Open Proposal Grant Program

Synopsis: The Johns Hopkins University School of Medicine - Neurofibromatosis Therapeutic Acceleration Program (NTAP) supports research projects designed to accelerate the development of effective treatments for NF1-associated pre-malignant peripheral nerve sheath tumors (e.g., cutaneous neurofibromas, plexiform neurofibromas, and atypical neurofibromas, also called atypical neurofibromatous neoplasms of uncertain biologic potential, ANNUBP) through the Open Proposal Program.

Priority research areas and **explicit exclusions:**
NTAP funds a focused, translational portfolio aimed at turning NF biology into meaningful therapies. Historically, funded projects cluster around several complementary areas: preclinical target identification and validation, small-molecule and biologic drug discovery and optimization, development of patient-derived and genetically engineered models for drug screening, biomarker development, and pharmacodynamic assays to support clinical translation. NTAP funding has emphasized projects positioned for rapid IND-enabling studies or early-phase trials, collaborative and open-data approaches to accelerate reproducibility, and work addressing unmet clinical needs in tumor control, neurological dysfunction, and pain in people with NF1 and cutaneous neurofibromas (cNF), plexiform neurofibromas (pNF), and atypical neurofibromas (aNF) or ANNUBP.

Moving forward, NTAP will focus its investment via the Open Proposal Program to address gaps in:

- Therapeutic target identification for cNF, pNF, aNF/ANNUBP
- Prevention of cNF, pNF, and aNF/ANNUBP tumor formation or progression
- Disease pathogenesis and mechanism studies for cNF, pNF, and aNF/ANNUBP
- IND-enabling studies for therapies being developed for cNF, pNF, and aNF/ANNUBP
- Early diagnosis/detection technologies for cNF, pNF, and aNF/ANNUBP
- Artificial intelligence applied to biomarker data (imaging, tissue, circulating markers, genetics, and genomics) for cNF, pNF, and aNF/ANNUBP
- Population science for cNF, pNF, and aNF/ANNUBP
- Symptom management for cNF, pNF, and aNF/ANNUBP.

Priority research areas for the NTAP Open Proposal Program include:

- Novel biology of NF1-driven cNF, pNF, and aNF/ANNUBP tumors that will lead to new or augmented therapies
    - Fund: New projects related to the pathogenesis and mechanism or tumorigenesis, including cancer neuroscience framework for translational studies
- IND-enabling translational drug development for therapies targeting cNF, pNF, and aNF/ANNUBP
    - Fund: Novel target development beyond or building on the MAPK/MEK pathway, target validation studies, next-generation therapies or combination approaches,

medicinal chemistry, ADME/PK, formulation, GLP toxicology, and IND-enabling studies for NF1-relevant targets or repurposed agents with preclinical efficacy.
- Tumor microenvironment and non-oncologic symptom management relevant to cNF, pNF, and aNF/ANNUBP
    - Fund: Mechanistic and translational studies into tumor–nerve interactions, immune and stromal contributors to cNF, pNF, and ANNUBP formation and progression.
- Adult NF1 & lifespan research relevant to cNF, pNF and ANNUBP
    - Fund: prevention of malignant transformation, survivorship, epidemiology, and real-world outcomes.

Explicit exclusions for the NTAP Open Proposal Program:

- Large multi-site clinical trials
    - However, awards may support a defined component of an already funded large-scale clinical therapeutic trial.
    - Opportunities for NTAP direct support of large clinical trials may be considered separately from the Open Proposal Program via conversations with NTAP leadership.
- Basic discovery projects without a clear translational path or defined milestones toward clinical readiness.
- Projects that duplicate current NTAP or major NF1 funder programs unless the proposal clearly addresses a gap in the existing or prior initiatives (examples include organoid development, gene therapy, new cell lines, new mouse models).
- Generalized sequencing studies (or other “omic” studies) without a clear translational objective (e.g., sequencing alone without a path to diagnostic or therapeutic target identification and validation).
- Projects that are focused on NF1 manifestations not directly related to cNF, pNF, and aNF/ANNUBP.
- Projects focused on NF2-SWN or the other forms of schwannomatosis.
- Projects that lack patient engagement or fail to include appropriate patient-centered endpoints when relevant.
- NTAP deeply values, supports, and participates in private-public partnerships regularly. These agreements are arranged collaboratively and honor NTAP’s core requirements for reasonable data sharing/reporting and feasible return on investment if the project funded by NTAP contributes to a commercially viable product.

