SELFRIDGES GROUP FOUNDATION

WESTON BRAIN INSTITUTE

PROGRAM DETAILS
Rapid Response: Ireland, Netherlands, UK 2018 (Fluid Biomarkers)

Background

The Weston Brain Institute (the "Institute") supports high-risk, high-reward translational research that accelerates the development of therapeutics for neurodegenerative diseases of aging. The Institute's programs in the Republic of Ireland, the Netherlands and the United Kingdom are supported by the Selfridges Group Foundation. The Institute was founded by The W. Garfield Weston Foundation, which supports the Institute's Canadian programs. The Selfridges Group consists of Brown Thomas and Arnotts in Ireland, Holt Renfrew in Canada, de Bijenkorf in the Netherlands, and Selfridges in the UK.

Neurodegenerative diseases of aging are among the most undertreated diseases today and require pioneering approaches to accelerate treatments. Early diagnosis remains a large challenge in the clinic, along with detection of subtypes of disease, predicting rate of progression of the disease, and using this information to enroll patients in clinical trials. Outcome measures for clinical trials are also needed to predict response to therapy, since these are diseases with many years of progression. Biomarkers for patient diagnosis, prognosis, stratification to clinical trials, and to predict response to therapy are crucial to enable new treatments to be developed for patients.

Biomarkers measured peripherally in patient-derived fluids (e.g., blood, CSF, saliva, stool) are relatively easy to access and generally low cost to collect and measure. The *Rapid Response: Ireland, Netherlands, UK 2018 (Fluid Biomarkers)* program was launched to provide seed funding, without requirement for preliminary data, to support high-risk, high-reward, translational research on novel biomarkers detected in patient-derived fluids.

Important things to know about the Institute:

- **We do not fund basic (also known as fundamental) research.** We only fund translational research.
- **Funds are provided contingent on meeting milestones.** If your project is awarded, funds are provided in tranches when experimental milestones are successfully completed.
- **Our application process is interactive**. You will likely receive feedback on your applications and may be asked to make modifications. We also encourage you to reach out if you have questions.
- **Many projects are declined at the Letter of Intent (LOI) stage**. Only ~15% of LOIs are invited to the Proposal phase, so that applicants and reviewers spend their time on Proposals that have an excellent chance of being funded. For previous Rapid Response programs, after the LOI phase, Proposal funding rates have ranged from 35-75%.
- **We provide more than funding.** Our grantees may also benefit from things like the expert advice of our scientific advisors, industry exposure, networking, and international collaboration opportunities.

Institute definitions:
A full list of our definitions is available on our website.

- **Neurodegenerative diseases of aging**: Alzheimer's disease, frontotemporal dementia, dementia with Lewy bodies, multiple system atrophy, Parkinson's disease, progressive supranuclear palsy, vascular contributions to the listed diseases, and prodromes to these diseases (e.g., mild cognitive impairment as prodromal to Alzheimer's disease; REM sleep behavior disorder as prodromal to Parkinson's disease).

- **Translational research**: Applied research towards developing therapeutics for the prevention and/or treatment of human disease. For example, for small molecule drug development, this includes target validation to phase IIa clinical trials. Basic/discovery research, including but not limited to understanding disease mechanisms and discovering genes implicated in disease, is not in scope.

- **Tool:** An item that accelerates development of therapeutics, e.g., imaging techniques or reagents, biomarkers, and diagnostics.
    - Tools must have direct impact on the translational development of therapeutics (as defined by the Institute, i.e., target validation to phase IIa clinical trials) for neurodegenerative diseases of aging and will be valued only on their ability to do this.
        - Any value the tools contribute to basic research will not be taken into consideration. For example, tools will not be valued for their ability to identify new targets or understand disease mechanisms.
    - Projects covering only the discovery/identification of a tool are out of scope.

- **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. Complementary approaches such as exercise, acupuncture, music, dietary and nutritional supplements are not considered therapeutics.

- **Novel biomarkers:** biomarkers that have been insufficiently studied.

Section 1 Scope

The *Rapid Response: Ireland, Netherlands, UK 2018 (Fluid Biomarkers)* program provides seed funding, without requirement for preliminary data, to test novel biomarkers in patient-derived fluids. Biomarkers must be previously identified and be for human disease diagnosis, prognosis, for patient stratification to clinical trials or to predict response to therapies (surrogate for a clinical endpoint).

For this program, **only biomarkers measured in fluid(s) are eligible** (e.g., blood, CSF, saliva, stool). Genetic biomarkers including somatic mutations, SNPs, epigenetics and gene products are in scope if they meet the other eligibility criteria. Biomarker discovery and unbiased screening approaches are not within the scope of this program.

Novelty of the biomarker will be a criterion for adjudicating applications. Applications focused on Abeta, tau or alpha-synuclein are discouraged unless there is an aspect of the work that is particularly

novel.

