

**Call for Proposals
University of Virginia
TransUniversity Microbiome Initiative
Pilot and Feasibility Grant Program**



Application Deadline:

Thursday, February 27, 2020

Purpose and Research Focus:

The mission of the TransUniversity Microbiome Initiative (TUMI) is to facilitate functional studies of the microbiome and the altering of its composition and activity to improve health. TUMI is funded by the Strategic Investment Fund and aims to support microbiome research across Grounds. The Pilot and Feasibility Grants are designed to bring together microbiome investigators from various departments and schools and to sponsor microbiome research within their subject areas. One of the major goals of TUMI is to involve undergraduate, graduate, and postdoc trainees in the proposed research. The Pilot and Feasibility Projects can focus on the microbiota at any body site of human, animal, plant, or water systems and its relevance to human health. Projects can focus on composition and/or function of bacterial, fungal, archaeal, or viral communities as well as their physiological and pathological effects on their hosts. Please reach out to the Program Manager (Casandra Hoffman, clh4he@virginia.edu) if you have questions regarding the relevance of your project to this funding opportunity.

Number of Awards and Available Funding:

Five \$60k, 1-year awards will be awarded semiannually. Funding announcements will be made in January 2020, January 2021, and June 2021.

Eligibility:

All faculty members of the University of Virginia are invited to submit proposals. We particularly encourage applications from established and early career investigators who wish to expand into studies of the microbiome.

Evaluation Criteria

TUMI Seed Grant proposals will be evaluated on three equally-weighted criteria:

1. How effectively will the proposed activities utilize TUMI Core Facilities, particularly the TUMI-sponsored gnotobiotic and metabolomics core facilities?
2. How likely are the proposed activities to lead to external funding to sustain the proposed research and/or support translation of an innovation into practice?
3. What is the potential scientific and clinical impact of the project?

Proposal Preparation:

Submit all documents as a single PDF via email to TUMI's Senior Research Program Manager, Casandra Hoffman (clh4he@virginia.edu). Complete proposals are due by 5PM on February 27, 2020. Awards will be announced in April 2020.

Format:

- NIH-style Specific Aims Page
- NIH Biographical Sketch

- Sections for the 6 page maximum (excluding references) main proposal include:
 - Background and Preliminary Results
 - Research Plan
 - Trainee Involvement: 1-2 paragraphs must be included that demonstrate the involvement of trainees (undergraduate, graduate, and postdoctoral research associates) in the proposed research activities.
 - Future Directions: 1-2 paragraphs must be provided at the end of the proposal articulating how this pilot award will provide necessary data to obtain extramural funding. Please be as specific as possible in the plan for follow-on funding, including information on previous related applications and outcomes, agencies and funding opportunities, etc.
 - Senior Investigators should indicate how this project represents a new direction in their research.
- Budget and Justification, 1 page maximum:
 - One year, \$60,000 budget
 - Salary support of \$10,000 or less allowed, though not for the PI.
 - Outline of Estimated TUMI Core usage: All awardees are required to use at least one of the TUMI Core Facilities. At least 50% of funds must be spent at one of the current TUMI Core Facilities: Gnotobiotic Animal Core, Metabolomics Core
 - Milestones: Funds will be released in two \$30,000 disbursements. The second disbursement is contingent upon reaching certain milestones (e.g. the use of the first \$30k, the completion of the first gnotobiotic experiment, the completion of the first metabolomics experiment, etc.). For more information, please reach out to the program manager (Casandra Hoffman, clh4he@virginia.edu).
- Data management and analysis plan
 - A summary for how will data be collected and stored
 - A summary of the data analysis plan, including any letters of support from the Bioinformatics Core or other bioinformaticians and biostatisticians that will aid in the analysis of collected data. For more information or help identifying bioinformaticians at UVA, please reach out to the program manager (Casandra Hoffman, clh4he@virginia.edu).

