I. Overview of the VCCBH and Rationale for Interdisciplinary Pilot Grants
Cardiovascular disease and stroke are leading causes of death and disability in the United States and are intimately related to cognitive impairment and dementia. The Vermont Center for Cardiovascular and Brain Health” (VCCBH) seeks to expand the University of Vermont’s (UVM’s) capacity to conduct research to reduce death and disability from these diseases through diverse, mutually reinforcing basic, clinical and population science perspectives. A core mission of the center is to provide support for junior investigators to conduct research that propels them to independence (in the form of an R01-equivalent grant award) using team-based, interdisciplinary mentorship, access to our research cores and our Pilot Grant Program. The latter will provide significant resources to foster interdisciplinary programs for junior faculty through an award of $200,000 over a two-year period. Research support will be provided by the VCCBH Study Design and Molecular Epidemiology and Customized Physiology and Imaging Cores. Access to these cores will advance grantees’ skills in study design, epidemiology, translational research, imaging, experimental instrumentation, and electrophysiology.

Please read this RFA carefully as it contains important information about eligibility and peer review criteria. If you have questions, or if you would like assistance identifying collaborators or resources to enrich your research application, please contact Dr. Owen Nadeau, Operations Administrator of the VCCBH at Owen.Nadeau@med.uvm.edu. We encourage you to start early in order to produce the most competitive application possible.

II. Components of the VCCBH Interdisciplinary Pilot Grants
Any individual with a full-time junior faculty appointment at UVM may apply for a VCCBH Pilot Project Grant. The main impetus behind the VCCBH Pilot Project Grant is to support cross-disciplinary research that will lead to extramurally funded research to impact our understanding of Cardiovascular and Neurovascular diseases. We plan to award one Pilot Project Grant for no more than $200,000 this year. Support for no more than $100,000 will be available for Year 1. Funding for Year 2 will be no more than $100,000 and will be contingent on meeting benchmarks in Year 1. Both the first and second year of funding are subject to the VCCBH External Advisory Board (EAB) approval. Multiple-PI (MPI) applications with two PIs are preferred but sole PI applications will be considered if there is sufficient departmental support. We encourage the MPIs to be from different backgrounds.

- Applications should meet each of the following expectations:
  - address a major issue in cardiovascular or neurovascular research.
  - have scientific excellence and rigor.
  - be innovative and of high impact, consistent with NIH review guidelines.
  - have a research strategy that leads to published manuscripts. The plan must be provided.
  - lead to high likelihood of obtaining extramural funding. The strategy must be provided.

We encourage applicants to consult with our Core Directors early in the preparation of their application. Allocation of Core effort to assist in grant preparation will be available on a first-come first-served basis. Brief descriptions of the Cores are included on page 6. Contacts:
- Study Design and Molecular Epidemiology: Dr. Peter Durda (Peter.Durda@med.uvm.edu)
- Customized Physiology and Imaging: Dr. Todd Clason (Todd.Clason@med.uvm.edu)
III. VCCBH Interdisciplinary Pilot Grant Eligibility

- Applicants will be early career faculty members at the assistant professor or faculty scientist level.
- Applicants may not have R01 or NSF equivalent funding; however, this does not include K99/R00 Career awards. If you aren't sure whether your funding disqualifies you, please inquire with Dr. Nadeau at the above address.
- Applicants should be in our Pipeline Investigator program or be Project Directors of this Center, but this is not required. To learn more or request to join the Pipeline, email Dr. Nadeau at the above address.
- Only one application per PI or multi-PI.
- VCCBH Interdisciplinary Pilot Grants are intended to encourage new cross-disciplinary and cross-departmental / college research. The conceptual development and execution of the project should be shared equally by each PI.