For this program, **only previously identified biomarkers are eligible.** An identified biomarker is defined as one that meets the following two conditions:

1. Specific item(s) or signature to be measured can be defined, for example,
    a. Single protein increased
    b. Two mRNA transcripts decreased
    c. Presence of a particular bacterium
    d. Precisely defined fingerprint
        i. If the biomarker is a fingerprint of a family of proteins or a signature of brain volume changes, the precise fingerprint or signature to be replicated must be previously determined. For e.g., omics studies for the purpose of identifying biomarker patterns or signatures are out of scope.
    e. Exact identities of multiple individual factors that may be useful individually or as a specific composite

2. In what it will be detected (i.e., which fluid), using what assay, and for which disease or clinically relevant subgroup, can be clearly stated;

The review committee will be more enthusiastic about very specific and well-defined biomarkers, and about projects with assays demonstrated to be up and running. Exploratory projects are not eligible. It is not in scope to know that a family of proteins is affected or that inflammatory markers are increased overall, if the specific item or signature that is the biomarker cannot yet be specified. For example, a single protein is not considered an identified biomarker if only the family of proteins were previously identified to be affected.

Use of existing clinical samples/data where possible is preferred. A letter of support from the samples/data provider indicating permission to use the relevant samples/data will be required in advance of funding. If already available, applicants should provide this letter at the Proposal stage. If the project will not rely on existing samples/data, applicant must provide justification for the need and feasibility to collect the required samples/data and protocols for collection and quality testing in the Proposal. Any samples used should have proper collection/storage procedures and adequate donor data, for example from biobanks or imaging banks.

The Institute encourages applicants to contact us with any questions regarding the program, including whether a potential idea is in scope.

Section 2 Funding Specifications

Total funding: The Institute will commit up to £540,000 to fund projects selected through this Program. Grants are contingent on the receipt of a sufficient number of high quality applications. If each project requests the maximum project budget, 3 projects will be awarded through this program.

Funds available per project:

- Up to £180,000 over up to 18 months is available per project. Start-up time (e.g., to obtain ethics

approvals) is not included in this duration.
- 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 described in the budget.
- Funds cannot be used for equipment purchases, computer purchases, administrative costs or indirect costs, unless prior written approval from the Institute has been obtained.
- Travel expenses to scientific conferences/meetings to present work funded by the Institute can be included in the budget.
- The amount granted may not be for the full amount requested.
- Up to 35% of the funds can be used to bring unique international resources into work led by Ireland, Netherlands or UK researchers. There are not any restrictions on funds for collaborations between these three countries.

Any grant provided by the Institute pursuant to this Program 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. If the funded project has the potential for significant commercial success, in the Grant Offer, the Institute may request, upon significant commercial success, repayment of grant funds to be used for further research funding.

Multiple institutions: In the event of collaboration between multiple institutions, it is the responsibility of the Principal Applicant (or Administrative Supervisor, if applicable) to distribute/manage funds appropriately.

Full or partial support of projects: The Institute 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. Applicants should make clear what part of the larger project the Institute 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 Grantee meetings. Continued support is not automatic and is contingent upon the grant progress being favourably reviewed by the Institute.

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

Section 3 Application Process

The application process consists of two stages: Letters of Intent (LOIs) and Proposals. To apply, applicants must submit an LOI to the Institute. Selected applicants will then be invited to submit a Proposal.

LOIs and Proposals are peer reviewed by a scientific review committee comprised of international experts in the field.

The LOI is brief but it is a significant stage of evaluation, focusing on the strength of central idea of the research project. Applicants whose LOIs meet the rigorous review criteria will be invited to submit a Proposal. The Proposal is longer, with more information regarding the experimental approach, team and environment, and milestones for the project. Budgets are only required at the Proposal phase. Proposal instructions and feedback from our scientific review committee will be forwarded along with the invitation.

Typically, only a small proportion of applicants are invited to submit full Proposals, and of those, many will be funded. This ensures LOIs 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 Rapid Response programs, ~15% of applicants submitting LOIs were invited to submit Proposals, and after the LOI phase, 35-75% of submitted Proposals were funded.

The grant agreement must be completed within 6 weeks of notification of selection; otherwise the Institute reserves the right to cancel the grant.

Section 4 Review Criteria

Criteria considered when reviewing LOIs:

- **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 clinical samples/data or patients sufficient?
- **Impact**: If successful, to what extent will this project significantly accelerate the development of therapeutics for neurodegenerative diseases of aging?
- **Fit**: Is the project, including its scale and scope, appropriate for this program?
- Other as needed.

Additional criteria considered when reviewing Proposals:

- **Experimental approach**: Are potential problem areas adequately considered and addressed? Is the plan to obtain clinical samples/data or patients feasible?
- **Development plan**: What are the steps after this study to continue development of this biomarker if successful?
- **Risk appropriateness:** Is the *scientific* risk (likelihood that the hypothesis will not be supported) commensurate with the potential reward of the project if successful? Has *executional* risk (likelihood that the project cannot be completed) been addressed as much as is reasonable?
- **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 aggressive for the research proposed? These are secondary considerations after the other criteria have been weighed.
- Other as needed.