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 cNF, pNF, aNF/ANNUBP, and a professional position that supports the effective execution of the proposed project is eligible.
2. Timeline - There are two cycles within which to apply for the Open Proposal Program. The due date for the letter of intent (LOI) is March 31 (cycle I) and July 31 (cycle II). LOIs will be reviewed by NTAP leadership to ensure eligibility and suitability for NTAP’s areas of focus as defined above. Feedback about the LOI will be provided to the corresponding investigator. The due dates for the full proposal application are April 30 (cycle I) and August 31 (cycle II). The decision notification date is July 20 (cycle I) and November 20 (cycle II).

	Cycle I	Cycle II
LOI Due Date	March 31	July 31
Application Due Date	April 30	August 31
Notification of Decision	No later than July 20	No later than November 20
Project Start Date	No later than December 1	No later than April 1

3. Project period – There is no fixed project period; investigators should propose a timeline that reflects the most efficient approach for achieving the proposed aims and deliverables. Projects may be supported for up to a maximum of 3 years. A detailed justification for the feasibility and the necessity of the proposed timeline for the study is required.
4. Budget
    a. NTAP's annual calendar year-based budget for the Open Proposal Program is $700,000/year across all Open Proposal Program projects. This can be allocated across several smaller projects, 2 mid-sized projects, or one larger project.
    b. NTAP supports investigators' salary within the limits of the most current NIH salary cap (https://grants.nih.gov/grants/policy/salcap_summary.htm).
5. NTAP will support indirect costs at a rate not to exceed 10% of direct costs per NTAP policy.
6. 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.
7. 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 (generally after a period of embargo, such as 12 months from the end of the original project period).
8. Application - All applications, review processes, and post-award management procedures are done through ProposalCentral (PC). (https://proposalcentral.com/ProposalGI.asp?SectionID=15052&ProposalID=-1) Investigators who are interested in submitting a proposal should read the requirements of funding (Appendix 1). If in agreement with all NTAP policies, please submit a letter of intent (LOI) by midnight EST on March 31 (cycle I), or July 31 (cycle II) (see Appendix 2). NTAP will invite full applications from approved LOI applicants. LOI is used to ensure eligibility and feasibility as well as to identify reviewers needed to enable rapid review and decision making after submission of the full proposal.
    a. If invited to submit a full application, please log in to PC via the link above and select "Apply Now" in the row entitled "Open Proposal Grant Program." Instructions for the full application are listed for reference in Appendix 2 and will be provided to investigators when invited to submit a full proposal.
9. Review – The LOI is internally reviewed for synergy with the NTAP mission and ongoing initiatives (http://www.n-tap.org). When a proposal is considered to be a good fit for the NTAP Open Proposal Program by NTAP leadership, the submitting PI will be contacted and asked to prepare and submit a full proposal. The full proposal will be again reviewed by NTAP leadership and then sent for peer review by a minimum of three independent, content expert reviewers. All submitted materials are reviewed within NTAP's strict confidentiality guidelines.

Detailed outcomes of the review, including quantitative and qualitative assessments, are shared with investigators.

10. Decision – Investigators will be notified of the outcome of the review by July 20 (cycle I), or November 20 (cycle II).
    a. 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 revisions, or (4) declining to fund the proposal. Commonly, in the review process the 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 of this process is to maximize the likelihood of success for each proposal via a collaborative process with the investigative team.
11. Project start date – The awarded project's start date is determined collaboratively between the applicant and their institution and Johns Hopkins University/NTAP. Broadly, NTAP suggests the project start dates of: December 1 (cycle I), or April 1 (cycle II).
12. 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 in the Open Proposal Grant Program. We are excited to work with you to accelerate the development of effective therapeutics for NF1-associated pre-malignant peripheral nerve sheath tumors.

