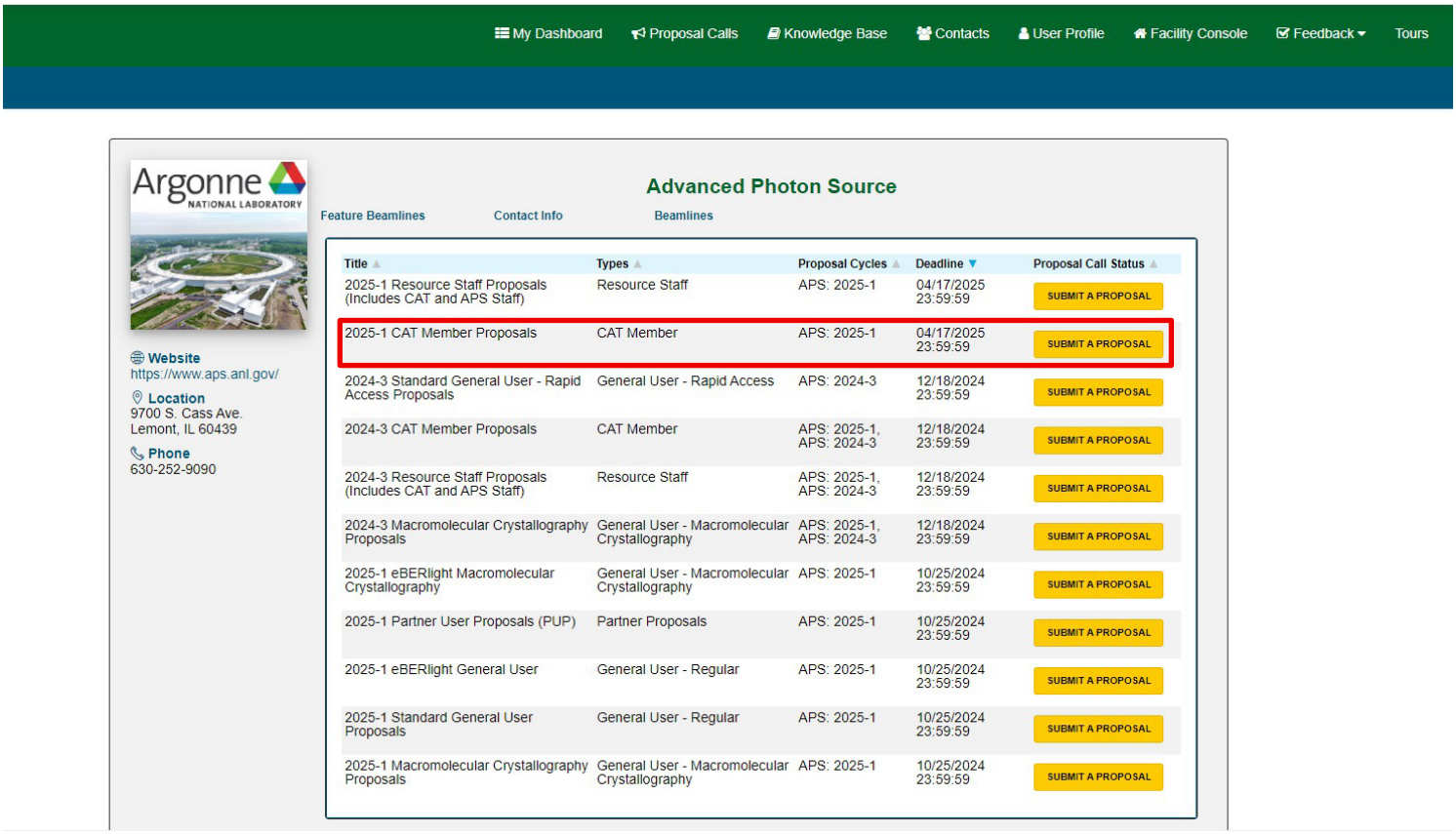
CAT Member Proposal questions

Dr. Renuka Kadivelraj
example template



Instructions

i) *indicates a required question; Other questions can be left blank
ii) Cyan highlights indicate Tab sections in submission form
iii) Yellow highlights indicate our suggested answers