Section 5 Eligibility of Applicants

For this program, the Institute is only able to accept LOIs and Proposals from PIs at eligible institutions

located in Ireland, the Netherlands, or the UK. Eligible institutions must be either registered with the Charities Regulatory Authority in Ireland, a Public Benefit Organization (PBO) in the Netherlands, or are a UK-registered charity. Qualified institutions/organizations in Ireland, the Netherlands, or the UK meeting the public benefit requirement towards research in neurodegenerative diseases of aging may also be eligible. Funds may be used to support the Ireland, Netherlands or UK portion of international collaborations.

Eligible Principal Applicants must be at or above the level of Postdoctoral Researcher or equivalent and at eligible institutions as described above. If the Principal Applicant is not appointed at the institution from which they are applying, they need to apply with a research supervisor (an "Administrative Supervisor"). Administrative Supervisors must hold an appointment at the institution from which they are applying, and will be responsible for the successful execution of the research and administration of the funds as per their institution's policy.

Each applicant may submit one LOI as Principal Applicant, and may appear as a Co-Applicant or Collaborator on an unlimited number of applications.

An LOI submitted to this Program does not need to be approved by the relevant institution on whose behalf or through which the LOI is being submitted. However, any Proposal submitted to this Program must be approved by the institution on whose behalf or through which the Proposal is being submitted.

Funds will be directed to the institution/organization on behalf of the principal applicant.

Section 6 Reports and Assessments

Grantees must complete the following if a grant is awarded. Templates for reports will be provided by the Institute.

- ***Milestone Reports.*** Payments are tied to successful completion of project milestones mutually agreed upon by the Applicants and the Institute. 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 Institute, a telephone discussion with the Principal Applicant and/or data underlying the research (solely for use in assessing progress).
- ***Grantee meetings*****.** At least one Applicant on the grant must attend an event to share progress of the project and have the opportunity to meet other funded researchers. Applicants will attend one Grantee meeting per year, unless otherwise notified by the Institute. Additional key personnel may also attend if approved by the Institute. Travel expenses for the Principal Applicant to attend one Grantee meeting per year in London, UK, should be included in the budget.
- ***Foundation Member Visits.*** With prior consent of Applicants, Foundation members may wish to visit researchers to see project work underway. These visits are not mandatory, and the Institute hopes that grantees will welcome this opportunity.

- ***Financial Accountability*.** Grantees are expected to account for the moneys expended under any Institute grant; any moneys spent either 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 Institute 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 Institute.

Section 7 Confidentiality

The Institute treats all LOIs, Proposals, research projects 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 Institute assessments. All Confidential Information will be used by the Institute and its scientific review committee for the purposes of reviews and assessments, 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:

a) was generally known to the public prior to the effective date of this Program announcement;
b) becomes generally known to the public through no unlawful or unauthorized act by any recipient of Confidential Information; or
c) was independently developed by the Institute or its scientific review committee without reference to the Confidential Information.

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

Section 8 General Information

Institutions and individuals affiliated with and applying through or on behalf of institutions (collectively, "Applicants") should carefully discuss the Program announcement and the terms of this document with the appropriate office at their institution before submitting an application. The submission of an LOI or a Proposal ("Proposals" and each a "Proposal") does not bind either the Institute 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 Institute reserves the right to alter, delete, or add additional terms in the grant agreement between the successful Applicants and the Institute.

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

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

Section 9 Other

Liability and Indemnity

Each Applicant pursuant to this Program acknowledges and agrees in responding to the Program announcement that the Applicant shall have no claim against the Institute, and its respective representatives, related companies or affiliates, should such Program response be unsuccessful for any reason. Each Applicant hereby remises and releases the Institute, its representatives and affiliates, from any cause of action, complaint, or claim in connection with the RFA process and its outcome.

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

Publication and Sharing Policy

The Institute expects results of funded research to be published as rapidly as possible in open access scientific literature or other forms of publication that are readily available to the research community, unless the Institute 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 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 2 months from the date of grant expiration. These abstracts may be made available to the public by the Institute.

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 Institute, in a manner proportionate to the contribution of the Institute. Any other use of the Institute's intellectual property, including its name, logo or trademark requires prior written permission of the Institute.

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 3 months of study completion. If sharing of such tools or reagents will jeopardize the Applicant's right to secure patents or copyrights necessary to protect the Applicant's ownership, then they should be made available as soon these rights have been secured. The Institute may let the public know of these tools or reagents so other researchers know they are available.

The Institute encourages sharing of data and making raw data publicly available where possible.

The Institute requires any clinical trial awarded under any of its funding programs be registered with clinicaltrials.gov, PD Trials.org, or other appropriate public registry.