Appendix 1: NTAP Policy

Data sharing policy:
A core mission of NTAP is the open and timely sharing of results (http://www.n-tap.org/mission-statement/). i.e., FAIR (Findability, Accessibility, Interoperability, Reusability) principles of key data (raw data, processed data). As such, all NTAP-funded investigators are required to identify and upload key data (raw data, processed data) to the Sage Bionetworks' Synapse Platform via the NF Portal. All data uploaded onto Synapse is confidential and visible only to the contributing investigator team, 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 investigator team after the period of embargo (generally 12 months from the original project end date).

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. NTAP is amenable to changes in the milestones or the deliverables throughout the award period, but these must be discussed with and approved by NTAP leadership and consideration must be made for the previously agreed upon timeline and budget.

Appendix 2: Detailed instructions for applying for the NTAP Open Proposal Grant Program via ProposalCentral

The submission of the Letter of Intent and full application is done through the ProposalCentral (PC) portal.

If you do not have a PC account, please use the following link to create an account Register.
Once you have created an account, you will receive an email with a confirmation number.
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).

Letter of Intent (LOI):
LOI is used to ensure eligibility and feasibility as well as to identify reviewers needed to enable rapid review and decision making after submission of the full proposal.
To start the LOI submission, please click HERE.

Please follow the PC directions for each of the required sections.

1. Title Page - Project title: Do not exceed 200 characters
2. Applicant - Principal Investigator (name, institution, ORCID, email address, phone number, etc.)
3. Lead Institution (for potential contract negotiation)
4. Key Personnel/Collaborators (name, institution, role, email address, phone number)
5. Proposal Attachments - Upload the following documents
    a. LOI document (maximum 3 pages) – Please include the following sections: Background/Rationale/Hypothesis, Specific aims, Broad schema of the experimental design and approaches, including any special techniques, expected outcomes/knowledge to be generated.
    b. One page for overview of total budget and summary of justification of the budget, expected timeline to achieve all stated goals (preferred in deliverable, tabular or GAANT chart format).

The LOI must be submitted by **midnight Eastern Standard Time on March 31 (cycle I), or July 31 (cycle II).**

Full Proposal:
Once your Letter of Intent is approved via a written letter by NTAP leadership, please access the full proposal by clicking the identifier number on your Home tab on PC. Please follow the ProposalCentral directions for each section, completing as thoroughly as possible.

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

1. Title Page - Project title: Do not exceed 200 characters
2. Download Templates & Instructions
3. Enable Other Users to Access this Proposal
4. Applicant - Principal Investigator (name, institution, ORCID, email address, phone number, etc.)
5. Lead Institution (for potential contract negotiation)

6. Key Personnel/Collaborators
7. Abstracts & Keywords – Abstracts are for a brief lay summary and a technical audience. Do not exceed 3,000 characters, including spaces, per abstract
8. Budget Summary
9. Organization Assurances – Human Subjects & Vertebrate Animals
10. Proposal Attachments: - Upload the following documents
    a. Letter of Introduction (maximum 3 pages): Summary of changes if a resubmission
    b. Proposal (maximum 5 pages): Outline of proposed scientific strategy; typewritten, single-spaced in typeface no smaller than Arial 11-point and 0.5" margins.
        i. Background
        ii. Rationale & Hypothesis
        iii. Gaps/Priority research areas
        iv. Project Goals
        v. Significance
        vi. Specific Aims
        vii. Preliminary Data
        viii. Experimental Design
        ix. Anticipated Timeline
    c. Citations or References (no page limit)
    d. Exhibit A: Proposed Scope of Work (refer to sample in Appendix 3 below) (no page limit)
    e. Exhibit B: Proposed Milestones/Deliverable Schedule relative to the Budget (refer to sample in Appendix 3 below) (no page limit). Instructions for Milestones/Deliverables are in Appendix 4 below.
    f. Exhibit C: Budget and Budget Justification (maximum 4 pages) (refer to sample in Appendix 3 below)
    g. Other support of applicant and key personnel (refer to sample in Appendix 5 below)
    h. NIH Biosketch for primary investigator(s) and all key personnel
    i. Letters of Support (as needed)
11. Validate - Click the "Validate" button to check for any missing required information or files.
12. Signature Page(s) – electronic signature for applicant
13. Submit - To submit your proposal, please click the "Submit" button.

