Weston Family Foundation

Weston Family Microbiome Initiative
Proof-of-Principle 2024 Program

Important Dates*

Information Webinar	May 1st and May 7th at 2:00 PM ET
Letter of Intent (LOI) Deadline	June 4th at 2:00 PM ET
Full Proposal Deadline	August 22nd at 2:00 PM ET
Anticipated Award Notice	October 2024

**Dates subject to change*

Program Information

The Weston Family Foundation is pleased to announce new programming in support of Canadian research efforts on the human microbiome. This program will provide funding to support innovative projects that:

1) Advance the application of the microbiome in improving human health
2) Foster greater collaboration within the Canadian research community
3) Position Canada as a global leader in the field of microbiome research

The **Proof-of-Principle** 2024 program, through the Weston Family Microbiome Initiative will provide research grants of **up to $300,000 over a maximum of 30 months** to support high-impact projects that seek to **identify, validate, or apply microbiome-based** biomarkers of disease and therapeutic response. Eligible projects must build on established responder/non-responder phenotypes towards the optimization of therapeutic or preventative strategies.

Stream 1: $300k – Project involving active patient engagement and testing.
Stream 2: $200k – Projects not working with patients (e.g. biobanked samples, animal studies, *in vitro*/*ex vivo* experiments).

Application Process

There are two stages to this application: Letters of Intent (LOI) and Proposals. **Applicants may submit a maximum of one application, when acting as a Principal Applicant, to the program**. Applicants invited to submit a full Proposal will receive instructions and reviewer feedback at the time of invitation. All applications will be rigorously peer reviewed by an international scientific advisory committee. LOIs and Proposals must be submitted using the Foundation's online grants management system, available at westonfdn.smartsimple.ca. Applicants are invited to contact staff at microbiome@westonfoundation.ca for any questions related to their application.

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About the Foundation

At the Weston Family Foundation (formerly The W. Garfield Weston Foundation), more than 60 years of philanthropy has taught us that there's a relationship between healthy landscapes and healthy people. That's why we champion world-class health research and innovation with the same passion that we support initiatives to protect and restore biodiversity on our unique landscapes. We take a collaborative approach to philanthropy, working alongside forward-thinking partners to advance Canada and create lasting impacts. We aspire to do more than provide funding, to enable others to find transformational ways to improve the well-being of Canadians.

Weston Family Microbiome Initiative

The human body is host to trillions of microbes. A wealth of research suggests that these organisms play important roles in bodily function, health, and disease. For example, the communities of bacteria living in the gut are thought to have a profound bearing on nutrition and are suspected to influence numerous and varied diseases, including gastrointestinal, immunological, cardiac, and neurological afflictions. For these reasons the microbiome represents a promising avenue for new strategies in disease treatment and preventative health. The success of fecal microbial transplants in treating infections caused by *Clostridium difficile* underscored the field's potential, with the successful approval of a new microbe-based therapy in late 2022. The Weston Family Microbiome Initiative (WFMI) will support high-impact Canadian research that strives to develop new therapies that harness the microbiome to improve human health and quality of life.

Important things to know about the WFMI:

- Funds are provided in tranches based on the successful completion of project milestones.
- The application process is interactive. Applicants are encouraged to connect with the Foundation to discuss their proposals. Applicants will receive feedback and recommendations from reviewers, and if warranted, will be given an opportunity to implement changes.

Program Details

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 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 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.

1) Project Scope

The Proof-of-Principle Program provides funding to innovative projects that seek to leverage the microbiome to deliver new interventions or preventative strategies for improving health. This includes modifying, manipulating, or exploiting the microbiome to confer health benefits or treat diseases.

For this iteration of the program, projects must be translational and seek to identify, validate, or apply microbiome-based biomarkers of disease and therapeutic response. The Foundation will consider all potential disease areas for which there is a hypothesized linkage to the microbiome, however, priority will be given to projects that focus on promoting healthy aging.

