# Motor Neuron Disease Translational Accelerator (MNDAcc)

Request for proposals

The Medical Research Council (MRC) and the National Institute for Health and Care Research (NIHR) are investing £6m in translational and experimental medicine research on motor neuron disease. The programme, referred to as MNDAcc (Motor Neurone Disease Accelerator) is intended to support diagnostics, treatment and prevention interventions emerging from a growing understanding of disease mechanisms.

MNDAcc is managed by Dementias Platform UK (DPUK) by providing infrastructure and key services. In addition, the UK Dementia Research Institute (UKDRI) is providing access to its scientific platforms and capabilities. MNDAcc has been designed to complement and support other recent MND research investments including (but not limited to) the BRCs, the MND Collaborative Partnership, the EXPERTS-ALS platform, and the MRC/NIHR funding highlight notice.

MNDAcc is a national RFP-based programme of experimental medicine and translational research. Proposals are invited from all UK-based MND and MND-FTD researchers (see guidelines below). While collaboration, including with industry, is encouraged, research groups may work singly or in multi-site consortia. This call seeks applications for human-based studies with a clear pathway to impact. Successful projects will include people with or at risk of MND and laboratory-based studies with samples, tissues, cell-lines or data derived from people with or at risk of MND, and appropriate controls.

The MNDAcc programme is supported by an Executive and a Scientific Steering Group (see annexe 1).

- The Executive is responsible for ensuring that the programme is delivered on time and according to the agreed scope. The Executive is chaired by an independent and internationally recognised researcher and includes a strong advocate for people affected by MND.
- The Scientific Steering Group (SSG) will oversee the peer review of the full applications and deliver funding recommendations to the Executive. The SSG is based on an MRC-appointed oversight panel and will be augmented by non-conflicted MND researchers with expertise relevant to the applications received.

**Proposals must focus on human-based approaches, should be hypothesis driven and should be achievable in 6-18 months.** In-scope projects include, but are not limited to:

- Projects to develop, validate or apply biomarkers for disease stratification, monitoring progression, clinical trials, etc.
- Projects to demonstrate target engagement.
- Early phase clinical trials and experimental medicine
- Leveraging existing cohorts to validate biomarkers
- Analysis of human samples and data generated from earlier clinical trials
- Evaluation of novel fluidic biomarkers for diagnosis, proximity, or monitoring
- Development of novel patient-derived cellular models of disease (e.g. organoids, iPSCs) with specific aim of supporting translational research
- Nested studies within existing MND research trials and consortia, where additional investment(/mechanistic insight) could increase impact

Ineligible/out of scope activities include:

- Fundamental or discovery neuroscience research
- Animal-based studies
- Sample characterisation or phenotyping projects
- Creating or expanding cohorts

MNDAcc has been designed to be flexible. There is no set budget limit for proposals. However, we expect to fund up to c.10 proposals across a range of values and it is therefore essential that applicants fully justify the requested budget. The MNDAcc Scientific Steering Committee will be asked to consider the overall value and impact of individual projects and the likely impact of the portfolio of projects, balancing high and low-cost proposals.

Applicants are invited to take advantage of DPUK and UKDRI scientific and technological platforms and resources. These include, for example, expertise in fluid based and digital biomarkers, proteomics, single cell and spatial transcriptomics, end-to-end data management, multi-modal data analysis, and networks for brain imaging (MRI, PET, MEG) and induced pluripotent stem cells. (Please refer to annex 2 for further details and contacts.) Whereas proposals that will benefit from these resources are encouraged to use them, proposals are not required to use these resources. Copies of data generated by MNDAcc will be stored in the DPUK Data Portal.

**Guidelines**

1. Lead applicants should be based at any eligible UK research organisation. For more information on eligibility criteria for individuals and research organisations see additional guidance at ukri.org Whereas individual research groups may apply, collaboration is encouraged when it serves the needs of the proposed project.

2. Proposals may involve collaboration with industry and financial or in-kind contributions from industry partners are welcome. However, MNDAcc funding cannot we provided to industry partners. Applicants preparing proposals involving an industry partner should review the MRC guidance to determine whether a submission under the Industrial Collaboration Framework is required.

