



# Penn Genetics

**Penn Genetics**  
**In partnership with**  
**the Institute for Translational Medicine and Therapeutics (ITMAT) and**  
**the Penn Center for Precision Medicine (PCPM)**

**announces the**

## **Translational Genetics Initiatives**

Proposals are due by **April 15, 2019** for a project start date of **July 1, 2019**  
Up to \$300,000 per year for up to 2 years

### **Overview**

Human genetics is transforming the way in which we practice medicine. Genetic variation influences risk of disease, guides preventive interventions, enhances the accurate diagnosis of disease, predicts prognosis and outcomes, influences response to treatment, helps identify novel targets for therapies, and enables new therapeutic approaches. Penn Medicine has established itself as a leader in the application of human genetics to biomedical discovery and clinical medicine. The **Penn Medicine Biobank (PMBB)** (<http://www.itmat.upenn.edu/biobank>) is one of the largest academic biobanks in the US, numbering > 60,000 participants and still actively recruiting. Participants consent to storage of biospecimens and their use in data generation, access to electronic health record (EHR) data, and permission for recontact. The PMBB has generated extensive genomic data, including ~12,000 whole exomes and ~20,000 genome-wide chip genotyping to date, and facilitates the access to linked EHR phenotype data and stored plasma and serum on all participants. *Importantly, all participants enrolled in the PMBB, both currently and prospectively, will have whole exome sequencing and chip genotyping performed.* Penn Medicine faculty therefore have a unique opportunity to leverage the genomic and phenomic data, as well as the stored biospecimens, in the PMBB for biological discovery and advancement of precision medicine. Through the program described in this RFA, we wish to catalyze the assembly of teams to harness human genetics in order to advance discovery, innovation, prevention, treatment, and cure for specific diseases with a genetic basis.

To capitalize on these opportunities, resources have been committed to establish Translational Genetics Initiatives (TGIs), led by Penn Genetics in collaboration with the Institute for Translational Medicine and Therapeutics (ITMAT) and the Penn Center for Precision Medicine (PCPM), that will strive to transform our approaches to human health and disease. We are seeking applications for TGIs from interdisciplinary groups of scientists and clinicians who propose innovative, translational genetic approaches to the diagnosis, sub-phenotyping, risk assessment, prevention, and/or treatment of human disease. To be considered translational, the proposed TGIs should consist of highly integrated and interdisciplinary programs with the ability to move scientific discoveries into the clinic, and with the potential for an impact on patient care and outcomes. *In addition, the project must make use of the Penn Medicine Biobank resources in some capacity (see below).*

Applications will be reviewed and selected by an Executive Steering Committee (ESC) comprised of Penn scientists and ad hoc experts as needed. The funding will be keyed to milestones. Funded projects will receive up to \$300,000 per year for a maximum of two years, with the second year of funding contingent on reaching

stated milestones and subject to approval by ESC. An important final milestone is to show convincing progress towards the utilization of human genetics in the diagnosis, prevention, or treatment of disease within the Penn Medicine.

### **Guidelines**

Translational Genetics Initiatives must be based around the application of genetic approaches to a specific disease or condition. They are not restricted to traditional Mendelian diseases but rather may consider the broad spectrum of disease in which there is thought to be a genetic component. The proposal must make use of the Penn Medicine Biobank in some capacity. This may include some combination of use of the genomic data, EHR phenotype data, or stored plasma/serum samples, and/or recall of PMBB participants for additional deep phenotyping studies. *Proposals that extend beyond simple analysis of PMBB data, especially those that engage PMBB resources to build new cohorts are strongly encouraged.* Specific questions about the data and resources available through the PMBB, including the number of current participants with a specific disease or diagnosis, should be sent to [biobank@pennmedicine.upenn.edu](mailto:biobank@pennmedicine.upenn.edu).

In addition, the following features of TGI applications are required:

- Jointly lead by 2 Principal Investigators with representative and complementary experience. It is expected that one PI will have basic science expertise and the other expertise in either human translational or clinical research.
- An integrated team of research scientists and clinical investigators
- An innovative proposal, rather than continuing ongoing research
- Anticipated ultimate impact on clinical care in some capacity
- Plan for sustainability

In addition, the following features are encouraged:

- Cross-departmental collaborations
- Contribution (funding or in-kind) by participating Departments/Centers/Institutes

The research proposal should utilize no smaller than Arial 11-point type (font) size and be no longer than 3 pages (including tables and figures). References are not counted toward the 3 page limit. The proposal should include the following:

- **Broad mission and specific objectives:** Describe briefly the translational vision for the TGI, the lack of information and unmet needs for the targeted disease, and the specific goals and objectives. Highlight how novel genetic approaches have the potential to transform care for the disorder. Specify how this represents a new direction rather than duplicating the applicants' past or ongoing research.
- **Clinical impact:** Describe how the TGI will accelerate advances in science that have the potential to change the standard for care in the future. Clarify how the interdisciplinary team approach will facilitate realizing this potential.
- **Approach:** List the aims and the general research strategies for a set of highly integrated scientific projects that address the overarching mission of the TGI. Specify how the Penn Medicine BioBank resources will be utilized. If gaps in existing facilities are perceived to be a challenge for execution of the proposed research, applicants are encouraged to describe ways that TGI funding could optimize facility services and operations.
- **Organization and leadership:** TGIs are multi-PI mechanisms and as such all TGI proposals are required to have at least two Principal Investigators with standing faculty appointments at Penn who complement each other with regard to scientific and clinical background and expertise. One PI should be identified as the administrative PI and will serve as the point person for communication. Describe and/or illustrate

the organizational framework for the proposed TGI. Provide evidence for the qualities and the capability of the PIs to lead this effort and to produce the expected results. Specify current strengths of the team and areas of opportunities for investment to build an outstanding TGI.

