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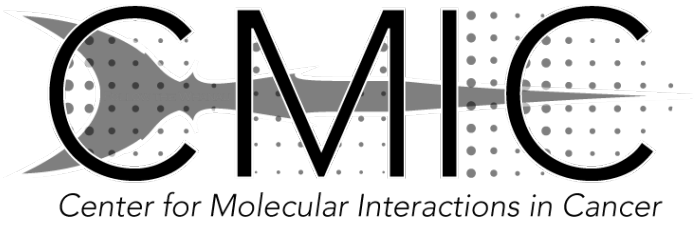

Request for Applications: Pilot Projects

Submission Deadline: June 15, 2024

Background

The objective of the Center for Molecular Interactions in Cancer (CMIC) is to use structural biology and quantitative biophysical approaches to conduct research aimed at understanding the molecular features of cancer, including initiation, progression, and treatment. The CMIC is funded through the NIGMS Centers for Biomedical Research Excellence (COBRE) award mechanism, which exists as part of the congressionally mandated Institutional Development Award (IDeA) program. This COBRE has funding available to support pilot projects for junior or mid-career faculty who would like to perform research that aligns with the scientific theme of the CMIC. For more information about the COBRE, please go to https://medicine.uams.edu/cmic/ or contact the Principal Investigator, Robert L. Eoff, PhD (rleoff@uams.edu).

Description of the Pilot Project Program

The CMIC Pilot Project Program provides up to $75,000 in direct costs for 1-year of support of basic or translational research projects that match the focus of the center. Two awards will be made annually. Funded pilot investigators will have access to the two CMIC Research Core facilities free of charge. Applicants are encouraged to take advantage of expertise available within other existing COBRE project teams and interact/collaborate with them. Funded COBRE pilot investigators will be required to participate in local, regional, and national COBRE and IDeA meetings, to give periodic progress reports when requested, and to submit a comprehensive final written report detailing studies performed and the findings.

Eligibility

1. The research project should be strongly focused on investigating molecular features of pathways or processes impacting cancer biology or therapy. Projects that plan to use the CMIC Research Cores (Structural Biology Core and Biomolecular Interactions Core) will be given priority. Basic science and translational projects are given equal priority. Projects must have clearly defined goals and outcomes to be competitive.
2. The applicant must have a PhD, MD, or equivalent degree.
3. Preference will be given to applicants who are early stage investigators in tenure track, with strong evidence of institutional support (designation of lab space, start-up funds, etc.), followed by young investigators with a clear path to obtaining an independent research position and mid-career faculty who are seeking a new direction for their research program.
4. It is important that applications indicate a clear path for subsequent extra-mural grant proposals for independent funding.

Projects that require performance of work at more than one institution will not be accepted. Third party sub-contracts are not allowed.

Applicants are highly encouraged to contact Robert Eoff (rleoff@uams.edu) to discuss eligibility and fit of the proposed research for the theme of the CMIC.

Application format

The application should include the following forms:

Form	Page Limit
NIH PHS 398 form – Face Page (https://grants/nih.gov/grants/funding/phs398/398_fp1.docx)	1 page
Project Summary	1 page
Specific Aims	1 page
Research Strategy	Up to 6 pages
NIH Biosketch for the PI and each of the key personnel (please use latest NIH biosketch (Non-Fellowship) format: https://grants.nih.gov/grants/forms/biosketch.htm	5 pages each
Budget Justification	No limit
Vertebrate Animals (if applicable)	No limit
Human Subjects and Clinical Trials Information (if applicable)	No limit

The **Research Strategy** should include a clear description of the major research objectives, methods used in the project, the expected results, and how successful completion will help the mission of the CMIC. A statement of plans for statistical analysis is required. The Research Strategy should include a statement of the relevance of the application to the focus of the CMIC. A brief description of the applicant's plan to obtain funding from data generated by the pilot award should be included.

Animal Studies: Institutional assurances (including review and approval by the UAMS IACUC) must be in place prior to funding if your project is selected. If animal studies are proposed, please be sure to include a completed NIH section "Vertebrate Animals" in the application (not subject to page limits).

Clinical Research: Institutional assurances (including review and approval by the UAMS IRB) must be in place prior to funding if your project is selected. If the use of human samples is proposed, please be sure to include a completed NIH section "Human Subjects and Clinical Trials Information" in the application (not subject to page limits).

Budget

There is a maximum of $75,000 in direct costs available for each project. Salary for the PI cannot be included in the budget.

Travel costs are only allowed for attending COBRE or IDeA meetings.

The following budget categories will not be supported: 1) equipment $5,000 or greater in cost; 2) patient care costs; 3) third party sub-contracts

Project Period: August 1, 2024 – July 31, 2025

Reporting Requirements

Pilot project awardees are expected to present their research at one of the semi-annual CMIC Advisory Committee meetings (preferably the in-person meeting) and provide a final progress report no later than 30 days after the end of the pilot project.

All publications resulting from work done with COBRE resources **must include an acknowledgement to NIGMS grant P20GM152281**. Any grant award received directly or indirectly as a result of COBRE support must be reported to Dr. Eoff immediately upon receipt.

