AIM
Autophagy, Inflammation & Metabolism
Center of Biomedical Research Excellence

bioMT | Institute for Biomolecular Targeting

AIM & Bio-MT Collaborative Pilot Awards

Inter- CoBRE collaboration initiative:
Request for Applications
February 6, 2020

The University of New Mexico's Autophagy, Inflammation, and Metabolism (AIM) CoBRE and the Dartmouth University Institute for Biomolecular Targeting (Bio-MT) CoBRE is offering collaborative pilot awards. These entities share missions to advance collaborative investigations of a number of processes affecting disease and health states including autophagy, inflammation, metabolism, whole genome CRISPR and drug screens, and protein chemistry and structural biology.

This program envisions collaborative teams with at least one investigator from each CoBRE/institution as joint-PIs, working collaboratively to develop a common research study and protocol that will be jointly implemented and supported by the two institutions. This innovative Pilot Program provides grants to investigators with the intention that they will use the funds to generate preliminary data to apply for external funding (preferably through NIH mechanisms, but also through other funding sources). We are currently accepting grant applications for the 2020 funding period. Proposals must be received by 5:00PM MST on **Monday, April 6th, 2020**, and the funding period is anticipated to be **May 5th, 2020 through October 31st, 2020.** If human studies are involved, IRB approval must be received prior to submission of the application. If animal studies are involved, IACUC should be in place by the time the funding commences. Proposals should articulate how work will be divided between the institutions, and how CoBRE scientific cores will be employed to further the work.

For these awards, proposals should incorporate a basic science approach and should address the topic of autophagy, inflammation, metabolism, cell biology and other areas in the context of a disease state that also meets the requirements of the Bio-MT Center. Applications are welcome from high-risk-/high-reward proposals that might prove innovative (and even disruptive vis-à-vis established paradigms) of high impact. A path for continuation and utilization of resources at the two institutions or nationally available resources accessible to users should be articulated.

Background and broader narrative: In September 2019, AIM and bioMT held a joint mini symposium with investigators form both institutions. This was viewed as a Phase I, first step toward establishing collaborative studies between the two CoBREs and the two Institutions. This collaborative pilot program is viewed as Phase II capitalizing on the contacts and interactions already in place and expanding it further to provide a path toward joint collaborative research programs and joint or individual grants emanating from these studies, which is considered to be Phase III of this inter-CoBRE initiative and program. We also envision that this program will be repeated (with further refinements) each year pending successful implementation and availability of funds. Below are descriptions of some of the facilities and the CoBREs involved, and the web sites describing activities and participants in the two centers are available on web sites: AIM: https://www.autophagy.center/ ; bioMT: http://biomt.dartmouth.edu/. Both sites have pages for "people" listing members and affiliates.

AIM supports the following scientific core facilities and capabilities:

Autophagy Core (Director: Larry Sklar, PhD)

1. Animal resource: Breeding pairs of autophagy and autophagy-related gene transgenic mice for research in pilot, mPI and main personnel laboratories (IACUC approval needed)
2. Cellomics high content microscopy: Quantitative microscopy for autophagy and lipid droplets as well as other intracellular profiles/organelles (e.g. lysosomes, peroxisomes, potentially mitochondria, nuclear translocation, etc.). Data generated are based on unbiased data collection and represent various numerical parameters (number/cell; area/cell, percent overlap, etc.), as well as statistics on large number of cells.
3. Amnis: as above (autophagy measures) for non-adherent cells.
4. High throughput screening (Link to UNM Center for Molecular Discovery: http://unmcmd.health.unm.edu/)

Inflammation and Metabolism Core (Director: Judy Cannon, PhD)

1. Seahorse: Oxidative phosphorylation vs glycolysis on adherent and non-adherent (special gel embedded) cells.
2. Amnis: flow cytometry for intracellular cytokines, and other profiles in inflammatory and immune cells, etc.

Bio-MT supports the following scientific core facilities and capabilities:

Molecular Tools Core (MTC) (Directors: Karl Griswold, PhD & Dale Mierke, PhD)

1. Enables research projects via acquisition or production of high quality recombinant proteins. We are developing optimization strategies spanning the molecular, cellular, and process levels in order to build an integrated pipeline capable of producing a wide spectrum of proteins and protein domain fragments.

   To provide the highest quality molecular tools for a specific project, the MTC will advise and work closely with researchers on construct design, expression host selection and on polishing strategies to produce large amount of pure proteins. The MTC will also execute or develop novel protocols for the production of recombinant proteins. Currently, we are producing proteins in mammalian cells and E. coli and will include insect cell and yeast expression systems in our toolbox in the near future. We are actively developing procedures to provide a robust quality control and characterization data package with the finished product, including spectroscopies and measurement of biomolecular interactions in close collaboration with the Molecular Interactions and Imaging Core (MIIC). The MTC recently incorporated the Crystallography Core Facility (CCF), providing the bioMT researchers the unique opportunity of designing, expressing, purifying, and crystalizing high quality proteins all in the same location.

