Programme Guide

Characterisation of Novel Biomarkers for Neurodegenerative Diseases of Ageing

I. Background

The Galen and Hilary Weston Foundation (the **"Foundation"**) supports neuroscience research that accelerates the development of therapeutics for neurodegenerative diseases of ageing. To help achieve this, the Foundation addresses gaps and inefficiencies in the funding market by supporting high-risk, high-reward translational projects, while leveraging world-class scientific expertise in a fast and flexible grant-making process.

Neurodegenerative diseases of ageing are among the most undertreated diseases today and require pioneering approaches to accelerate treatments. Biomarkers for human diagnosis, prognosis, stratification to clinical trials, and to predict response to therapy are crucial to enable new treatments to be developed.

The *Characterisation of Novel Biomarkers for Neurodegenerative Diseases of Ageing* programme (the **"Programme"**) was designed by the Foundation to support longer and larger studies of translational research focused on novel biomarkers with compelling preliminary data. Biomarkers are biological indicators found in human tissues, blood and other bodily fluid that can be used to measure various aspects of health or disease. They are vital to the diagnosis of disease, to monitoring its progression, and to developing new, effective treatments.

Important things to know about the Foundation:

- **We do not fund basic (also known as fundamental) research.** We only fund translational research.
- **Funds are generally provided contingent on meeting milestones:** if your project is approved for funding, grants are provided in tranches as experimental milestones are successfully reached.
- **Our application process is interactive:** you will likely receive feedback on your applications and be asked to make modifications, although we welcome applicant questions and challenges regarding said feedback. Generally, the Foundation welcomes questions and comments from prospective and actual applicants.
- **The majority of applications are declined at the project synopsis stage:** all synopses are rigorously reviewed and, on average, 15% of applicants who submit a synopsis are invited to forward a full proposal. We do this intentionally to ensure that applicants and reviewers direct their attention to applications that have a high probability of being approved for funding. A declination at the project synopsis stage does not mean that the Foundation will not review a similar synopsis in future competitions.

Key Foundation definitions:

- **Neurodegenerative diseases of ageing:** progressive diseases that are underpinned by or associated with significant loss of neurons in the central nervous system and with disproportionate incidence in the elderly. Specific neurodegenerative diseases of ageing that are in scope for this Programme include:
  - Amyotrophic lateral sclerosis (Lou Gehrig's disease)
  - Dementia with Lewy bodies
  - Familial Alzheimer's disease
  - Frontotemporal dementia
  - Multiple system atrophy
  - Parkinson's disease
  - Progressive supranuclear palsy
  - Other rare forms of dementia
  - Vascular contributions to the listed diseases and dementia (but not stroke-mediated vascular disease)
  - Prodromes to the listed diseases/conditions, such as: Mild cognitive impairment as prodromal to Alzheimer's disease
    REM sleep behaviour disorder as prodromal to Parkinson's disease
- **Translational research:** Applied research towards developing therapeutics for the prevention and/or treatment of human disease.
- **Tool:** An item that accelerates development of therapeutics (e.g., animal model, imaging techniques or reagents, biomarkers, or diagnostics.)
- **Therapeutic:** A pharmacological approach (including small molecules, biologics, cell therapies and vaccines, including drug repositioning and repurposing), medical device, surgical intervention, or magnetic or electrical brain stimulation. Therapeutics can be for symptomatic relief, disease modification, or prevention of human disease. Complementary approaches such as acupuncture, music and social interaction are not considered therapeutics.
- **Clinical samples/data:** Human-derived specimens/ resources or data (e.g., tissue, fluid, and imaging scans.)
- **Novel biomarkers:** biomarkers that have been insufficiently studied.

II. Programme scope

The Programme funds testing of novel biomarkers in human samples / data to accelerate the development of therapeutics for neurodegenerative diseases of ageing, as defined by the Foundation.

Candidate biomarkers should be novel and have strong preliminary data to justify testing in human samples / data / cohorts, both of which are criteria for adjudicating applications. **Note that the Foundation will not fund projects exclusively focused on sporadic Alzheimer's disease (familial Alzheimer's disease is acceptable inasmuch as existing biomarkers do not represent a viable alternative to the biomarker approach proposed for this project)**; we further discourage projects advancing biomarkers related to alpha-synuclein for Parkinson's disease unless there is a component of the project that would be considered unique or novel.

Characterisation of novel biomarkers using existing cohorts that are longitudinally tracked is encouraged and will be given priority over projects that use small sample sizes and/or cross-sectional cohorts.