IV. Overview of Application and Review Processes

1) A Letter of Intent (LOI) is required (due February 3, 2023) and must include all the following (or it may not be considered):
   a. The LOI will be one page that:
      • addresses the scope of the research (possible specific aims),
      • states how this award would propel the investigator(s) to further funding,
      • states there is no overlap with existing research, or explains perceived overlap,
      • briefly describes the role of each MPI,
      • lists any involved mentors.
   b. NIH 5-page biosketch of the applicant(s).
   c. A signed letter of assurance from the applicant’s chair(s) that their department(s) will provide matching funds (25K/year for 2-PI applicants and 50K/year for single-PI applicants). Please reach out to us for assistance and information on requesting this support, and we will assist you with communications with your chair as needed.

2) After review of LOI’s, a request for submission of a complete application will be issued by Feb. 24, 2023. While not all LOI’s will be selected, it is to the investigators’ advantage to continue work on an application while awaiting this decision.

3) The completed VCCBH Interdisciplinary Pilot Grant Application packet is due May 26, 2023. It must include the following sections. Applications not including each point here may be administratively withdrawn.
   - Cover page:
     • Title of the project.
     • If applicable, a statement that IACUC or IRB approval will be obtained prior to the Oct 2 start date of project.
     • Budget requested.
     • Indication of core usage (or non-usage).
     • PI Assurance: I certify that the statements herein are true and accurate to the best of my knowledge. I agree and accept responsibility for the scientific conduct of the project and to provide the required progress reports if the grant is awarded.
     • Signature of the applicant(s).
     • Chair Assurance and Signature of the applicant(s)’ Department Chair(s)

Using PHS398 forms and instructions, the following sections are required:
• Face Page (signed by institutional signing officer)
• Project Summary (Page 2)
• Specific Aims page that includes the following:
  • Clear statements of the aims and hypotheses being tested.
  • We recommend a central figure illustrating the project aims.
  • We recommend a limit of one to two specific aims that can reasonably be completed within the funding period.
• Research Strategy (6 pages) that includes the following subsections:
  • Background and Supporting Literature (< 1 page): state the research problem, with review of relevant literature.
  • Significance (<1 page): briefly describe how the proposed research is novel in approach, methodology, theoretical concept or intervention, with a brief description of how environment will contribute to probability of success.
  • Innovation (<1 page): illustrate how this research challenges and seeks to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches, methodologies, instrumentation or interventions.
  • Preliminary Data (1-2 pages): if available, provide this to assist the reviewers in determining the feasibility and justification for the project. Preliminary data in some cases may not be directly related to the proposed research but will demonstrate feasibility.
• Research Design and Methods (2-4 pages):
  o Provide the methods proposed to address the proposed aims. The experimental design should provide a clear explanation of key methods and data analysis approaches (including statistical analysis plan and power calculations).
  o Discuss usage of VCCBH Cores. Use is encouraged but not required. Discussion is required.
  o Present the strategic plan for how the proposed research and its results will increase competitiveness for a new extramurally funded, research grant.
  o All applications must discuss consideration of sex as a biological variable. If applicable, provide information on consideration of race/ethnicity.
  o Provide a timeline for the proposed research, submission of an extramural grant application.
  o Describe any perceived scientific overlap with existing funded research, and if there is a perception of overlap, why it isn’t present.
  o Provide a list of anticipated manuscripts.
• References (no page limit)
• Animal and/or human welfare assurance if applicable (no page limit) see PAR-18-266 and SF424 (R&R) Application for instructions.
• Budget with detailed justification. The budget is limited to no more than $100,000 annually inclusive of all costs (i.e., fringe if salary is requested).
  o Present the budget in tabular form as no more than one page.
  o Provide details for use of either or both Scientific Cores, including fees for the work of each Core.
  o PI salary is an allowable budgetary item up to 15% effort annually for each MPI at the NIH cap (fringe will be applied, please confirm rates with your Department Administrator).
  o Provide detailed justification of less than one page (use of salary as a budget item will require assurance that remaining funds are sufficient to complete the project).
  o Travel may not be included in the budget unless this is necessary for collaboration or learning new skills and techniques that require in person experience, with strong justification.
  o Conference travel is not allowed. Note, the Cardiovascular Research Institute of Vermont provides travel grants.
  o Publication fees, including article processing charges for open access publishing, are allowed.
• NIH 5-page Biographical Sketches for Principal Investigator(s), other key personnel, and mentor(s) (if applicable)

• Senior Mentor letter(s):
  o We require inclusion of at least one Senior Mentor who may or may not be part of the VCCBH mentor group (see Page 8). The Senior Mentor is expected to interact closely with the applicant in grant preparation and monitoring progress during the funding period.
  o In a letter of no more than 1 page, describe the mentor's experience, relationship to applicant(s), and mentoring plan.

