



Open Proposal Grant Program

Synopsis: The Johns Hopkins University School of Medicine - Neurofibromatosis Therapeutic Acceleration Program (NTAP) supports research projects designed to accelerate development of effective treatments for NF1 associated pre-malignant peripheral nerve sheath tumors (e.g., Cutaneous neurofibromas, Plexiform neurofibromas, and Atypical neurofibromas) and on preventing the progression to malignant tumors through the Open Proposal Program.

Key Information about the Open Application Program:

1. Eligible Investigators - Any investigator (regardless of their location or primary research focus) who has a proposal related to NF1 associated peripheral nerve sheath tumors including cutaneous neurofibroma, plexiform neurofibroma and atypical neurofibroma (also called atypical neurofibromatous neoplasms of uncertain biologic potential, ANNBP) and a professional position that supports the effective execution of the proposed project is eligible.
2. Timeline - There is no deadline to apply for Open Applications. The Open Proposal Program reviews applications on a rolling basis throughout the year.
3. Project period – There is no set time frame for the project period. Rather, the investigator should propose a time period that reflects maximal efficiency for the project and deliverables proposed. Many Open Application projects are 2-3 years, however, shorter or longer project periods can be supported with the appropriate justification.
4. Budget
 - a. There is no limit for direct and total costs but the direct costs should be appropriate and well justified to perform the proposed research. Opportunities to leverage NTAP support or planned submissions for follow-on funding should be presented.
 - b. NTAP supports investigators' salary within the limits of the NIH salary cap (https://grants.nih.gov/grants/policy/salcap_summary.htm).
 - c. NTAP supports indirect costs at a maximum of 10% of direct costs.
 - d. NTAP supports the effort fee for key data upload to Synapse and annotation of the uploaded data up to \$10,000 per project based on the type and amount of data to be generated.
5. Funding model – NTAP uses a milestone and deliverable based funding model. If a proposal is selected for funding the investigator is asked to finalize a milestone and deliverable schedule. Each milestone has a budget amount associated with it. Payment is made by NTAP to the investigator/institution based on evidence that the milestone has been completed.
6. Data sharing policy – A core mission of NTAP is the open and timely sharing of results (<http://www.n-tap.org/mission-statement/>). As such, all NTAP funded investigators are required to upload key raw data to the Sage Bionetworks' Synapse Platform. All data uploaded onto Synapse is confidential and visible only to the contributing investigators, NTAP leaders and limited Sage staff until it is ready to be shared with designated collaborators or released to the public with permission of the investigative team after the period of embargo (generally 18 months from the end of project).

7. Application - All applications, review processes, and post-award management procedures are done through ProposalCentral (PC).
<https://proposalcentral.com/GrantOpportunities.asp?GMID=229>.
- To start the application, please log in to PC via the link above and select “Apply Now” in the row entitled “Open Proposal Grant Program.”
 - Please follow the PC directions for each section completing each as thoroughly as possible (see Appendix A and D below).
 - The Open Proposal Grant Program proposal is limited to 5 pages total for the sections including: background, hypothesis & rationale, specific aims, preliminary data, experimental design, project goals and anticipated timeline. This brief application format is intended to focus the application on core information and enable rapid peer review. Additional details requested by reviews will be conveyed to the investigator(s) during the review and decision process.
 - For questions about using the PC system - Please check the online “help” or contact customer service link in the top right corner of PC page, email (pcsupport@altum.com) or call (1-800-875-2562).
 - For questions about the contents of the application, please email (info@n-tap.org) to the NTAP.
8. Review – The submitted proposals are internally reviewed for synergy with the NTAP mission and ongoing initiatives (<http://www.n-tap.org>). Proposals of interest to NTAP leadership are referred for additional peer review by members of the NTAP Scientific Advisory Board and appropriate experts. All submitted materials are reviewed within NTAP’s strict confidentiality guidelines. Detailed outcomes of the review including quantitative and qualitative assessments are shared with investigator(s).
9. Decision – Investigators will be notified of the outcome of the review as soon as feasible, but no later than two months after submission.
- The outcome of the review may include: (1) agreement to fund the proposal without changes, (2) acceptance of some portions of the proposal, but not others, (3) agreement to fund the proposal after appropriate revisions, (4) declining to fund the proposal. Commonly, reviewers ask for additional details, clarifications or revisions based on key critiques through the review process and before the final decision for funding is made. The goal is to maximize the likelihood of success for each proposal via a collaborative process with the investigative team.
10. Information about previously funded Open Proposals can be found at the NTAP website:
<http://www.n-tap.org/apply-for-funding/open-proposals/>

Thank you for your interest to the Open Proposal Grant Program. We are excited to work with you to accelerate development of effective therapeutics for NF1 associated pre-malignant peripheral nerve sheath tumors.