Award Terms:

- A progress report is due at 6 months into the project period. The report will contain a one-page synopsis of scientific progress and a list of resulting collaborations, microbiome program core utilization, publications, grants that were applied for, and grants awarded.
- A final progress report is due within one month after the close of the project period. The report will contain a one-page synopsis of scientific progress and a list of resulting collaborations, microbiome program core utilization, publications, and grants.
- The awarded funds will be disbursed in two parts. The second disbursement requires that certain milestones or benchmarks have been met. Milestones and/or benchmarks will be determined by the PI and TUMI. Funds that are not used by the end of the 12 month (1 year) period will be returned to TUMI.
- Awardees will be asked to highlight research activities at the annual Trans-University Microbiome Initiative symposium.
- Awardees must acknowledge TUMI support in resulting publications.
- The project title, PI name, and key personnel names will be published on the TUMI website as an announcement (no financial or project details will be included).
- Awardees are required to inform the Trans-University Microbiome Initiative in the event that the Pilot/Feasibility Project receives external funding or a project results in a publication during the project period.

Additional Information about TUMI

TUMI SPACE AND RESOURCES

The TransUniversity Microbiome Initiative is located both in the Department of Medicine, Division of Infectious Diseases and International Health and Department of Pediatrics, Division of Pediatric Gastroenterology, Hepatology & Nutrition, in close proximity to the University of Virginia's Children's Hospital (<5 minute walk within the UVA hospital system) and the University of Virginia's Ivy Translational Research Building (<10 minute drive, home to Administrative and Data Science Cores). The University of Virginia's Trans-University Microbiome Initiative (TUMI) has two dedicated procedure rooms currently under renovation for microbial and tissue culture, 16S DNA extraction, and sample storage.

Within this space will be the following equipment:

- Bio-Rad CFX96 real-time PCR detection systems, Eppendorf conventional gradient PCR instruments, OptiMax thermocycler
- Class II Biosafety cabinets
- Incubators, shaking incubators, Fisher Scientific jacketed CO2 incubators
- Refrigerators and -20°C freezers
- Eppendorf microcentrifuges, Beckman L7-55 ultracentrifuge, Sorvall refrigerated benchtop centrifuge, Avanti J-30I centrifuge with multiple rotors, International PR-J swinging bucket centrifuge, Sorvall RC5B Super speed centrifuge
- Milli-Q water purification system
- Vortex mixers, pH meter, hot plate stirrers, balances including Mettler balance
- Ultrasonic bath sonicator and Ultrasonic W-375 sonicator/cell disruptor
- Fisher Isotemp water bath
- Autoclave and dishwashing facility
- Spectronic 601 spectrophotometer
- Bio-Rad Gel Doc system
- Qiacube HT (DNA extractor) (to be purchased by 06/2020)
- Illumina MiSeq (to be purchased by 06/2020)

Affiliate resources, including the University of Virginia's Biomolecular Analysis Facility and Genome Analysis and Technology Core, provide use of an Agilent Bioanalyzer and LC-MS-MS mass spectrometer.

TUMI AND TUMI-ASSOCIATED CORE SERVICES

Gnotobiotic Animal Lab

Gnotobiotic Animal Center, directed by Sanford Feldman, has obtained equipment through our efforts and those of the Trans-University Microbiome Initiative (TUMI) and the Virginia Equipment Trust Fund to generate and maintain germ-free mice. We are now in our eighteenth month of breeding, maintaining, and validating the germ-free state of this colonies of Swiss Webster and C57BL/6 mice.

The equipment produced by Class Biological Clean (CB Clean, LLC) in our possession is located in the Life Sciences Annex (LISA) at Fontaine Research Park. We maintain four large flexible film isolators for production of germ-free mice, two isolators for each strain in case one isolator should become contaminated and require

removal from service. We have forty small flexible film isolators for carrying out experiments distributed in the LISA facility, and have sufficient steam sterilizer capacity to support this activity. Our gnotobiotic facility is producing transgenic animals in a germ-free state for experiments as well, germ-free transgenic strains are maintained as cryopreserved embryos and produced by trans-cervical embryo transfer as needed for experiments.

Germ-free mice that are used in experimentation are transferred to “semi- rigid” isolators where they are associated with microbial flora that constitutes the experiment of the researcher in question. Only a single experimental microbial association can be done in one semi-rigid isolator, which is then solely dedicated to the experiment for its duration. Currently we have two semi-rigid isolators for this purpose. In addition to the semi-rigid isolators, an alternative method of housing germ-free mice that have been associated with a specific microbiome is in biocontainment caging. We have unused biocontainment caging sufficient to hold 72 boxes of mice. Each box can then represent a unique microbiome-associate for the duration of a particular experiment.