Proposal Form Section

***Proposal Title** (*text entry*): The evolution and regulation of human UDP-glucose dehydrogenase

Proposal Call: (*populates automatically*)

***Proposal Type** (*select CAT Member*): CAT Member

***Primary Area of Research** (*select from dropdown, pick one*):

Biological and life sciences
Chemistry
Earth Sciences
Engineering
Environmental sciences
Instrumentation related to user facilities
Materials science
Medical applications
Optics (excluding x-ray optics)
Physics

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Polymers
Purchase of specialty service or materials
Other

Additional Area(s) of Research (*can pick multiple*):
Biological and life sciences
Chemistry
Earth Sciences
Engineering
Environmental sciences
Instrumentation related to user facilities
Materials science
Medical applications
Optics (excluding x-ray optics)
Physics
Polymers
Purchase of specialty service or materials
Other

***Keywords** (can pick multiple from list): Macromolecular Crystallography

***Please suggest the most appropriate review panel for your proposal** (*select from dropdown, pick one*):
CAT Member/Resource Staff proposals only

***Abstract** (text entry maximum 2000 characters, including spaces):

UDP-glucose dehydrogenase (UGDH) is a NAD-dependent oxidoreductase that synthesizes UDP-glucuronic acid, the metabolite required for glucuronidation which is the major detoxification pathway in the Phase II metabolism of drugs and toxins. The human enzyme (hUGDH) has evolved to display an atypical mode of allostery where the downstream, feedback inhibitor, UDP-Xylose (UDP-Xyl) binds in the active site of the substrate, UDP-Glucose (UDP-Glc), to inhibit and alter the conformation of the hUGDH hexamer from the active, E state to the inactive, E-Omega state. Our aim is to understand the allosteric mechanisms that control hUGDH and its analogs from other clades by studying the restructuring of the NAD binding (NB) and sugar binding (SB) domains. We have identified a distinct lineage of vertebrate UGDH variants that increase affinity for the inhibitor, UDP-Xyl, by conserving (i) a buried, unsatisfied threonine (Thr127; T-variant) and ii) an intrinsically disordered C-terminus (the ID-tail). We will examine the crystal structures of UGDH from Archaea, Bacteria and Eukarya to understand the evolution of the atypical allosteric mechanism of hUGDH. The long-term goal is to combine co-evolution analysis with protein engineering and functional studies to characterize these structural features.

Collaborator Names: To be added to an APS proposal (e.g., appear in the search list), a person must be a registered APS user with a badge number and an ORCiD listed in their APS registration record AND have logged into UPS and completed their UPS profile.
*Principal Investigator (PI) (*choose one from list*): Zachary Wood
Co-Principal investigator (Co-PI) (*choose one or more from list*)
Co-proposers (*choose one or more from list*): Renu Kadirvelraj

Funding Source(s) Section

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*__Funding Sources__ (*select one or more from the list below, related questions asked for each selection*): National Institutes of Health

__Funding Source Details__ (*not required but helpful*):

*__Grant Number__ (*required for ♦certain funding sources, see list*): RNIHX…..