Appendix A: Detailed instructions for applying for the NTAP Open Proposal Grant Program via ProposalCentral

1. Go to <https://proposalcentral.com/> and login under the “Applicant or Awardee” section. If you do not have an account, please click “Need an account?” or refer to the “How to Register as a ProposalCentral user” tutorial.
2. Click the gray Grant Opportunities tab in the upper right.
3. Select the grant maker you’re looking for (e.g., JHU-NTAP---Neurofibromatosis Therapeutic Acceleration Program) from the drop-down menu at the top of the page. Alternatively, type “Open” in the Search box.
4. To download the instruction of Open Proposal Grant Program, click document symbol next “Open Proposal Grant Program.”
5. To start the grant application, click “Apply Now.” You can also download the instruction of Open Proposal Grant Program by click “Program Guidelines” once the application has opened.
6. Please follow the ProposalCentral directions for each section completing (section #1 - #11) as thoroughly as possible.
7. Once the application has opened, select “Open Program” under “Choose sub-program.”
8. Enter a project title. Do not exceed 200 characters.
9. Select “Yes” or “No” under “Resubmission” section
10. Click a save button.
11. You can now navigate to any section with the proposal to add data and/or files and review the information.
12. Click the “Validate” button to check for any missing required information or files.
13. After you complete all the proposal sections, click one of the Print buttons below to open and print the cover/signature pages and application files.
14. To submit your Proposal, please click the “Submit” button.

Appendix B: The documents including proposal (scientific strategy) should be uploaded as PDF or Word document attachments to the application workspace in ProposalCentral. The proposal components are:

1. Title of Project (Do not exceed 200 characters)
2. Name of primary investigator (PI) and key investigators
3. Abstracts (for a technical audience and a brief lay summary) (Do not exceed 3,000 characters including spaces)
4. **Letter of introduction and summary of changes if a resubmission (3 pages maximum)**
5. Proposal (maximum 5 pages): Outline of proposed scientific strategy; typewritten, single-spaced in typeface no smaller than Arial 11-point and 0.5" margins.
 - a. Background
 - b. Hypothesis & Rationale
 - c. Significance
 - d. Specific Aims
 - e. Preliminary Data
 - f. Experimental Design
 - g. Project Goals
 - h. Anticipated Timeline
6. Citations or References (no page limit)
7. Proposed Scope of Work (refer to sample in Appendix C below)
8. Proposed Milestones/Deliverable Schedule relative to the Budget (refer to sample in Appendix C below)
9. Budget and Budget Justification (maximum 4 pages) (refer to sample in Appendix C below)
10. Other support of applicant and key personnel (refer to sample in Appendix D below)
11. NIH Biosketch for primary investigator(s) and all key personnel
12. Support letters (as needed)

Appendix C: Example of Exhibits (Scope of Work, Milestone/Deliverable Schedule, Budget and Budget Justification)

TITLE: Transition to 5D and Sun screening of plexiform neurofibroma models in 96-well format

PI: Jane Doe, Ph.D. (State University)

Exhibit A: Scope of Work (Statement of Work)

I. Scope of Work

INSTITUTION has performed an initial library screen of compounds against plexiform neurofibroma (PN) cells growing on 1536-well plates using Dark-n-Glo to assay proliferation. One surprising and interesting result from that work is that there is a group of compounds that show altered response in cells that express DGDP.

INSTITUTION X has shipped a set of 20 selected compounds to State University with the expectation that we will perform 5D and Sun Screen assays of the results from the initial screens. We believe that this collaborative approach will both provide important scientific knowledge and practical application. The latter will result from the development of a 96-well format Dark-n-Glo assay procedure that will be useful for general confirmatory testing. We expect that these results should directly reproduce those of the initial screen, i.e., that the outcome is independent of the platform (1536-well vs. 96-well) or performance site (INSTITUTION X vs. State University). Further, we will begin transition to a 5D culture, 96-well format assay that we predict will advance from confirmation to a sunscreen of initial results. We hypothesize that cells growing in 5D matrices, as compared to those growing in 2D on plastic, will exhibit drug sensitivity that is a better predictor of eventual clinical effectiveness.

The primary goals are: (1) To perform an initial sunscreen assay of 20 compounds (selected and provided by INSTITUTION X) against PN cells in a 96-well format, and (2) To establish a secondary screening protocol of 5D PN cell cultures in a 96-well format to assay 20 compounds (selected and provided by INSTITUTION X).

II. Project Goals

The project goals are...

III. Specific Aims

Aim 1: Test...

