

**Manchester BRC Next Generation Phenotyping and Diagnostics Theme (NGPD)**

**‘Genome Editing Service’ Funding Call (Round 2) Remit**

**Call Summary/Remit:**

Following on from the success of the first Manchester BRC Next Generation Phenotyping and Diagnostics Theme (NGPD) ‘Genome Editing Service’ call in 2023, the second call is now open for applications.

NGPD invites researchers and collaborators to apply for up to £20,000 for projects accessing the platforms/services offered by the University of Manchester [Genome Editing Unit](https://www.bmh.manchester.ac.uk/research/platforms/) (GEU). These include:

* Generation of genetic mutation cell models (including human-derived cell lines, primary cells or induced pluripotent stem cells (iPSCs))
* Downstream functional assays
* CRISPR-based diagnostics development (including SHERLOCK and DETECTR platforms)

No staff posts will be funded through this call, but applicants will have access to an Experimental Officer based at the UoM GEU, to support their project. FTE contribution required by the experimental officer, to deliver the project, must be specified in the application.

*Projects must:*

* Relate to phenotyping and diagnostics of disease, rather than therapeutic interventions.
* Clearly define the role of the Experimental Officer and benefits this contribution will have.
* Be of an appropriate scale and able to be initiated without a great delay (e.g., with ethics already in place where necessary).
* Have a duration of up to 13 months max.
* Align with the remit of the NGPD Theme programmes (as detailed in Appendix 1).

*Priority will be given to projects which:*

* Span across 2 or more of our BRC research themes and/or clusters.
* Create novel resources that can be adapted for additional projects and/or develop new technologies.
* Have opportunity for translation, including diagnostic development or pre-clinical therapeutics.
* Promote collaboration between an NHS Trust and UoM core facilities.

Further details on the projects delivered during Round 1 of this call can be found in Appendix 2 below.

**Applicant Eligibility:**

* This call is open to both BRC and non-BRC associated staff, and we encourage applications led by:
* Early Career Researchers
* Nurses, Midwives and Allied Health Professionals
* The lead applicant must hold an appropriate contract with a BRC partner organisation and/or with a Higher Education Institute (HEI) within the Greater Manchester area. This contract must exceed the duration of the proposed project.
* The call is also open to Children’s research.

**Finances:**

* Projects of approximately £5,000-20,000 will be funded. Total amount available, for all awarded projects (across two financial years), is £40,000 (100% of directly incurred costs only).
* Funds are **only** available for:
* Core Facility lab costs
* Project-related consumables
* Additional non-staff costs (e.g. PPIE/EDI etc.)
* No **salary** funding will be awarded. The Experimental Officer’s services will be provided as an in-kind resource contribution.
* Equipment purchases are capped at £5,000 per item and must be justified against the duration of the project).
* The BRC cannot fund pre-clinical/animal model work

Funding will be awarded in 2 payments across 2 financial years: Up to 31st March 2025 and 1st April 2025 – 31st March 2026. Project costings submitted must reflect this.

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| **BRC Financial Year** | **Total Funding Available** | **Funding to be spent between:** |
| FY3 Present to 31st March 2025 (Project Year 1) | £20,000 | 10th February - 31st March 2025 |
| FY4 01st April 2025 to 31st March 2026 (Project Year 2) | £20,000 | 01st April 2025 – 31st March 2026 |

* Please review the NGPD Terms and Conditions document before applying.
* For further information on the services and capabilities of the GEU, lab costings and how the GEU can support your application, please visit the UoM Core Facilities [website](https://www.bmh.manchester.ac.uk/research/platforms/) and/or contact:

Polly Downton (Experimental Officer) polly.downton@manchester.ac.uk

Antony Adamson (GEU Manager) Antony.Adamson@manchester.ac.uk

**Application Process:**

* Applications are subject to a review by an appointed NGPD Theme review panel.
* Awards are made based on scientific merit, relevance to our focus areas and impact on patient health outcomes.