Biomarkers must be under development for human disease diagnosis, prognosis (including rate of progression), stratification to clinical trials, measuring disease progression, and/or to predict / measure response to therapy (*e.g.*, a surrogate for clinical endpoint.)

Biomarkers should measure pathology of the disease (*e.g.*, fluid, imaging or tissue-biopsy-derived biomarkers) and not be based on cognitive, neuropsychological or behavioural phenotypes (e.g., gait, grip strength, and cognitive tests). Genetic biomarkers, including somatic mutations, single nucleotide polymorphisms, epigenetics and gene products, are in scope provided they meet all eligibility criteria.

For this Programme, only biomarkers that meet the following three criteria are eligible:

1. **Description of the biomarker:**

   a. Specific item(s) or signature to be measured can be defined, for example:

      i. Disease-specific EEG signature.
      ii. Specific brain structure with reduced volume or other anatomical change (e.g., MRI analysis).
      iii. Single protein changed (e.g., measured in fluid or by neuroimaging approaches).
      iv. Precisely defined fingerprint: if the biomarker is a fingerprint of a family of proteins or a signature of brain volume changes, the precise fingerprint or signature must be previously determined. For example, 'omics' studies for the purpose of identifying biomarker patterns or signatures are out of scope.
      v. Exact identities of multiple individual factors that may be useful individually or as a specific composite.

   b. Method: type of assay or technique that will be used for the detection of the biomarker can be stated clearly.

   c. Human population: Disease population or clinically relevant subgroup the biomarker is being developed for use in, or that you wish to study the biomarker in, can be stated clearly.

   d. Type of specimen: The type of specimen (e.g., which fluid or tissue) that will be used for the detection of the biomarker can be articulated clearly.

2. **Detection:** Specific item(s) or signature to be measured has been shown to be detectable in humans, or in the kind of human-derived samples/data that will be tested in the proposed study.

3. **Rationale:** Compelling data exist to justify carrying out the proposed work. The most compelling data are likely in humans, or in human-derived samples / data with a relevant disease and will likely allow for a power calculation such that the statistical significance of the result of the study can be determined. Data from pathophysiologically relevant animal models could be considered if those animal data are compelling.

If the proposed assay is different than the one used for initial biomarker identification, or if the assay will be used in a different type of specimen (*e.g.*, different tissue/fluid or different species), then preliminary data must be provided to demonstrate that the assay functions appropriately. For example, if a biomarker was identified using an assay in cerebrospinal fluid and you are proposing to use the same assay to measure the biomarker in blood, there must be preliminary data demonstrating that the assay is effective in blood.

Below we have listed some common steps in the biomarker development pathway and outlined which are in scope (or out of scope) for the Programme.

- Biomarker identification and discovery and unbiased screening approaches: out of scope for this Programme.
- Initial experiment(s), defined as the first time measuring the chosen biomarker in human samples in the population of interest versus controls using the proposed assay: in scope for this Programme.
- Replication of initial experiments / replication studies, defined as repeating the same experiments using the same samples from the same cohort and the same assay, and not considered to be validation: out of scope for this Programme unless the application also proposes the initial experiment or a validation step.
- Validation of the biomarker, defined as conducting the same work as the initial experiments, except using a different, independent set of human samples, data or cohort at the same or different research site: in-scope for this Programme.

Wherever possible, the biomarker under study should be compared against the current commonly used biomarker(s), diagnostic criteria, or pathology of the disease of interest, and a rationale should be provided for the selection. Alternatively, applicants should provide justification if the novel biomarker under study will not be compared to commonly used biomarker(s), diagnostic criteria, or pathology of the disease of interest.

Any human samples / data used should have, as applicable, proper collection, processing, shipping and storage procedures, and adequate donor data. Use of existing human samples, data, and/or cohorts where possible is preferred. A letter of support from the provider indicating permission to access the relevant human samples, data, and/or cohorts will be required before funding is released, if the project is approved for funding. If already available, applicants should include this letter with their full proposal.

If the project will not rely on existing human samples, data, and/or cohorts, applicants will be asked to provide:

1. Justification for the need for, and assessment of feasibility to, collect the required human samples/data, including plan for recruitment of participants, as needed.

2. Information on the protocols that will be used for collection and quality testing of human samples/ data. Any human samples / data used should have proper collection, processing, shipment, and storage procedures:

    a. As a first choice, where relevant and appropriate, applicants should follow ADNI / PPMI / GENFI guidelines for their biomarker based on the type of human sample / data, disease being investigated and/or the method of data collection and/or analysis (e.g., imaging technique, assay).