• All documents must be prepared in 11-point Arial font with 0.5-inch margins, be assembled into a single PDF in the order listed above and submitted via email (Owen.Nadeau@med.uvm.edu). Applications should not be sent to SPA.

V. Evaluation
• VCCBH leadership will solicit the input of qualified reviewers to hold a study section.
• Applications will be scored using a NIH-style Overall Impact Score from 1 (outstanding) to 9 (poor).
• Reviewers will be encouraged to comment on the following individual criteria: significance, innovation, investigator(s), environment, approach, potential for extramural funding, potential for enhanced productivity. Summary Statements of the written critiques will be provided to the applicants.
• The EAB must approve the funding decision.

VI. Evaluation Criteria
• Primary considerations:
  • Does the proposal address a significant problem in Cardiovascular and Brain Health?
  • If successful, will the results have a substantial impact on the field?
  • Is the proposed research innovative?
  • Is the proposed research achievable during the funding period?
  • Are the investigators qualified to lead the proposed research?
  • Are there two PIs? Are they from different backgrounds? (both are encouraged but not required)
  • Does the proposed research have high potential to lead to future extramural funding?

• Other considerations:
  • Is adequate mentoring planned?
  • Use of VCCBH Research Cores?

• Examples of a responsive application might include (but are not limited to):
  • Gathering proof-of-concept or feasibility data for a larger extramural grant application.
  • New research topics and directions.
  • Innovative technology development.
  • New collaboration among basic, clinical and/or population science.
  • Development of new methodologies, assays or biological / pathological specimens.

VII. Funding Contingencies
• Funding decisions will be announced in August. At month 9 of the award, a progress report will be due, with Year 2 funding awarded contingent on adequate progress, and on EAB / NIGMS approval. We discourage requests for carry forward, but will allow carry forward of up to $30,000 from Year 1 into Year 2 only.

VIII. Awardee Requirements
• The PI will submit projects for approval to the IACUC or IRB as necessary. Funds will not be released until the project is approved by the IRB or IACUC so we suggest approval be sought upon application.
• The PI is required to present their work at a VCCBH Conference before or following the end of the funding period—To schedule see Catherine Cate (HeartBrainHealth@med.uvm.edu).
• The PI will provide occasional study updates at monthly VCCBH Work in Progress meetings and is encouraged to attend these monthly meetings.
• The PI is encouraged to attend monthly VCCBH conferences, an Annual Symposium, and engage with others in the Center to grow collaborations.
• A final progress report is due 60 days before the end of the funding period in Year 2.

IX. Action Dates
• RFA Announced December 6, 2022
• Application LOI due: February 3, 2023, 5 pm eastern time. Email to Owen.Nadeau@med.uvm.edu
• Notification to apply: February 24, 2023
• Application due: May 26, 2023, 5 pm eastern time. Email to Owen.Nadeau@med.uvm.edu
• Funding Decision Announced: July 14, 2023

X. Restrictions
• If an investigator has departmental or extramural funding, the specific aims of the proposed research should be distinct from already established support and the application should clearly establish the need for additional funding.
• An investigator can only obtain the VCCBH Interdisciplinary Pilot Grant once.
• An applicant who is unsuccessful in obtaining the VCCBH Interdisciplinary Pilot Grant may, in subsequent years, resubmit the same or a similar application or a substantially different application.

XI. Questions
• Dr. Owen Nadeau, Operations Administrator, VCCBH (Owen.Nadeau@med.uvm.edu).
Research Cores: Vermont Center for Cardiovascular and Brain Health Interdisciplinary Pilot Grants.

