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.

Toward this end, 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). We are seeking applications for TGIs from interdisciplinary groups
of scientists and clinicians who propose innovative, translational team approaches to the diagnosis, sub-
phenotyping, risk assessment, prevention, and/or treatment of specific genetic diseases (either Mendelian or
complex genetic disorders). 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 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 for the first year, and an additional $300,000 will be made available for a second year based on
reaching stated milestones and subject to approval by ESC, for a potential total award of up to $600,000. 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 Health System.

Guidelines

Translational Genetics Initiatives must focus on a particular type or class of genetic condition, which can be a single-gene disease or a complex genetic disorder. The proposal must also make use 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. Applications might also include prospective targeted recruitment of patients with the disease of interest into the PMBB. Specific questions about the data available through the PMBB, including the number of current participants with a specific disease or diagnosis, should be sent to biobank@pennmedicine.upenn.edu.

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

- At least two ‘multiple PIs’ who complement each other with regard to background and expertise
- 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, cross-school, and/or cross UPHS-CHOP collaborations
- Contribution (funding or in-kind) by participating Departments or 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 the novel approaches that have the potential to transform care for the genetic 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:** A TGI is expected to have at least two ‘multiple PIs’ who complement each other with regard to scientific and clinical background and expertise, preferably one focused on more ‘basic’ research and one focused on ‘human’ research. 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 that are relevant to your TGI, with a short-term (e.g., 2-year) and 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 (e.g., P01s, foundation support, increased clinical revenues, philanthropy, etc.) should be discussed.

**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): A letter of support from the PIs' Department Chairs is encouraged. Support (including in kind) from participating departments (or centers/institutes) will be considered favorably in the review process. One example could be support for consenters to prospectively recruit patients of interest into the PMBB.

**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?
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](http://www.itmat.upenn.edu/membership.shtml)
- All proposals are due by April 15, 2019 at 12PM.

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 Varone 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 pre-submission inquiries; please put “TGI pre-submission 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).