3. Applicants may only serve as principal (lead) investigator on a single proposal. A principal investigator may however participate on other proposals as co-applicant and individuals may serve as co-applicants on multiple proposals.

4. Projects can be no longer than 24 months in duration. It is anticipated that most will run for 6-18 months (with an additional 3-month, unfunded set up time permitted).

5. Funds may be used to cover:
    - Scientific, medical, and technical personnel
    - Research consumables and reagents.
    - Appropriate CRO costs
    - Service costs commensurate with the specific use of equipment

    Ineligible costs include:
    - Conference and other meeting registration and travel
    - Publishing costs
    - Industry partner costs

- PhD studentships

Modest travel costs may be included but only when travel is necessary for the successful delivery of the research. Funds may not be used for the purchase of equipment unless the applicant can demonstrate that the proposed equipment is an essential component of the project and is otherwise unavailable (including via a collaborator).

6. Applications should be costed under MRC's standard 80% of FEC methodology https://www.ukri.org/councils/epsrc/guidance-for-applicants/costs-you-can-apply-for/principles-of-full-economic-costing-fec/ Permitted exceptions (see MRC Guidance for Applicants) will be funded at 100% FEC. Successful applicants will receive MRC award letters under MRC standard grant terms and conditions https://www.ukri.org/manage-your-award/meeting-ukri-terms-and-conditions-for-funding/

7. It is the responsibility of the applicants to obtain all relevant clearances and/or approvals for the proposed work.

**Selection criteria**

Applications will be assessed according to the following criteria:

- In scope and responsive to the call remit including relevance to and impact on people affected by MND/FTD
- Vision of the project
- Feasibility of project plan:
    - project plan & milestones,
    - methodology, experimental and statistical design
    - risk mitigation and management
    - research environment and infrastructure
    - data management and sharing plans
    - resources requested
- Translational pathway
    - The applicant should outline a translational pathway which should describe plans for ensuring that the project outcomes result in patient impact.

**Application process**

There are two stages to this application process. Both should be submitted using the templates provided via the MNDAcc website

**Step 1: Expression of interest.**

EOIs will be evaluated by the MNDAcc Executive to determine compliance and relevance to the call. EOIs should be structured as follows:

1. Project title
2. Start/end dates
3. Investigator details:
    a. Principal investigator
    b. Co-applicants
    c. Contributions to the project of each applicant (400 words)
4. Scientific aims

a. study rationale (400 words)
b. expected translational impact (400 words)

5. Summary of project plan (600 words)
6. Resources requested (table)

Expressions of interest will be censored at the maximum word count for each section.

**Step 2: Full applications**

Applicants will be informed in December 2023 if a full application is invited. Full applications will be peer reviewed by the Scientific Steering Group with additional peer reviewers as required. Full applications will be structured as follows:

a. Project title
b. Start/end dates
c. Investigator details: List of investigators and contribution to the project
d. Lay summary
e. Scientific abstract
f. Scientific aims and translational impact
g. Background and preliminary data
h. Translational pathway
i. Risk mitigation
j. Research plan to include:
    i. Collaboration contributions and management
    ii. Experimental plan
    iii. Project timeline and go/no go milestone decision points
    iv. Risk Management
    v. Future plans
    vi. References
k. Detailed Budget and justification of resources requested
l. Intellectual property disclosure
m. Data Management Plan

Any queries related to this RFP should be directed to MNDAcc@psych.ox.ac.uk

**Important dates:**

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|---|---|
| Request for proposals announced: | 8 October 2023 |
| Information Webinar: | 16 October 2023 |
| Expression of interest (EOI) deadline: | 1 December 2023 |
| Full applications invited: | 15 December 2023 |
| Full application deadline: | 2 February 2024 |
| Peer review and rebuttals completed: | 22 March 2024 |
| Recipients announced | April 2024 |