- **Metrics of success:** Provide a list of no more than five specific metrics over 2 years that are relevant to your TGI. Comment on potential impact over a longer-term (5-year) time line. Scientific and clinical metrics should be emphasized; however, training metrics may also be included. Potential metrics may relate to novel discoveries based on observational or experimental research, development of new diagnostic, prevention or treatment modalities, advancing innovative clinical trials, and/or improvements in clinical outcomes.
- **Sustainability:** It is recognized that changes in clinical care and outcomes may require long-term investment beyond the initial 2-year funding period. A goal of this program is to stimulate the development of programs that will continue to exist and have impact. Thus, plans to promote the sustainability of the TGI beyond the initial 2-year funding period to achieve these. Explain how the initial funding will be leveraged to promote sustainability.

### **Required documents**

- **Submission:** Please submit online at [www.med.upenn.edu/apps/itmat/pg](http://www.med.upenn.edu/apps/itmat/pg). Please ensure that you choose **Translational Genetics Initiatives** when submitting your application. Please refer to Document Submission Section for specific instructions related to this system.
- **Abstract:** The abstract text should be no longer than 250 words.
- **Research proposal:** See guidelines above
- **Budget** (does not count toward 3-page limit): A high-level budget is requested at the time of the application. **Support for faculty salaries and benefits will not be provided through this mechanism.** Budgets must be submitted on the approved excel template available on the website.
- **Budget justification** (does not count toward 3-page limit): Please provide a short justification for all personnel, supplies, and equipment that will be expensed to this project. Please provide a distinct justification if resources are to be spent on services provided from outside Penn.
- **NIH biosketches** (do not count toward 3-page limit): NIH format biographical sketches should be included for the PIs and other key faculty members of the TGI.
- **Departmental letters of support** (do not count toward 3-page limit): Letters of support from the PIs' Department Chairs that includes explicit description of any tangible in-kind or financial contributions from the Department. One example could be support for consenters to prospectively recruit patients of interest into the PMBB. Letters of support from Center/Institute directors are not required but will be considered favorably in the review process.

### **Review Process**

An initial review by the ESC will be performed to select those applications most competitive for funding. These applications will be reviewed by scientists and clinicians with content expertise. Final funding decisions are anticipated by June 2019, with a TGI initiation date of July 2019.

Review criteria will include:

- **Impact:** What is the likelihood that the proposed program of research will translate discoveries to clinical practice and have a transformative impact in the targeted disease?
- **Innovation:** Is the proposed TGI creative and significant? If successful, will the work in this TGI produce shifts in clinical practice by using novel concepts, methodologies, and/or interventions?
- **Investigative Team:** Do the proposed TGI PIs have a strong track record of leadership of interdisciplinary and translational science? Does the team have sufficient interdisciplinary breadth and depth to carry out the proposed research?

- **Approach:** Are the general strategies and translational approaches sufficiently rigorous to ensure generation of important data? Are metrics of success and plans for sustainability presented and reasonable?
- Tangible commitments from participating departments and active engagement with the PMBB regarding recruitment will be viewed favorably in review.

**Ongoing review and evaluation:** Funded TGIs will be expected to submit semi-annual progress reports, which will be evaluated by the ESC and possibly by outside advisors. Metrics of success and progress toward achieving scientific milestones will be considered. Continuation of funding for the second year will depend on documented progress toward established milestones.

**Support for TGIs not selected in the current round:** Compelling components of unfunded applications may be supported with seed funds to facilitate further development of future TGIs for funding in future years.

#### **Other**

- To apply you must be a registered member of the Institute for Translational Medicine and Therapeutics (ITMAT). You can register to become a member at <http://www.itmat.upenn.edu/membership.shtml>
- All proposals are due by **April 15, 2019 at 12 PM.**

#### **Document Submission**

All applications should be submitted via ITMAT's Pilot Grant System at [www.med.upenn.edu/apps/itmat/pg](http://www.med.upenn.edu/apps/itmat/pg).

**PLEASE ENSURE THAT YOU CHOOSE "TRANSLATIONAL GENETICS INITIATIVES" WHEN SUBMITTING YOUR GRANT PROGRAM.** You will need your PennKey logon and password to access this system. Once you start an application, you can proxy someone (grants manager, post doc, etc.) to finish it for you.

- Each PI must be an ITMAT member.
- Each PI must have the approval of their respective Business Administrator.
- **Penn Faculty** should select the Business Administrator or Grants Manager that normally signs off on all of their research proposals.
- **CHOP Faculty** must select Amanda Varrone as their Business Administrator.
- If your grants are managed by a division within the **Department of Medicine**, please select Susan Wahl as your Business Administrator. She will coordinate divisional/departmental approval.
- Please ensure that the documents you upload are the final documents. We will not update or replace files.
- All documents must be uploaded by noon on the due date of the proposal to ensure time for all approvals. All approvals must be completed by 5 pm on the due date.
- Once all approvals are completed, the grant will be received by Penn Genetics.

#### **Application or Funding Questions**

We encourage presubmission inquiries; please put "TGI presubmission inquiry" in the title of your email and send to Rebecca Helgesen at [rebecca.helgesen@uphs.upenn.edu](mailto:rebecca.helgesen@uphs.upenn.edu). Direct any other programmatic or budget questions to Rebecca as well. For questions about the Penn Medicine Biobank and its utilization, please contact [biobank@pennmedicine.upenn.edu](mailto:biobank@pennmedicine.upenn.edu). For technical questions related to completing the online application, please contact Andrea Albelda at [aalbelda@pennmedicine.upenn.edu](mailto:aalbelda@pennmedicine.upenn.edu).