Application Submission

The submission deadline is 5 PM, June 15th, 2024.

Applications should be submitted by e-mail to Robert Eoff (RLEOFF@UAMS.EDU). Electronic submissions are required. An application assembled into one PDF document is preferred. Late or incomplete applications, or applications not conforming to the page limits will not be reviewed.

Questions

For questions, please contact Robert Eoff, PhD (RLEOFF@UAMS.EDU). For a brief summary of CMIC Research Core services and instrumentation, please refer to the menus below.

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Structural Biology Core Services

Sample Preparation

Protein Expression and Quality Control

Technique & Applications	Instrumentation Available
• Bacterial protein expression • Insect cell protein expression • mamalian cell culture and protein expression • Sample homogeneity	• 3 Innova 44R shakers • Biosafety cabinet • 3 Multitron shakers with integrated CO_2 • 4 CO_2 incubators • NanoTemper Tycho NT.6

Protein Purification

Technique & Applications	Instrumentation Available
• Cell harvesting and lysis • Preliminary purification • Affinity chromatography • Ion-exchange chromatography • Size-exclusion chromatography	• Two Beckman JXN26 floor centrifuges • Avestin Emulsiflex • Akta Pure 25 L • Dedicated lab bench

X-ray Crystallography

Sample Crystallization

Technique & Applications	Instrumentation Available
• Crystallization screening • Crystallization optimization • Crystal harvesting	• Mosquto LCP • RockImager 1000 • Zeiss stereomicroscope

Data Collection, Structure Solution and Refinement

Technique & Applications	Instrumentation Available
• Evaluation of crystal diffraction • Collection of high-resolution diffraction data • Anomalous data collection • Phase determination • Model building & refinement	• 0.5 share SER-CAT: 2 tunable beamlines suitable for high-resolution and Se-Met • 2 Linux workstations

Cryo-EM

Specimen Preparation

Technique & Applications	Instrumentation Available
• Grid preparation • Specimen vitrification • On-site negative stain screening • On-site cryo-EM screening • Gradient fixation	• FEI TF20 • Vitrobot Mark IV • GloQube® Plus Glow Discharge System • Biocomp gradient station, fractionator, and flow cell • 3 Dry shippers

Data Collection, Structure Solution and Refinement

Technique & Applications	Instrumentation Available
• Single particle cryo-electron microscopy • Cryo-electron tomography • Particle selection and classification • Structure determination, classification, and refinement	• NIH National Centers for Cryoelectron Microscopy • NIH Service Centers for Cryoelectron Tomography • 4-GPU system • 600 TB storage server

Biomolecular Interactions Core Services

Size & Composition

Size-Exclusion Chromatography with Multi-Angle Light Scattering

Technique & Applications	Instrumentation Available
• Molecular Weight (<1 kDa-1 GDa) • Distribution of oligomeric states • Homogeneity of solution • Useful for a variety of biomolecules • Label free measurements in solution • Typically requires 10-100 µL sample at nM to µM concentrations	• Wyatt Dawn Heleos II light scattering detector • Wyatt Optilab T-rEX refractive index detector • Shimadzu HPLC with UV detector • ASTRA software

Mass Photometry

Technique & Applications	Instrumentation Available
• Molecular Weight (30 kDa-5 MDa) • Distribution of oligomeric states • Homogeneity of solution • Useful for a variety of biomolecules • Label free measurements in solution • Typically requires 5-20 µL sample at pM to nM concentrations • Single molecule analysis	• Refeyn Two MP + software

Dynamics & Equilibria

Isothermal Titration Calorimetry

Technique & Applications	Instrumentation Available
• Macromolecular & small-molecule binding analysis • Range of Kd = nM - mM • Enthalpy, entropy, thermal capacity, & stoichiometry • Label free measurements in solution • Typically requires ~300-500 µL sample at 10-1000 µM concentrations	• MicroCal PEAQ-ITC + software

Microscale Thermophoresis

Technique & Applications	Instrumentation Available
• Wide range of interactions (from ions to MDa complexes) • Range of Kd = pM - mM • Label free measurements in solution • Typically requires ~10-20 µL sample at pM to nM concentrations	• Nanotemper Monolith X + software

Circular Dichroism

Technique & Applications	Instrumentation Available
• Study secondary structures of biomolecules • Built-in Peltier temperature control for thermal stability studies • Label free measurements in solution • Typically requires ~100 µL sample at µM concentrations	• Jasco J1100 + SpectraManager software

Fluorescence Anisotropy

Technique & Applications	Instrumentation Available
• Robust analysis of interactions • Range of Kd = pM/nM - mM • Typically requires ~50-100 µL sample at nM-µM concentrations	• Biotek Synergy H4 + Gen5 software

Total Internal Reflection Fluorescence Microscopy

Technique & Applications	Instrumentation Available
• Visualization of single molecules • Rapid timescale dynamics • In vitro and live-cell options	• Olympus IX73 Two Deck with cellTIRF-1Line System + software