**Website: www.mandacc.com**

**Email: info@mndacc**

**Annex 1 – Membership of MNDAcc Executive**

Chair: Professor John Gallacher, University of Oxford

MRC NMHB Board Chair

Patient / carer representative to be nominated by MNDA/MNDS

**Membership of MNDAcc Scientific Steering Group**

Chair: Christian Haas (DZNE) or Ludo Van Den Bosch (VIB)

Professor James Rowe, University of Cambridge

Member of MND collaborative – Pam Shaw

MRC NMH Board panel member

MRC Experimental Medicine panel member

Other members will be co-opted according to the needs of expert scientific review

**Annex 2 – DPUK and UK DRI – Technical and scientific resources contact list**

**Facilities and technologies available to MNDAcc include:**

- **The MNDAcc hub at DPUK Data Portal**
  - End-to-end data management
  - Data and tissue discovery
  - Research ready data
  - Multi-modal analysis
  - Security to ISO 27001

  Contact: Emma Squires, emma@chi.swan.ac.uk

- **DPUK Trials Delivery Framework**
  - 'Great Minds' research Register
  - Clinical Studies Research register
  - DPUK trials delivery network

  Contact: Research registers Dr Ivan Koychev, ivan.koychev@psych.ox.ac.uk
  Trials network: Dr Vanessa Raymont, vanessa.raymont@psych.ox.ac.uk

- **DPUK Experimental Medicine Incubator**
  - Vascular health
  - Neuroinflammation
  - Synaptic health

  Contact: Professor James Rowe, James.Rowe@mrc-cbu.cam.ac.uk

***Applicants will be able to access UK DRI Platforms benefitting from prioritisation and heavily subsidised rates identical to those offered to full UK DRI Group Leaders.***

- **UK DRI Biomarker Factory**
  - Ultrasensitive immunoassay laboratory for biofluid sample analysis
  - Refinement of existing blood biomarkers
  - Identification of novel biomarkers through a combination of 'omics-based discovery studies, semi-targeted and targeted assays of neuroimmune and lysosomal function, and in-depth molecular analysis
  - Technologies: Quanterix *Simoa HDx, Merck SMCxPRO, O-Link Signature 100 platform, MesoScale Discovery platform, BioRad platform with Luminex technology and general plate reader equipment*

Contact: Dr Amanda Heslegrave, a.heslegrave@ucl.ac.uk

- **UK DRI Proteomics Platform**
  - Access to Mass spectrometers, proteomic techniques and associated expertise.
  - Access to expert informatics advice and analysis of mass spec data.
  - Improvement of proteomic experimental design to strengthen reproducibility.
  - Quantification techniques such as TMT and DIA, Proximity labelling, PTM analysis, Small cell number analysis (<2,000 cells), Subcellular fractionation.

Contact: Dr Beth Geary, BGeary001@dundee.ac.uk

- **UK DRI Single Cell and Spatial Transcriptomics Platform**
    - UK DRI is providing services in single cell RNA sequencing and associated techniques and bioinformatics from our UCL Platform Lab.
    - We also have access to a range of single cell and spatial transcriptomics equipment through both local labs and a network of collaborators.
    - Technologies being used include: Single-cell: 10x Genomics workflows (scRNAseq, scATAC-seq and 'Multiome'); Spatial: Nanostring GeoMX, Nanostring CosMX, BGI Stereoseq.

Applicants interested in using these technologies as part of their project can contact Sam Jackson in the first instance to discuss needs: sam.jackson@ukdri.ac.uk

- **Other UK DRI capabilities**
    - Novel iPSC-based models for drug screening, target identification and validation, including isogenic lines for rapid i-Motor Neuron differentiation, degron-based models, 2D/3D systems, organoids, neuromuscular 'assembloids'
    - High-throughput screening approaches for drug discovery including phenotypic cellular analysis (multiplex high-content imaging, morphological profiling, fluorescence-based pathway sensors)
    - Machine learning approaches and informatics analysis for ALS-linked genetic variation (including GWAS, mendelian mutations, AnswerALS risk scores)
    - Predictive computational models using pathway and biomarker analysis to complement polygenic risk score for patient stratification

Contact: Dr Giovanna Lalli (UK DRI Director of Scientific Affairs) g.lalli@ukdri.ucl.ac.uk