Eligible projects will be in one of the four priority areas:

- *Mechanism*: Investigate mechanisms to identify functional biomarkers of response or non-response.
- *Modulation*: Modulate the composition or function of the microbiome towards promoting a responder phenotype for an intervention or preventative strategy.
- *Diagnostic*: Leverage validated community or functional microbiome biomarkers to predict disease, progression, or response to intervention.
- *Intervention*: Develop novel therapeutic intervention by targeting established microbiome biomarkers with a population (disease or stratified).

Projects must build on a compositional or functional (preferred) microbiome biomarker and established responder/non-responder phenotype.

Interventions and Preventative Strategies of Interest

Projects should seek to develop therapeutic or preventative strategies that leverage the microbiome towards improving health, including:

- Health Canada or FDA approved and/or investigational drugs, such as small molecules, biologics, and live biotherapeutic products.
- Dietary substrates, including, but not limited to, prebiotics, fibres, oligosaccharides, but excluding complete diet changes.

- Microbial-derived products, such as fecal microbiome transplants (FMT) and probiotics.

Microbiome biomarkers

Microbiome biomarkers are community, chemical, transcriptional, or proteinaceous signatures that are observed within a given microbiome. *Community biomarkers* give information on the structural composition of a microbiota as well as the changes in individual members within the community. *Functional biomarkers*, such as chemical, transcriptional, and proteinaceous, describe the function of the members within a microbiome. Biomarkers have been traditionally used to diagnose illnesses and monitor response to therapy. Microbiome biomarkers represent a new modality of biomarkers that can leverage the information of the microbiome in assessing disease and health status. These biomarkers have the potential to predict response to therapy, improve response to therapy, or stratify individuals for tarted therapy.

Example: Levodopa is the most widely used treatment for Parkinson's disease. However, its efficacy is hindered by limited brain absorption resulting from peripheral nervous system metabolism. While carbidopa inhibits peripheral metabolism, there remains significant variability in response and dosage for these medications to achieve optimal therapeutic effect. The gut microbiome has been shown to be associated with levodopa/carbidopa dosage, whereby some microbial genes strongly correlate with therapeutic dosage[1]. Characterizing the microbiome of Parkinson's disease patients, researchers identified key bacterial species and metabolic pathways that contribute to levodopa degradation by the microbiome[2]. The authors modified carbidopa to inhibit microbiome metabolism of levodopa and demonstrated that the new drug combined with existing therapies could promote serum levodopa in preclinical *in vivo* models[2].

A strong application will have a clear and well supported hypothesis that identifies a microbiome-based biomarker and has defined criteria for a response/non-response phenotype. Projects are encouraged to investigate functional omics data, including metabolomics, proteomics, and transcriptomics.

Applicants are encouraged to consult with the Foundation should they have any questions regarding the eligibility of their proposed project. Please note that the Foundation prefers projects that involve human participants or human-derived samples where possible.

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[1] van Kessel SP, Frye AK, El-Gendy AO, Castejon M, Keshavarzian A, van Dijk G, El Aidy S. (2019). Gut bacterial tyrosine decarboxylases restrict levels of levodopa in the treatment of Parkinson's disease. Nat Commun. 10(1):310. doi: 10.1038/s41467-019-08294-y. PMID: 30659181; PMCID: PMC6338741.

[2] Maini Rekdal V, Bess EN, Bisanz JE, Turnbaugh PJ, Balskus EP. (2019). Discovery and inhibition of an interspecies gut bacterial pathway for Levodopa metabolism. Science. 364(6445):eaau6323. doi: 10.1126/science.aau6323. PMID: 31196984; PMCID: PMC7745125.

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2) Eligibility of Applicants

The Foundation is only able to accept Letters of Intent ('LOIs' and each an 'LOI') and Proposals ('Proposals' and each a 'Proposal') from institutions (or individuals affiliated with and applying through or on behalf of institutions) that are Canada Revenue Agency-qualified donees in Canada. Funds can also be used to support the Canadian portion of collaborations with members from other geographies.