    Alternatively, if data from the proposed study will be shared through a public repository that has specific guidelines for human samples/data collection and sharing, following those specific guidelines is acceptable.

    b. As a second choice, applicants may use other established guidelines, if sufficient justification is provided that these guidelines are more appropriate for their biomarker of interest.

    c. As a third choice, justification should be provided for the adoption of protocols that do not adhere to the above principles. Details of your protocol should be well documented for future human samples/data sharing purposes.

We expect results of funded research to be published as rapidly as possible in open-access scientific journals or other forms of publication that are readily available to the general public or the research community. Where possible, applicants should consider sharing raw human samples / data with the research community through a public database or repository (*e.g.*, GAAIN, Neurovault, BioRxivs, NIAGADS). Applicants should take into consideration the requirements for disseminating data to a repository (*e.g.*, obtaining participant consent) in the design of the project where possible.

The Foundation encourages applicants to contact us with any questions regarding the Programme, including whether a project concept is in scope.

If you have further questions,
please email Dr. Jeffrey Coull
Jeffrey.coull@westonfoundation.ca
to discuss your application.

III. Funding specifications

The provision of grants is contingent on the receipt of a sufficient number of high-quality applications.

Funding guidelines:

- A maximum of £350,000 over up to 3 years is available per project. If the proposed project requires a budget outside of this range, please contact Dr. Jeffrey Coull to discuss.
- Funds will be granted only for direct costs that are appropriate and justifiable for the work proposed.
- Each item and its cost must be clearly articulated in the budget.
- Funds cannot be used for equipment purchases, computer purchases, administrative costs or indirect costs, unless prior written approval from the Foundation has been obtained.
- Travel expenses to scientific conferences / meetings to present work funded by the Foundation can be included in the budget. Applicants should further make provision for the principal applicant to travel to London, UK once per year to present their research to the Foundation's trustees and staff.
- The Foundation reserves the right to grant an amount that does not match the amount requested.
- Funds can be distributed within the UK and Ireland in any manner without restriction. In addition, up to 35% of the funds can be used to bring unique international resources (from other countries) into work led by researchers in the UK and Ireland.

Any grant provided by the Foundation pursuant to this Programme shall be directed to the institution and not to any individual. Responsibility for the planning, direction, and execution of the proposed project will rest solely with the applicants.

Multiple institutions: In the event of collaboration between multiple institutions, it is the responsibility of the principal applicant to distribute / manage funds appropriately.

Full or partial support of projects: The Foundation can support a full project or parts of a project. If the application is for part of a larger project, the criteria for granting will be applied only to the part of the project proposed to be supported by the Foundation. Applicants should make clear which part of the larger project the Foundation funding would support.

Conditional funding and milestones: Grants are conditional on grantees meeting pre-determined milestones and providing deliverables, including submission of progress reports and participation in annual meetings through which progress can be shared with the Foundation. Continued support is not automatic and is contingent upon the grant progress as interpreted by the Foundation.

Supplemental funding: The Foundation encourages grantees to seek additional funds to further their work. The Foundation has no guaranteed policy for renewal or continuation of grants. At its discretion, the Foundation may seek to further support clearly successful projects.

IV. Application process

The application process consists of two stages: project synopsis submission and review and full proposal submission and review. To apply, applicants must submit a project synopsis to the Foundation using the form provided on the Foundation's website (www.galenhilaryweston foundation.org). Selected applicants will then be invited to submit a full proposal.

All synopses and full proposals are reviewed by a scientific review committee comprised of international experts in the field of biomarkers and/or neurodegenerative diseases of ageing.

Synopses are reviewed with the objective to determine the strength and uniqueness of the central idea of the prospective research project. The full proposal must contain significantly more detail, with sections seeking information on experimental approach, team and environment, and envisioned milestones for the project. Budgets are only required in the full proposal phase. Proposal instructions and feedback from our scientific review committee will be forwarded along with the invitation to submit.

As previously noted, only a small proportion of applicants are invited to submit full proposals, and of those, many will be funded. This ensures synopses are easy to submit so that promising ideas are not missed, while ensuring applicants taking the time to write full proposals have a very good chance of being funded. In past Programmes supported by the Foundation, approximately 15% of applicants submitting synopses (or letters of intent) were invited to submit full proposals, and more than 50% of full proposals were approved for funding.

If your proposal is approved for funding, we will forward you a detailed grant agreement, which, under normal circumstances, must be executed, without amendment, within 6 weeks of receipt.