*__Percentage__ (*total percentages must add up to 100% in order to be able to complete the section*):

♦ DOE, Office of Basic Energy Sciences (BES)
♦ DOE, Office of Biological and Environmental Research (BER)
♦ DOE, Office of High Energy Physics (HEP)
♦ DOE, Office of Workforce Development
♦ DOE, Other (includes LDRD)
Foreign
♦ Homeland Security
Industry
♦ National Aeronautics and Space Administration (NASA)
♦ National Institutes of Health (NIH): 100
♦ National Nuclear Security Administration (NNSA)
♦ National Science Foundation (NSF)
Other
♦ Other U.S. Government
♦ U.S. Department of Agriculture (USDA)
♦ U.S. Department of Defense (DOD)

Experiment Time Request Section

__Proposal number__ (*pre-filled by the system*)

*__Run Cycle__ (*choose one from available/offered dropdown*): APS 2026-3

*__1st choice resource__ (*choose one from available/offered dropdown*): 22-ID-D

*__1st choice instrument__ (*choose one from available/offered dropdown, offerings are based on the resource choice*): 22-ID-D Goniometer MD3 single axis (Arinax) with Eiger 16M detector

*__1st choice technique__ (*choose one from available/offered dropdown, offerings are based on the resource choice*): Macromolecular Crystallography

*__Shifts Requested This ETR__ (*text entry*): 7 (1 share = 3 shifts)

__Minimum useful shifts This ETR__ (*text entry*):

*__Lifetime Shifts Requested__ (*appears on first ETR only*): 7

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(Optional: 2nd choice resource, 2nd choice instrument, 2nd choice technique)

Additional Questions (for proposal type = APS CAT Member Proposal)

General:

***CAT Affiliation:** Select from drop down menu

- BIO-CAT
- DCS
- DND-CAT
- GM/CA-XSD
- HPCAT-XSD
- IMCA-CAT
- LRL-CAT
- LS-CAT
- MR-CAT
- NE-CAT
- SER-CAT

Affiliated institution: Select from drop down menu

- BIO-CAT affiliated institutions:
  Illinois Institute of Technology
- DCS affiliated institutions:
  Army Research Laboratory
  Lawrence Livermore National Laboratory
  Los Alamos National Laboratory
  Sandia National Laboratory
  Washington State University
- DND-CAT affiliated institutions:
  Dow
  DuPont
  Northwestern
- GM/CA-XSD affiliated institutions
  NCI
  NIGMS
  SAB
- HPCAT-XSD affiliated institutions

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Evans-LLNL

Gramsch-CDAC

Seagle-SNL

Somayazulu-HPCAT

Sturtevant-LANL

Yoo-SSAA

- IMCA-CAT affiliated institutions

  Abbvie

  Bristol-Myers Squibb

  Evotec

  Janssen

  Merck

  Novartis

  Pfizer

  Relay Therapeutics

- LRL-CAT affiliated institutions

  Eli Lilly and Company

- LS-CAT affiliated institutions

  Cayman Chemical Company

  Grand Valley State University

  Medical College of Wisconsin

  Michigan State University

  Northwestern University

  University of Illinois Chicago

  University of Michigan

  University of Wisconsin-Madison

  Vanderbilt University

  Wayne State University

- MR-CAT affiliated institutions

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ANL/CSE

ANL/ER

BP

EPA

IIT

ND

UF

UOP

- NE-CAT affiliated institutions

  Columbia University

  Cornell University

  Harvard University

  Massachusetts Institute of Technology

  Memorial Sloan-Kettering Cancer Center

  Rockefeller University

  Yale University

- SER-CAT affiliated institutions

  University of North Carolina at Chapel Hill

  University of Notre Dame

  University of South Carolina

  University of South Florida

  University of Virginia

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Amgen Inc.
Bayer
Center for Disease Control (CDC)
Duke University (Medical Center)
Emory University
East Carolina University
Georgia Institute of Technology
GlaxoSmithKline
MDAnderson Cancer Center (University of Texas)
National Institute of Health (NIH)
Rosalind Franklin University of Medicine and Science
Saint Jude Children's Research Hospital
Scripps Research Institute
University of Alabama at Birmingham
University of Arkansas College of Medicine
University of Georgia
University of Kentucky
University of Missouri Kansas City
University of North Carolina at Chapel Hill

***Will the data collected be considered proprietary (e.g., work that will not be made available in the open literature)?**

yes
no

***What mode(s) of access would you consider for this work? (Note: not all beamlines support all modes of access, choose all that apply.)**