The Study Design and Molecular Epidemiology Core provides services unavailable elsewhere at UVM, including up-front and ongoing assistance to VCCBH Project Directors, Pilot Grant Awardees and Pipeline Investigators on their study design, data analysis plans, biostatistical support and data reporting. Active learning approaches are applied. It draws on the Laboratory for Clinical Biochemistry Research (LCBR) resources, including in developing and conducting assays, and accessing a biorepository with >4 million aliquots of biological samples from >100,000 research participants. It will identify LCBR resources and studies to afford effective translation of VCCBH Investigator findings to population or clinical research settings. This allows basic science-oriented VCCBH Investigators to translate their findings to human populations; for epidemiology and clinical-research oriented VCCBH Investigators to scale their findings to large populations; and engagement in outcomes research. Core co-Directors are Neil Zakai, MD, MSc (Associate Professor of Medicine and Pathology & Laboratory Medicine) and Peter Durda, PhD (Faculty Scientist, Pathology & Laboratory Medicine).

*Pilot Awardees are provided up to 6 hrs. of biostatistician time annually on a first-come, first-serve basis. Pilot Award recipients will budget in their application for study design, assay reagents, laboratory technician time and statistical support if their need is greater than resources offered through the Core.

The Customized Physiology and Imaging Core provides state-of-the-art capabilities for fixed and live cell and in vivo imaging, the capability of simultaneous electrophysiology, on-site fabrication of needed devices, and analysis services. This Core provides extensive training to PDs and other VCCBH users by providing high-level pre- and post-experiment technical and analytical support. This enables investigators to perform sophisticated imaging / electrophysiological experiments that are not possible in their own laboratories or elsewhere on campus. Investigators are provided training to develop a deep understanding of the microscopes and electrophysiology instrumentation so that they have the capability and flexibility to tailor the experimental system to answer key questions. Coupled with that, investigators are encouraged to learn design principles of chambers, holders, and other key accessories and their fabrication by 3D printing to optimize experimental approaches. Lastly, investigators are provided training to learn sophisticated image and electrophysiological analysis to maximize extraction of critical information. This Core is directed by Mr. Todd Clason, MS (Department of Neuroscience).

* Pilot awardees are provided free consultation and training on Core instrumentation, as well as discounted hourly fees for equipment access. They will budget in their application to offset imaging costs, should investigators need extensive instrument time.
Cover Page (must be included in application): Vermont Center for Cardiovascular and Brain Health Interdisciplinary Pilot Grants.

Project Title:

If applicable, a statement that IACUC or IRB approval will be obtained prior to the Aug 8 start date of project.

Total Budget requested.
   Year 1:
   Year 2:

Indicate briefly in bullet form how you will use Research Cores (or state, “use not proposed”)
   Study Design and Molecular Epidemiology
   Customized Physiology and Imaging

PI Assurance:
I certify that the statements herein are true and accurate to the best of my knowledge. I agree and accept responsibility for the scientific conduct of the project and to provide the required progress reports if the grant is awarded.
Name and Signature of the applicant(s).

Chair Assurance:
I approve submission of this application and agree to provide matching funds of 25K/awardee/year.
Name Signature of the applicant(s)’ Department Chair(s)

Contact information (name, email, best phone number for each PI):
List of VCCBH Senior Mentors: Vermont Center for Cardiovascular and Brain Health Interdisciplinary Pilot Grants.

George Wellman, PhD, Professor of Pharmacology; George.Wellman@med.uvm.edu

Michael LaMantia, MD, MPH, Associate Professor, Medicine and Neurological Sciences; Director, Center on Aging, Chief of Geriatrics, UVM Medical Center, Michael.LaMantia@uvm.edu

Marilyn Cipolla, PhD, Professor, Neurological Science; CVRI Board Director, Marilyn.Cipolla@uvm.edu

Ira Bernstein, MD, Professor and Chair, Obstetrics & Gynecology; Emeritus Senior Associate Dean for Research, UVM; CVRI Board Director, Ira.Bernstein@med.uvm.edu

Sayamwong Hammack, Professor, Psychological Science; Associate Director of the Undergraduate Neuroscience Program, Sayamwong.Hammack@uvm.edu