Available equipment in the MTC:

- AKTA Pure 25 chromatography systems for purification of native and recombinant proteins equipped with:
  - Multi-wavelength UV and fluorescence detectors.
  - Capillary loops, superloops, and sample pumps for loading small and large

volumes of sample.
    - Pre-packed columns for size exclusion, ionic exchange and affinity chromatography.
- Beckman Avanti J-25and Optima L-70 centrifuges for low- and high-speed centrifugation.
- Bio-Rad Trans-Blot Turbo and Mini Trans-Blot Cell for membrane transfers.
- Bio-Rad PROTEAN IEF Cell for isoelectric focusing.
- Horizontal and vertical gel electrophoresis systems for protein and nucleic acid analysis (Bio-Rad and Invitrogen).
- Shaking incubators for cell culture (37ºC and low temperature).
- Electroporator for fungal, bacterial and eukaryotic cells.
- Microfluidizer LM10 for cell disruption.
- NT8 Drop Setter automated nanoliter/microliter drop dispensing.
- Formulator Screen Builder automated preparation of custom crystallography screens.
- Rock Imager images screen plates at scheduled intervals and allows users to remotely monitor drops.

Molecular Interactions and Imaging Core (MIIC) (Directors: F. Jon Kull, PhD & Henry Higgs, PhD)

1. To quantitatively characterize the molecular interaction of biomolecular systems, the MIIC will provide expertise in the sample preparation (working with the MTC), data collection, and analysis for a range of instrumentation including isothermal calorimetry, surface plasmon resonance, fluorescence-based measurements (fluorescence polarization, alpha-screen), and nuclear magnetic resonance. The MIIC has equipment available for

2. bioMT members for label-free analysis of biomolecular interactions, including drug target identification and validation, and for numerous imaging applications to characterize biological systems.

Available equipment in the MIIC:
- Biacore X100 to measure biomolecular interactions in real-time.
- LI-COR Odyssey for quantitative, highly sensitive near-infrared fluorescence detection.
- Bio-Rad GelDocXR for high-resolution nucleic acid and protein gel imaging.
- Synergy Neo2 Hybrid Multi-Mode Microplate Reader for numerous HTS applications with multi-detection modes.
- DeNovixDS-11 FX+Spectrophotometer/Fluorometer for a variety of micro-volume nucleic acid and protein analyses.

Microscopy (Contact: Zdenek Svindrych, PhD)
1. We provide microscopy support to the bioMT community. With a broad range of microscopes available at Dartmouth (either located in one of the imaging cores – Class of 1978 Life Sciences Center and Dartmouth-Hitchcock Medical Center, or in individual labs), we can cover many applications. The MIIC uses microscopy for both biochemical and cellular studies, and will help individuals design and implement methodologies to answer specific research questions.

Available microscopes and Image Processing Software:
- Laser scanning confocal (Nikon A1RSi with FLIM/FCS, Zeiss LSM880 with Airyscan, Zeiss SLM800 with Airyscan).
- Spinning disk confocal (AndorDragonfly 302, AndorW1 with Mosaic and Micropointphotostimulation/photoablation).
- Total Internal Reflection (Nikon/AndorTIRF, Olympus TIRF).

- Mutliphoton (Olympus FVMPE-RS with MaiTaiDeepSeeand FLIM/FCS).
- Epifluorescence (Nikon Ti-E - inverted, Nikon 90i – upright, Nikon SMZ1500 – dissecting stereo zoom).
- Amaris workstation with Measurement Pro, ImarisTrack, ImarisColoc, ImarisXT, ImarisCell, ImarisVantage, and Filament Tracker.
- NIS Elements workstation with Deconvolution.

FUNDING
It is anticipated that up to **two** pilot awards will be funded in this cycle (contingent on the availability of funds), with an award date of **May 5, 2020 and end date of October 31, 2020.** Awards will be for amounts of up to $20,000 (per award) for Direct Costs, each split $10,000 per institution. It anticipated that the proposals will operate under a "shared protocol, separate budgets" model. Budgets may include lab supplies and salary support for graduate students or other personnel as needed to complete the proposed work. Budget justifications should stipulate what work will be done and where it will be done. The CoBREs reserve the right to recoup unspent moneys at the end of the award period.

ELIGIBILITY
We welcome faculty applicants from the University of New Mexico Health Sciences Center and Dartmouth University. To be eligible for funding, applicants must be **PI-eligible employees** of these two universities. Since it is a common goal of CoBRE Centers to mentor and support junior investigators, funding priority will be given to early-career researchers who have not received research funding as a PI on a federally funded grant. Senior investigators will also be considered if they can demonstrate that their application represents a significant change in the scope of their current research program. Non-tenure track, Research faculty are encouraged to apply. If so, a letter of support from mentor will be required.

Important: IRB and/or IACUC approval must be secured prior to submission of the pilot award application and notice of such approval should be included with the proposal.