The Principal Applicant must be a researcher working in Canada at least 50% of the time and at or above the level of Assistant Professor or equivalent, at a CRA-qualified donee in Canada. Postdoctoral Fellows may apply as Principal Applicants, however, in such cases the project must include an Administrative Supervisor acting as a co-applicant, who has authorization to administer research accounts and is granted the relevant signing authorization. Projects must align with the scope of the Program as outlined below. An LOI submitted pursuant 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 pursuant to this Program must be approved by the institution on whose behalf or through which the Proposal is being submitted. Applicants who have participated in previous WFMI POP grants are encouraged to join this competition.

3) Funding Specifications

Overall funds: The Foundation will commit up to ~ **$3,000,000** to projects selected through this program (approximately ~ 10 projects). Grants are contingent on the receipt of a sufficient number of high-quality applications. The Foundation reserves the right to expand the funding envelope should it deem there to be many high-quality Proposals submitted in this call.

Project Funding

- Grants will provide up to $300,000 CAD for clinical projects that involve active patient engagement and testing, and up to $200,000 CAD for projects not working with patients (e.g. biobanked samples, animal studies, in vitro/ex vivo experiments).
- Funds will be used over up to 30 months.
- Funds will be granted only for direct costs that are justifiable for the work proposed.
- Items and cost must be clearly described in the budget of the full Proposal.
- Funds cannot be used for equipment purchases, computer purchases, administrative costs, or indirect costs, unless written approval from the Foundation is received.
- Funds cannot be used for institutional overhead.
- The granted funds may deviate from the full amount requested.

- Travel expenses to scientific conferences/meetings to present work funded by the Foundation can be included in the budget.
- Each item and its cost must be clearly described in the budget (provided at the Proposal stage).
- Budgets should be developed to account for rising costs during the tenure of the project.

Any grant provided by the Foundation pursuant to this Program shall be directed to the institution and not to the individual affiliated with and applying through the institution. Responsibility for the planning, direction, and execution of the proposed project will rest solely with the Applicants in collaboration with their respective institution.

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 a portion of any project, e.g., the cost of a clinical trial may exceed the project budget of this Program, but Applicants may seek partial support for that trial. In the case of the latter, applicants should provide proof of the necessary resources to complete the full project.

Conditional funding and milestones: Grants are conditional on grantees meeting pre-determined milestones and providing deliverables, including submission of progress reports and/or participation in Foundation sponsored assessment meetings. Continued support is contingent upon the progress reports being favourably reviewed by the Foundation.

Supplemental funding: The Foundation encourages grantees to seek additional funds to further their work once the term of the initial grant has expired. The Foundation has no guaranteed policy for renewal or continuation of grants. The Foundation may, at its discretion, seek to further support clearly successful projects. Grantees are also eligible to apply for funding through other Foundation programs and RFAs.

4) Information Webinar

The Foundation will host Information Webinars on **May 1st and May 7th, 2024, at 2:00 PM ET.** Details will be forwarded to interested applicants in advance of the meeting and can be found on the Foundation website. Applicants are asked to indicate their intention to join the meeting by emailing microbiome@westonfoundation.ca or by signing up at the event page through the Foundation website.

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5) Application Process

The application process consists of two stages: Letters of Intent (LOIs) and Proposals. Applicants must submit a LOI to the Foundation to be considered for Proposal submission to the Program. Each LOI will be reviewed internally by the Foundation and peer reviewed by a scientific advisory committee.

The LOI stage of the application process is a brief but significant stage of evaluation. It is expected that only a small proportion of applicants will be invited to submit full Proposals, and of those, many will be funded. This ensures that LOIs are easy to submit so that good ideas are not missed, while ensuring that applicants that take the time to write full Proposals have a very good chance of being funded. In past Programs more than 50% of submitted Proposals were funded.

Applicants whose LOIs meet the review criteria and are favourably reviewed will be invited to submit a full Proposal. Proposal instructions and feedback from the scientific review committee will be forwarded along with the invitation. Applicants will be required to obtain and submit relevant institutional signatures at the Proposal stage. Complete Proposals will be peer reviewed by the scientific review committee. Unsuccessful applications will receive written feedback from the scientific review committee. No appeal process is currently available.