Aim 2: Determine...

Exhibit B: Milestones/Deliverables & Payment schedule

Milestone 1 (Month 6, January 1, 2025 – June 30, 2025) – \$19,050 (total budget)

1. Establish Dark-n-Glo assay in 96-well format at State University to provide confirmatory sunscreen assay for results from INSTITUTION X.
2. Define efficacy and potency for 20 selected compounds against PN cells.

Milestone 2 (Month 12, July 1, 2025 – December 31, 2025) – \$19,050 (total budget)

3. Establish Dark-n-Glo assay in 96-well format with 5D culture conditions to provide transition to a secondary screen for initial hits.
4. Define efficacy and potency for 20 selected compounds in 5D cultures of PN cells.

Exhibit C: Budget & Budget Justification (for January 1, 2025 – December 31, 2025)

I. Budget

Personnel

Richard Roe (Technician)(40% effort) \$15,892

SUBTOTAL: \$15,892

Supplies

Cell Culture Supplies \$7,350

96-well Dark-n-Glo assay Supplies \$9,390

SUBTOTAL: \$16,740

Equipment

Eppendorf 5430R (centrifuge w/ buckets) \$3,878

SUBTOTAL: \$3,878

Publication Costs

Standard fees, applicable \$1,500

SUBTOTAL: \$1,500

Data upload and annotation

\$2,500

SUBTOTAL: \$2,500

TOTAL due (Direct Costs): \$40,510

TOTAL due (10% maximum indirects): \$4,051

GRAND TOTAL: \$44,561

II. Budget Justification

Personnel (\$15,892)

Mr. Richard Roe is an experienced cell culture technician who has become familiar with the culture of the PN cell models, including in 5D. He will commit 40% of his effort to complete the work on this project. Budget request: \$12,553 salary; \$3,339 fringe benefits

Supply Costs (\$16,740)

Cell culture supplies: (Note: Cell culture supply costs have been extrapolated from those incurred so far on this project) media, serum, tissue culture plastic, reconstituted basement membrane, medical gases; sub-total= \$7,350

96-well Dark-n-Glo assay supplies: (Note: costs in 96-well format estimated from scaling the A MYSTERY INSTITUTION standard protocols), Greiner Bio-One 96-well assay plates, Dark-n-Glo reagent, 2 multi-channel pipettors and racked repeater tips; sub-total=\$9,390

Equipment Costs (\$3,878)

We will need a refrigerated centrifuge that can accommodate 96-well microplates to generate even coating of reconstituted basement membrane for transition to 5D cultures. The State University Office of Vice-President for Research has committed more than half (\$4,290) toward the cost of this necessary equipment to support our efforts and to reflect that we expect the equipment to be useful beyond the term of the supplementary project.

Eppendorf model 5430R: refrigerated centrifuge with conventional rotor and swinging bucket rotor for 96-well microplates, quote price \$8,168 less institutional commitment of \$4,290.

Publication Costs (\$1,500)

We expect to publish the results of this project and request funds to partially offset the costs associated with doing that.

Data upload and annotation Costs (\$2,500)

The costs are for the efforts of key data upload to Synapse and annotation for the uploaded data.

Appendix D: Instruction & Example for Other Support of lead investigator and key personnel

Provide active support for all key personnel (PI(s), Co-Investigator(s)). Other Support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards. Training awards, prizes, or gifts do not need to be included. Please specify any existing or pending support that has any scientific or budgetary overlap with the NTAP proposal responsive to this RFA. Please specify the plan to address any potential areas of overlap identified.

There is no "form page" for other support. Information on additional support should be provided in the *format* shown below, using continuation pages as necessary. Include the principal investigator's name at the top and number consecutively with the rest of the application. The sample below is intended to provide guidance regarding the type and extent of information requested.

Sample

DOE, JANE

ACTIVE

2 R01 NC 00000-13 (Doe) 03/01/2020 – 02/28/2025 3.60 calendar

NIH/NCI \$186,529

New therapy development for cutaneous neurofibromas

The major goals of this project are to define the effect of Selumetinib on peripheral nerve tumors in children with NF1

PENDING

CTF 950000 (Anderson) 07/01/2024 – 11/30/2027 2.40 calendar

Children's Tumor Foundation \$82,163

Drug screening of plexiform neurofibroma models in 96-well format

The major goals of this project are to identify FDA approved drugs on plexiform neurofibromas *in vitro* cell culture models

Role: Co-Investigator

OVERLAP

There is scientific overlap between aim 2 of NIH/NCI and aim 1 of the application under consideration. If both are funded, the budgets will be adjusted appropriately in conjunction with agency staff.