DEADLINE FOR SUBMISSION
Deadline for this submission cycle is 5:00PM MST Monday, April 6, 2020.

APPLICATION GUIDELINES
Applications should be prepared in general accord with the NIH PHS 398 application guidelines (Revised 1/2018) available from
https://grants.nih.gov/grants/funding/phs398/phs398.html

Applications must be submitted electronically as a signed pdf document by **5:00PM** on the deadline date. **Applications received after this time will not be reviewed**.

Please include the following sections in your application:

1. Form page 1: Face Page (https://grants.nih.gov/grants/funding/phs398/fp1.pdf). **YOU DO NOT NEED TO OBTAIN OSP SIGNATURE;**
2. Form page 2: Project Summary/Abstract (https://grants.nih.gov/grants/funding/phs398/fp2.pdf). **FOR THE PURPOSES OF THIS CALL, YOU MAY LEAVE THE "RELEVANCE" SECTION BLANK;**
3. Form page 4: Detailed Budget for Initial Budget Period (https://grants.nih.gov/grants/funding/phs398/fp4.pdf).

4. A detailed budget justification
5. A research proposal of no more than three pages (Specific Aims + 2 additional pages) that contains the following sections. **Each section must be addressed separately with its own heading**:

a. Specific Aims
b. Research Strategy
   i. Significance
   ii. Innovation
   iii. Approach
   iv. Collaboration logistics and anticipated benefits and products
c. A statement to indicate how the project will use AIM and bioMT core facilities. If core facilities are not relevant to the project, please explain.
d. List formal mentors (if applicable, as for mPIs).
e. Grant submission plan to include a description of planned NIH or other funding agency submissions
f. Literature cited (not included in the page limit)
g. Reporting plan/schedule that should last past the expiration date of the grant[1]

Please use 11-point Arial font with one-inch margins on all four sides. Write concisely and limit the amount of general background to the essentials that reviewers will need to be aware of and appreciate the proposed research. A list of current and pending support. Provide a listing of all current research support from all sources. For each source listed, please provide the following information: Name of funding source, title of project, project start/end dates, and amount of direct costs available (or available to you if a multi-PI grant), and percent effort. If you are a junior faculty member, please include the following details of your startup package in this list: amount initially provided, current unspent balance, and expiration date or other restrictions if any. An NIH style biosketch (https://grants.nih.gov/grants/forms/biosketch.htm) must also be included.

REVIEW PROCESS

Given that an important goal of CoBRE Centers is to enhance the odds of investigators obtaining NIH funding for their project(s), NIH review criteria and procedures will be used. Each proposal will be scored according to the five NIH criteria: Significance, Investigator, Innovation, Approach and Environment. For information on these criteria and procedures see NIH notices **NOT-OD-09-024** and **NOT-OD-09-025.**

It is anticipated that there will be two reviewers per proposal who will be selected to avoid conflict of interest.

The initial scientific review will be organized and provided by AIM. Prioritization of applications will be proposed by the AIM CoBRE Executive Committee in consultation with BioMT leadership. The final approval will be made by BioMT. Furthermore, final funding decisions will be made by the PIs of the two CoBRE Centers after joint discussion: Vojo Deretic, PhD at AIM and Dean R. Madden, PhD at BioMT. Note re approvals: If and when P20 funding is utilized, representatives of NIH/NIGMS must also approve all pilot award proposals prior to funding and commencement, otherwise while these pilots represent CoBRE initiatives

[1] In preparing the report, there is an initial report due 2 months after the conclusion of the funding (max 1/2 page narrative) but it is important to consider periodic reporting process that extends past these deadlines to capture future publications and grants resulting from this support. Also, please provide a plan/statement to cite P20s (CoBRE grants) that provided this support in publications.

if they are supported by unrestricted funds they do not require EAB and NIH program approvals.

CONDITIONS OF AWARD

IACUC or IRB applications must be submitted well in advance of the submission deadline, and approvals must be in-hand by the time of proposal submission. Awardees will be required to sign a memorandum of agreement as a condition of project funding. This memorandum will serve to indicate the recipient's willingness to:

1. Attend AIM and/or Bio-MT functions,
2. Take advantage of AIM and Bio-MT mentoring and support activities,
3. Participate in annual External Advisory Committee (EAC) meetings and program review for AIM and/or Bio-MT,
4. Cite AIM and Bio-MT and NIGMS in any publications stemming from their pilot project,
5. Present their work at any local or national meeting as requested, and
6. Submit an annual progress report (see

QUESTIONS

All questions on the AIM CoBRE pilot program or related to this announcement should be directed to Sally Ann Garcia (sangarcia@salud.unm.edu) in the AIM program office (505-272-2281) or to Mark R. Burge, MD (mburge@salud.unm.edu , phone 505-272-4658).

All questions on the Bio-MT CoBRE pilot program or related to this announcement should be directed to Dean Madden (Dean.R.Madden@dartmouth.edu) in the Bio-MT program office.