Contracting must be completed within four weeks of notification of selection as a grantee. If contracting is not completed at this point, the Foundation reserves the right to cancel the grant.

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

6) Important Dates*

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7) Review Criteria

The following criteria will be considered in reviewing LOIs and Proposals. At the LOI stage, the primary focus of review will be the scientific idea itself. At the Proposal stage, reviewers will place increased consideration on the strength of the methodology, milestones and contingencies, budgeting, and the suitability of the project team and research environment.

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LOI Stage

Innovation: Does the project challenge or significantly expand current paradigms in the field? Will the work refine, improve or be a new application of existing knowledge, technologies, or methods? Does the project demonstrate potential to lead to novel applications?

Potential for Impact: If successful, will the project accelerate the development and application of new technologies or approaches for the prevention and/or treatment of human disease? Will the work performed pave the way for more advanced applied therapeutic studies? If unsuccessful, will the insights gained make a significant contribution to the field or foster a new line of research? How will the project impact the health of Canadians near-term/long-term?

Likelihood of Success: How likely is it that the stated goals will be achieved? Are the project goals grounded in the state of the field and strength of the team?

Experimental Overview: Does the project propose reasonable, testable, and clear hypotheses? Are the proposed strategies and methodologies well-reasoned and appropriate for the work being undertaken?

Preliminary data: Up to one page of preliminary data can be attached to the application to support the rationale, hypothesis, and feasibility of the study.

Additional Criteria Considered at the Proposal Stage

Integrated Development Plan (IDP): If the project is successful, what are the next steps needed to advance the application of the discovery to real-world application? What additional resources (financing, infrastructure, collaborators) will be needed? What is the timeline to delivery? Please consider both short-term and long-term steps.

Experimental Approach: Are the methodologies described in sufficient detail to present a compelling action plan for addressing the proposed hypotheses? Are methods well established and have they been demonstrated to be effective in the scientific literature? If not, are the appropriate experiments in place to validate new methods/processes? Are there alternative methodologies that should be considered based on effectiveness or cost? Have limitations been considered?

Team and Resources: Does the project team have the capabilities and capacity to reliably execute the proposed experiments and analyses? Does the proposed project capitalize on any unique resources or competencies? Does the team have experience in translating

scientific findings? Have strategic partners been identified that will facilitate the mobilization and application of newly discovered knowledge?

Budget and Timeline: Are the proposed budget, milestones, and length realistic yet aggressive for the proposed research?

Milestones: Has the team identified critical milestones and relevant contingencies? Does the applicant indicate a well-thought-out strategy with go/no-go check-points that will help mitigate risk? Have potential problem areas been adequately considered and addressed? What are next steps if work is unsuccessful?

8) Regulatory and Ethics Approval

It is highly recommended that applicants initiate the process of seeking Health Canada Approval for studies, where required, at the Proposal stage or earlier. Obtaining necessary regulatory approval can introduce significant lag into a research project and be a major hurdle to success. While not essential for funding approval, the review panels look favourably upon those projects that proactively seek to understand and address necessary regulatory approvals (Health Canada, ethics) in advance of the launch of the project. Approval of ethics will be a critical first milestone of projects selected for funding.

The Foundation will permit a maximum period of six-months from the project start date for grantees to secure the required regulatory approvals. Projects facing longer approval timelines will require a project exemption, to be granted at the sole discretion of the Foundation on a case-by-case basis.

9) Power Calculations

Applicants should provide appropriate power calculations to justify project scale and demonstrate statistical significance of proposed studies and prospective outcomes (as necessary). This Proof-of-Principle 2024 grant call provides for larger project budgets compared to previous offerings of the Program with the intent of ensuring properly powered studies. It is highly recommended that applicants include a power calculation in the LOI and Proposal phase of the application, and that recruitment should exceed the calculated number of subjects based on the calculation. If a power calculation is not possible due to a lack of previous research, the power calculation of the current gold standard option or closest related therapeutic option should be included.

