, progressive disease affecting many body systems. They are caused by mutations in genes which code for lysosomal enzymes, which break down large toxic molecules in the cell. When these enzymes don't work properly these substances build up, causing damage to the heart, kidneys, blood vessels, muscles, brain and skeleton, depending on which enzyme is affected. Fabry disease is the most common LSD and causes nerve pain, strokes, and progressive heart and kidney disease.
Some LSDs can be treated with enzyme replacement therapy (ERT). This involves a weekly or fortnightly infusion treatment given directly into the vein. However, current treatments are only partly effective as they work less well than natural enzymes and cannot access certain body tissues. They also cause immune reactions, leading to severe allergic-type reactions, and further reduce the effectiveness of the treatment. Patients find these side effects and the frequency of the infusions a major burden.
We are using artificial intelligence-led protein design to help design new treatments for Fabry disease. These enzymes are designed to work more effectively and not cause immune reactions. They are designed to be better than current treatments so they can be given less often and work more effectively. The first stage of testing is to see whether they cause fewer immune reactions than existing treatments. We will do this by testing them in samples of patients' blood in the laboratory.

Who can participate?
Anyone with a confirmed diagnosis of Fabry disease who is over 16 years old and is not taking any regular immune-suppression medication (such as for a kidney or heart transplant). We are not able to enrol patients who have received experimental gene therapies for Fabry disease.

What does the study involve?
We would like you to donate an extra sample of blood and urine, usually taken at a single visit at the same time as your routine NHS clinic bloods. You can also choose to have a 24-hour ambulatory blood pressure and vascular stiffness monitor, which you take home and post back to us.

What are the possible benefits and risks of participating?
There are no direct benefits to taking part, but you will be contributing to research which may help improve treatments for people with Fabry disease.
There are no significant risks to taking part: blood tests may be uncomfortable and leave a small bruise but will be taken at the same time as your usual blood tests. The 24-hour ambulatory blood pressure cuff is inconvenient but should not be painful.

Where is the study run from?
The study is being run from the Clinical Research Centre at the University of Edinburgh (UK)

When is the study starting and how long is it expected to run for?
August 2024 to December 2026

Who is funding the study?
The study has been funded by the Engineering and Physical Sciences Research Council (EPSRC) (UK)

Who is the main contact?
Dr Eve Miller-Hodges, eve.miller-hodges@ed.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
340344

Central Portfolio Management System (CPMS)
63395

Study information

Scientific Title
Intelligent De-immunization of Enzyme Replacement Therapies (IDERT)

Acronym
IDERT

Study objectives
This study aims to test the immunogenicity of novel engineered enzymes against patient samples, in order to design better treatments for patients with Fabry disease

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 04/06/2024, South West - Cornwall & Plymouth Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)3071048071; cornwallandplymouth.rec@hra.nhs.uk), ref: 4/SW/0061

Primary study design
Observational

Secondary study design
Cross sectional study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Fabry disease

Interventions
Collection of blood and urine samples
24-hour non-invasive home measure of blood pressure and blood vessel function (optional)

Intervention Type
Other

Primary outcome(s)
Cross-reactivity of existing patient anti-drug antibodies to the new designed enzymes tested using enzyme-linked immunosorbent assays (ELISA) in patient sera and reported relative to wild-type enzyme and existing treatments at a single timepoint

Key secondary outcome(s)
Associations between immune-reactivity to the new designed enzymes compared to the clinical phenotype of the patient (defined as classical or late onset); sex; prior treatment exposure (type of enzyme replacement therapy), plasma lyso-GB3 (measured using liquid chromatography tandem mass spectrometry) and ambulatory blood pressure and vascular stiffness (measured using Mobil-o-Graph NG 24hr ABPM System) at a single timepoint

Completion date

30/12/2026

Eligibility

Key inclusion criteria
1. Diagnosis of Fabry disease (biochemical and/or genetic diagnosis)
2. Aged 16 years or over
3. Able to give informed consent
4. Not on immunosuppressive medications (e.g., previous transplant) which could impact immunogenicity
5. Never received gene-therapy for Fabry disease
6. No upper age limit

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. On immunosuppressive medication (equivalent to >7.5 mg prednisolone daily)
2. Treated with gene therapy for Fabry Disease
3. Unable to give informed consent

Date of first enrolment
01/08/2024

Date of final enrolment
30/12/2026

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
University of Edinburgh
Old College
South Bridge
Edinburgh
Scotland
EH8 9YL

Sponsor information

Organisation
University of Edinburgh

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Not defined

Funder Name
UK Research and Innovation

Alternative Name(s)
UKRI

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 this study will be de-identified and may be available for use in future ethically-approved studies, on request.

IPD sharing plan summary

Available on request