In association with TUMI, the Gnotobiotic Animal Core will: a) expand cage capacity, b) allow Veterinary Services to rederive transgenic mice into germ-free conditions, and c) provide germ-free enclosures at other locations across the University to receive mice in biocontainment caging from the main facility at Fontaine prior to experimentation. Anaerobic, microaerophilic, and fermenter capacity will be coordinated to allow for the isolation and culture of difficult to grow members of bacterial communities. Because the microbiome encompasses far more than bacteria, this capacity will also allow ultimately allow us to incorporate studies of the virome and fungome to complement TUMI.

In addition to the expansion of resources, TUMI will also subsidize experiments in the Gnotobiotic Animal Core through the award of TUMI pilot and feasibility grants, making the use of our Core less costly to users.

Useful Information for Gnotobiotic Animal Facility Budget Preparation:

Thus far, only one experiment has been done at the Gnotobiotic Facility. Sandy Feldman, who runs the facility has been unable to accurately estimate costs for when animals for multiple experiments are housed. With that being said, here are the costs associated with the first germ-free experiment at UVA.

The primary cost was the purchase and shipping of germ-free animals from Taconic. The cost of purchasing mice is considered part of the funds used at a TUMI core.

Additional pricing information can be found at <https://www.taconic.com/mouse-model/black-6-b6ntac>

C57BL/6, Germ-Free, M, 6 weeks

Qty 16

Cost Ea. \$565.00

Extended \$9,040.00

Shipping \$419.00

Handling \$0.00

Mouse Total **\$9,459.00**

Housing per diem at Snyder (UVA Gnotobiotic Facility)

(\$3.16/day, may change based on # of germ-free mouse facility users)

This cost includes experimental administration of bacterial species.

[4 cages * 30 days * \$3.16 = \$379.20]

16 germ-free mouse experiment total : \$9,459.00 + \$379.20

Metabolomics Core

The Metabolomics Core is nested in the Biomolecular Analysis Facility. The major goal of the facility is to provide access to advanced mass spectrometry instrumentation and qualified staff at the University so that investigators can not only obtain high quality data for complex, scientifically significant research but also interact directly with the staff to provide effective experimental planning and design. The BAF and the Trans-University Microbiome Initiative (TUMI) have recently hired a dedicated Metabolomics Staff Scientist, Nishikant Wase, who will perform metabolomics extractions and targeted and untargeted metabolomics profiling via both liquid chromatograph and mass spectrometry. With Dr. Wase's help, we will characterize a library of known metabolites to identify host and bacterial metabolites in microbiome-related samples. In addition to running samples for metabolomic profiling, the BAF will work closely in the development of sample storage and processing, and metabolite extraction protocols from urine, blood, stool, saliva, breastmilk, and cord blood, and be available for post-experiment data analysis as needed. The BAF also provides internal and external controls for samples, ensuring quality control for longitudinally collected samples.

The Mass Spectrometry section of the BAF identifies and quantitates proteins and other types of molecules either individually or in complex mixtures with a Thermo Velos Orbitrap (High Resolution and Mass Accuracy) and a Thermo Electron TSQ Quantum Access MAX (Multiple Reaction Monitoring). The Core or individual researchers (open access) perform quality control on molecules using a Bruker MicroFlex MALDI-TOF.

The ability of the BAF to determine the absolute quantitation of small molecules and metabolites was recently strengthened by the addition of a Thermo Orbitrap ID-X with both LC and ZipChip (CE) interfaces. The purchase of this instrument was supported by TUMI and the Commonwealth of Virginia Equipment Trust Fund in 2019, demonstrating the recognition by the University of the importance of metabolomics in the future of biomedical research. In addition to these investments, the University provides support in the BAF through subsidies for users (40% copay for UVA users), which will be applied to all fees incurred by TUMI users.

Microbial Culture and Repository Services

Will be developed in the coming months. More information coming soon.

Bioinformatics Services

Will be developed in the coming months. Two TUMI-supported faculty and two additional bachelor's/master's-level bioinformaticians will be hired in July 2020. More information coming soon.