V. Relevant dates

The relevant dates for the 2024 Programme are as follows:

Programme launch:
25 January 2024

Deadline for submission of project synopses:
12 April 2024, 5:00pm BST

Deadline for submission of full proposals:
2 August 2024, 5:00pm BST

Notification of successful applicants:
November 2024

All project synopses must be submitted via the Foundation's website (www.galenhilaryweston foundation.org). It is anticipated that invitations for applicants to submit a full proposal will be extended in May 2024. All successful applicants will be required to enter into a comprehensive grant agreement prior to receiving research funding from the Foundation.

VI. Review criteria

The criteria considered when reviewing synopses include, but may not be limited to:

- **Innovation:** How novel is the work and biomarker under study?
- **Experimental approach:** Are the overall strategy, methodology and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Is the availability and quality of human samples/data and/or cohorts sufficient?
- **Likelihood of success:** How likely is this project to succeed (in advancing development of a new biomarker for disease diagnosis and prognosis, for stratification to clinical trials or to predict response to therapies)?
- **Impact:** If successful, to what extent will this project significantly accelerate the development of therapeutics for neurodegenerative diseases of ageing?

Additional criteria considered when reviewing invited full proposals include, but may not be limited to:

- **Experimental approach:** Are potential problem areas adequately considered and addressed? Is the plan to obtain human samples/data/cohorts feasible?
- **Development plan:** What are the steps after this study to continue development of this biomarker if successful?
- **Team and environment:** How well-suited are the team and environment for this work? Does the work take advantage of unique features of either?
- **Budget and timeline:** Are the proposed budget, milestones and length realistic yet ambitious for the research proposed? These are secondary considerations after the other criteria have been weighed.

VII. Eligibility of applicants

For this Programme, the Foundation is only able to accept project synopses and full proposals from investigators affiliated with eligible institutions located in the UK or Ireland.

Institutions applying to this Programme must be a registered with the relevant regulatory authority in the UK or Ireland. Other qualified organisations in the UK or Ireland that meet the public benefit requirement towards research in neurodegenerative diseases of ageing may also be eligible; please contact the Foundation if you would like to ascertain your eligibility.

Foundation grants may be used to support the UK or Ireland portion of international collaborations.

Eligible principal applicants must be at or above the level of lecturer, assistant professor or equivalent and hold an appointment at eligible institutions (as described above) from which they are applying.

Principal applicants must further be a researcher physically present and working in the UK or Ireland at least 30% of the time.

Each applicant may submit one synopsis per round as principal applicant but may appear in other roles such as co-applicant or collaborator on an unlimited number of applications.

A project synopsis submitted to this Programme does not need to be approved by the relevant institution on whose behalf or through which the synopsis is being submitted. However, any full proposal submitted must be duly approved by the institution on whose behalf or through which the proposal is being submitted.

VIII. Reports and assessments

Grantees must complete the following if a grant is awarded *(the Foundation will provide templates for reports)*:

- **Milestone reports:** Payments are tied to successful achievement of project milestones mutually agreed upon by the applicants and the Foundation. A milestone report is due prior to each scheduled payment being made.

- **Progress reports:** A progress report includes a written report with budget and, if requested by the Foundation, a telephone discussion with the principal applicant and/or data underlying the research (solely for use in assessing progress).

- **Grantee meetings:** Principal applicants must attend one event annually to share progress of the project and/or to have the opportunity to meet with other funded researchers. Additional key personnel may also attend if approved by the Foundation. Travel expenses for the principal applicant to attend one grantee meeting per year in London, UK, should be included in the budgetary module of the full proposal.

- **Foundation member visits:** With prior consent from the grantee, Foundation members may wish to visit researchers to see project work underway. These visits are not mandatory and are uncommon, however the Foundation hopes that grantees will welcome this opportunity.

- **Financial accountability:** Grantees are expected to account for the monies expended under any Foundation grant; any monies spent that are not in accordance with the approved research project or prior to pre-approval of any material change in the project are both recoverable and subject to restitution by the grantees to the Foundation and may be cause for immediate termination of funding. Any funding provided beyond what is needed for the agreed upon research must be returned to the Foundation.

IX. Confidentiality

The Foundation treats all project synopses, full proposals, research project details and associated research information (collectively, the **"Confidential Information"**) in confidence using reasonable care in protecting such Confidential Information from disclosure to third parties who do not participate in the grant review process and Foundation assessments.

All Confidential Information will be used by the Foundation and its scientific review committee for the purposes of review and assessment and will be shared only in accordance with the sharing policy as set out herein. Notwithstanding the foregoing, Confidential Information shall not include any information that:

- was generally known to the public prior to the effective date of this Programme announcement;

- becomes generally known to the public through no unlawful or unauthorised act by any recipient of Confidential Information; or,

- was independently developed by the Foundation or its scientific review committee without reference to the Confidential Information.