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| **Project duration - Up to 13 months** |
| **Funding Call Opens** | 20th Dec 2024 |
| **Funding Call Closes** | 29th Jan 2025 |
| **Panel Review** | w/c 3rd Feb 2025 |
| **Award Letters Issued** | w/c 3rd Feb 2025 |
| **Project Start Date** | 10th Feb 2025 |
| **Project End Date** | 31st March 2026 |

Appendix 1. Theme details

**Theme programmes are as follows:**

**1. MULTIDIMENSIONAL DATA INTEGRATION TO IMPROVE BIOMARKER DISCOVERY**

*Leads: David Wedge and Rachel Lennon*

Fibrosis, eye disease and cancer collectively present an enormous healthcare burden. We have existing multidimensional data in these exemplar domains to test the below hypotheses:

**1)** Improved phenotyping can detect early stages of fibrosis.

**2)** Integration of genomic and image data improves risk profiling.

**3)** Multimodal tests applied across a range of ethnicities will improve prognosis across cancer types.

**2. DATA MINING TO ADVANCE THE UTILITY OF EXISTING DIAGNOSTIC DATASETS**

*Leads: Graeme Black and Andrew Morris*

We will improve diagnostic sensitivity by the integration of orthogonal datasets and will test the below hypotheses:

**1)** Understanding genomic variant impact improves patient stratification and allows identification of therapeutic targets.

**2)** Machine learning image analysis can identify new imaging biomarkers.

**3. CLINICAL VALIDATION OF TRANSLATABLE DIAGNOSTIC METHODOLOGIES**

*Leads: Tracy Hussell and John Grainger*

We will advance high throughput diagnostics by testing the below hypotheses:

**1)** Near-patient diagnostics can accelerate real-time tailoring of patient management.

**2)** Immunophenotyping can identify disease endotype, progression and treatment response.

Appendix 2. 2023-2024 NGPD GEU projects

**2023/2024 Funded Projects:**

**Ruling out infection with pan-bacterial detection from sterile sites.**

*PI: Dr Danielle Weaver*

*CoI: Prof Tim Felton, Dr Antony Adamson, Dr Stephanie Thomas*

*Award: £4200*

*Outputs: Opportunity for translation/IP, grant applications/industry investment, data for publication.*

This project aimed to develop CRISPR diagnostic reagents for identification of bacterial presence in clinical samples. We have designed and validated Cas12 guide RNAs for universal detection of clinically-relevant species of bacteria in *in vitro* DETECTR assays.

**Using genetic manipulation techniques to functionally validate informatics findings associated with albinism.**

*PI: Dr Panagiotis Sergouniotis*

*CoI: Prof Graeme Black, Prof Sue Kimber, Dr Antony Adamson*

*Award: £19339*

*Outputs: Grant applications, data for publication.*

This project aimed to genetically modify a patient-derived iPSC line to correct several disease-associated single nucleotide variants (SNVs). We have used CRISPR-cas9 genome editing to successfully correct the first of these variants and also generate a parallel KO cell line; subsequent rounds of modification to stack additional SNV corrections into modified cells are ongoing.

**Functional characterisation of genetic variants of relevance to hypertension and antihypertensive treatment.**

*PI: Ms Amber Emmett*

*CoI: Prof Maciej Tomaszewski, Dr James Eales, Dr Xiaoguang Xu*

*Award: £14470*

*Outputs: Grant applications, data for publication.*

This project aimed to experimentally validate bioinformatic analyses identifying disease-associated SNVs in kidney proximal tubule cells. Gene expression analysis in response to inflammatory and metabolic stimuli prioritised potential variants, which have subsequently been introduced into proximal tubule cells using CRISPR-cas9 genome editing. Phenotypic analysis of modified cells to validate SNV effect is ongoing.

**Development and validation of a diagnostic assay for the risk of uveitis in patients with juvenile idiopathic arthritis.**

*PI: Dr John Bowes*

*CoI: Dr Antony Adamson*

*Award: £2000*

*Outputs: Opportunity for translation/IP, grant applications/industry investment, data for publication.*

This project aimed to identify and test potential CRISPR diagnostic assays for identification of genomic variants associated with uveitis risk in Juvenile Idiopathic Arthritis (JIA) patients. Eight relevant variant sequences were screened and three taken forward for experimental testing of SHERLOCK (Cas13) diagnostic reagents. A Cas13 guide with potential to successfully discriminate genomic variants was identified.