10) Reports and Assessments

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Grantees are responsible for the completion of the following if a grant is awarded:

- **Milestones.** Proposed projects must include clear milestones that guide the continuation of research (go/no-go). Pre-determined milestones, as agreed upon by the Applicants and the Foundation, will be used to determine reporting dates and the distribution of payment tranches. A brief milestone report will be required in advance of payment.

- **Progress Reports.** A progress report including a brief written report with budget, telephone discussion with the Principal Applicant and, if requested by the Foundation, data underlying the research (solely for use in assessing progress), is due at minimum every 12 months unless otherwise notified by the Foundation. Submission dates and reporting frequency will be linked to project milestones and the nature of the research, as agreed upon by the Applicants and Foundation. As this is a pilot program, the Foundation is eager to connect with researchers regarding their progress, successes, and challenges. The Foundation kindly invites Grantees to take a proactive approach to communication throughout the Project. **New to 2024**, progress reports must be submitted in accordance with the project schedule, as detailed in the grant agreement. Failure to submit reports on time may result in termination of the project.

- **New to 2024 - Clinical Project Report.** For projects involving active patient engagement, grantees will be required to provide brief quarterly updates capturing trial approvals, patient recruitment and patient retention.

- **Assessment Meeting.** The Foundation, at its discretion, may require at least one Applicant on the grant to attend an assessment meeting to report on the progress of the project and have the opportunity to meet other funded researchers. Assessment meetings will be held once a year unless otherwise notified by the Foundation. Additional key personnel may also attend if approved by the Foundation. Travel expenses to required assessment meetings will be covered by the Foundation per Foundation guidelines.

- **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 Foundation hopes that grantees will welcome this opportunity.

- **Financial Accountability.** Grantees are expected to account for the moneys expended under any Foundation 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 (i) recoverable by, and subject to

restitution by the grantees, to the Foundation and (ii) may be cause for immediate termination of funding by the Foundation. Any funding provided beyond what is needed for the agreed upon research must be returned to the Foundation at the completion of the research funded by the Foundation.

- **Impact Monitoring Reports.** Grantees are expected to report impacts related to the funded work, including, but not limited to, academic and media publications, patent and patent licensing, novel academic and commercial partnerships, and follow-on funding. As a number of these items may occur after the grant completes, the Foundation would expect the grantee to report on these metrics annually for up to 3 years after the grant completion.

11) Confidentiality

The Foundation 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 Foundation assessments. All Confidential Information will be used by the Foundation 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 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 or other owner(s) of such Confidential Information notice of such disclosure request as soon as is reasonably practicable.

Participating scientific reviewers will be subjected to the Foundation's standard non-disclosure agreement for such engagements.

12) Other

Liability and Indemnity

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Each Applicant pursuant to this Program acknowledges and agrees in responding to the Program announcement that the Applicant shall have no claim against the Foundation, and its respective representatives or affiliates, should such Program 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 RFA process and its outcome.

The Foundation's role in grants awarded pursuant to this Program is that of a funder. It is not the sponsor of funded projects. The Foundation will not assume any liability associated with funded projects and each Applicant who is ultimately awarded a grant pursuant to this Program 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.

Intellectual Property Policy and Intellectual Property Agreements among Collaborators

The Foundation acknowledges that any intellectual property ("IP") that arises from research funded through this Program is not the property of the Foundation. The Foundation does require that researchers and collaborators agree on any material IP issues prior to submission of a Proposal.

Publication and Sharing Policy

The Foundation expects results of funded research to be published as rapidly as possible in the open access scientific literature or other forms of publication that are readily available to the research community, unless such publication will jeopardize the Applicant's right to secure patents or copyrights necessary to protect the Applicant's ownership. 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 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.

The Foundation expects that all tools/reagents (i) funded by and (ii) that result from funded projects will be made readily available to the community for research purposes either freely or at reasonable prices. The Foundation may let the public know of these tools/reagents, so researchers know they are available.

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