If the Foundation or any of its scientific review committee members is requested to disclose Confidential Information pursuant to a legal or governmental proceeding, the Foundation shall give the applicant, grantee or other owner(s) of such Confidential Information notice of such disclosure request as soon as is reasonably practicable.

X. General Information

Institutions and individuals affiliated with and applying through or on behalf of institutions (collectively, the **"Applicants"**) should carefully discuss the Programme announcement and the terms of this document with the appropriate office at their institution before submitting an application.

The submission of a project synopsis or full proposal does not bind either the Foundation or the applicants by any commitment to provide or receive funding, respectively. Successful applicants will be required to agree to terms substantially similar to those contained in this document and the Foundation reserves the right to alter, delete, or add additional terms in the grant agreement between the successful applicants and the Foundation.

The Foundation reserves the right to accept or reject any or all grant applications at its discretion and to negotiate the terms of the specific grant agreement with applicants.

The Foundation, at its sole discretion, may change the timeline of the application process.

XI. Other

Liability and indemnity

Each applicant to this Programme acknowledges and agrees in responding to the Programme announcement that the applicant shall have no claim against the Foundation, and its respective representatives, related companies or affiliates, should such Programme response be unsuccessful for any reason.

Each applicant hereby remises and releases the Foundation, its representatives and affiliates, from any cause of action, complaint, or claim in connection with the request for applications process and its outcome.

The Foundation's role in grants awarded pursuant to this Programme is that of a funder. The Foundation is not the *sponsor* of funded projects. As such, the Foundation will not assume any liability associated with funded projects and each applicant who is ultimately awarded a grant pursuant to this Programme releases the Foundation from any and all liability with respect thereto and further indemnifies the Foundation, and its respective representatives and affiliates, from any claim or loss whatsoever associated with the applicable grant.

Publication and sharing policy

The Foundation expects results of funded research to be published as rapidly as possible in open-access scientific journals or other forms of publication that are readily available to the research community, unless the Foundation agrees there is a greater public good served by proceeding otherwise. Such publication should be consistent with high standards of scientific excellence and rigor and provide sufficient detail so that the research community can benefit from the findings from, or in connection with, the funded project.

A lay person abstract of the research proposal must be submitted prior to funding. A lay person abstract of the research results must also be submitted no later than two (2) months from the date of grant expiration. These abstracts may be made available to the public by the Foundation.

Any presentation, releases, papers, interviews, publication or other forms of communication dealing with the awarded project or the results from the awarded project must acknowledge the funding provided by the Foundation, in a manner proportionate to the contribution of the Foundation. Any other use of the Foundation's intellectual property, including its name, logo or trademark requires prior written permission of the Foundation.

All tools or reagents (i) funded by and (ii) that result from funded projects should be made readily available to the research community either freely or at reasonable prices within three months of study completion. If sharing of such tools or reagents will jeopardise the grantee's right to secure patents or copyrights necessary to protect the grantee's ownership, then they should be made available as soon these rights have been secured. The Foundation may let the public know of these tools or reagents so other researchers know they are available.

The Foundation encourages sharing of data (inclusive of raw data) publicly wherever possible.

The Foundation requires any clinical trial awarded under any of its funding Programmes be registered with clinicaltrials.gov, PDTrials.org, or other appropriate public registry.

Intellectual property

The Foundation acknowledges that any IP that arises from a project funded under this Programme (the "Funded IP") is not the property of the Foundation.

That said, the Foundation reserves the right to impose certain conditions on the Funded IP, if appropriate in its sole opinion, including to ensure sufficient United Kingdom and Ireland public benefit in line with its charitable objects or to comply with legal requirements.

Specifically, if, in the sole opinion of the Funder, the grant recipient does not take steps to promptly achieve practical application of the Funded IP within the UK or Ireland and for the benefit of UK or Ireland residents and/or seeks to achieve practical application in a jurisdiction other than the UK or Ireland prior to achieving practical application in the UK or Ireland, then the Funder may require the grant recipient to: (a) terminate or convert any exclusive rights granted to a third party in connection with the Funded IP, as well as any background IP necessary to enable the full practical application of the Funded IP, to non-exclusive rights; and/or (b) promptly locate, and grant to a new entity acceptable to the Foundation the rights to apply the Funded IP, all improvements thereto made by the grant recipient and the principal investigator necessary to enable full practical application of the Funded IP in the UK or Ireland.