Remote
Mail-in
On-site

***Is this research required for a student's thesis?**

yes
no

***Is this proposal related to another proposal?**

yes
no

If yes:
***What changes are being made to this proposal since the previous proposal submission?** (*text entry, 2000 characters including spaces*)

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*__Please indicate the related proposal number__. (*text entry*)

Safety:

*__Does this research involve the use of radioactive samples/materials, sealed sources, or x-ray generating devices?__

yes
no

If yes:
__Please indicate the type of radioactive material involved__ (*pick all that apply*):
--samples/materials
--irradiated materials
--sealed sources
--radiation generating devices (RGDs)

*__Does this research involve the use of any of the following__ (*pick all that apply*):
--explosives or energetic materials
--a new class 3 or class 4 laser that has not been approved by the Argonne Laser Safety Officer
--nanoparticles (one or more dimensions is 100 nm or less), including thin films, powder, and solutions
--samples/materials that require a BSL-2 (biosafety level) facility
--human subjects or human tissues, body fluids, or cells in culture
--plant pathogens, soil microbes, animals, insects, or insect/animal tissues, body fluids, matter, cells in culture
--none

APS Experiment Time Request (ETR) Questions

If you will require use of laboratory space during the requested scheduling period, provide details here. (*text entry, 2000 characters including spaces*)

*__Will you be bringing any electrical or hazardous equipment to the facility during this scheduling period?__

yes
no

If yes:
*__Please describe the equipment and its intended use__. (*text entry, 2000 characters including spaces*)

*__Would the work associated with this request for time involve any of the following (choose all that apply):__

- Pure gases (or single gas component) greater than 1.3 ft3, 36 L or 1 lb. (inert gasses excluded)
- Liquids greater than 5 gal. or 19 L
- Solids greater than 18.1 kg or 40 lbs.
- None of these apply

Preferred experiment dates for this request, enter date span(s) in format MM/DD/YYYY.

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Unacceptable experiment dates for this request, enter date span(s) in format MM/DD/YYYY.

Export Control Follow on ETR question (for ETR #s 2 or later only)

***By submitting this Experiment Time Request (ETR), I certify that the funding sponsor, proposal scope, and/or research samples/specimens have not changed since the original proposal was submitted.**

yes
no

If no:
If you answered "no" to the prior question, please describe the change(s). (*text entry, 2000 characters including spaces*)

Export Control/S&T Matrix Research Screening Questions

1) ***Are there any restrictions, contractually or otherwise, on public dissemination of the work (e.g., research, experiment) described in this proposal? Public dissemination includes presenting at conferences or open meetings, publications, or web source information**.
   yes
   no

2) ***Are you bringing any items (including specimens/samples), technical data, software, or services owned or funded by a nuclear, defense, military, space, intelligence agency, or a defense contractor of the United States or of another country?**
   yes
   no

3) ***For work (e.g., research, experiment) conducted at the user facility, are any items, technical data, software or services designed, developed, or modified exclusively for military applications, military training, spacecraft, launch vehicles, or national security or intelligence collection and analysis?**
   yes
   no

4) ***Would the research results be directly useful for- or would the research involve- a nuclear reactor application (e.g., commercial nuclear fuel, molten salts or other nuclear reactors, nuclear grade graphite, uranium enrichment)?**
   yes
   no

5) ***Are you bringing any items (including specimens/samples), technical data, or software to the user facility that require restricted access?**
   yes
   no

6) ***For DOE National Lab PIs or employees, please affirm that your research has been screened by your National Lab against the DOE "Science and Technology Risk Matrix" critical**

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and emerging research areas and technologies. Note: If no or unsure, you should contact your home institution's office responsible for screening research for the DOE S&T Risk Matrix. The User Facility must be consulted to determine if research restrictions can be accommodated.

Yes, I affirm my work has been screened
No, my work has not been screened
I am not a DOE national lab PI or employee