NTAP uses a milestone and deliverable-based funding model. At the time of application, the investigator team is asked to provide a draft milestone and deliverable schedule relative to the requested budget and timeline provided in the Budget Period Detail and the Budget Justification. Each specific aim should be broken down into key milestones/deliverables with an associated timeline and budget. If a proposal is selected for funding, the investigator team may be asked to modify and then finalize the milestone and deliverable schedule based on reviewers' feedback and iterative discussions to ensure the research objectives can be met. Payment is made by NTAP to the investigator/institution based on evidence that the milestone has been completed. The milestones and deliverables are also used to identify key data elements to be uploaded to the NF Data Portal (a required element of NTAP funding).

The budget justification should provide a narrative explaining why all elements in the budget are required for the success of the project. The justification should address the specific role and percent effort of all personnel (for each year personnel effort is requested) and all non-personnel costs for the entirety of the project. Please also include justification for the anticipated timeline for project completion and the anticipated fluctuation of personnel or other costs over the life of the project, as

appropriate. Specific justification and quotes should be provided for any equipment being purchased, especially for the experiments in the proposal.

The maximum budget allocated to the Open Proposal Program annually is $700,000 across all funded projects. The requested budget and budget elements for each individual proposal must be very well supported by the budget justification. NTAP will consider (and may request) changes (increases or decreases) to the budget depending on changes in the scientific plan (and associated changes to the budget justification).

NTAP supports investigators' salary within the limits of the NIH salary cap (https://grants.nih.gov/grants/policy/salcap_summary.htm).

NTAP supports indirect costs at a maximum of 10% of direct costs.

NTAP will support budget costs for studies that are related to, but not funded by, other ongoing research efforts. There cannot be direct scientific or budgetary overlap between the NTAP proposal responsive to this program and any other projects active during the period of the award.

Appendix 3: Example of Exhibits document (Scope of Work, Milestone/Deliverable Schedule, Budget and Budget Justification, Payment Schedule, Data Sharing Plan)

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)

Please note, all of the text in this example is imagined and designed to give a sense of structure and level of detail desired in the Scope of Work. Investigators are asked to create Scope of Work specific to their project.

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.

II. Project Goals

The project 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).

III. Specific Aims

Aim 1: Determine the sunscreen effect of 20 selected compounds in PN cell lines
Aim 2: Establish a protocol for 5D PN cell culture

Exhibit B: Milestones/Deliverables & Payment Schedule

Please note, all of the text and estimated budget amounts in this example are imagined and designed to give a sense of structure and level of detail desired in the milestone/deliverable schedule. Investigators are asked to create milestone/deliverable schedules, timelines and budget amounts specific to their project.

Milestone 1 (0 months, April 1, 2026, $72,000)

1) Sign final contract
2) Register with Synapse and complete an orientation meeting with SAGE Bionetworks
3) Define key data elements and their associated annotations for data upload to Synapse

Milestone 2 (6 months, September 30, 2026, $72,000)

This milestone is about Specific aim 1:

1) Establish a 2D cNF cell culture model system for drug screening (Aim 1)
    - We will use four pairs of established cNF and immortalized cNF cells which are derived from human (two female, two male) cNF patients with NF1-/-
    - The cell proliferation will be assessed using MTS assay
    - The cell imaging will be molecular probes' Live/Dead assay
2) Identify effective compounds (i.e. cytotoxic to cancer cells but less toxic to normal cells) for cNF cell model and other cells such as Schwann cells, endothelial cells, fibroblasts. All these cells are derived from human cNF patients (female, male) with NF1-/- (Aim 1)
3) Submit and obtain approval IACUC for the proposed animal study
4) Create annotation language and submission of generated data to Synapse
    - Key raw data: cell proliferation assay, Live/Dead imaging
    - Key protocol of the experiment

Deliverables:

- IACUC approval
- Results of drug screening
- Upload key raw data to Synapse and annotate the uploaded data
- Upload key protocol to Synapse

Milestone 3 (12 months, March 31, 2027, $72,000)

This Milestone is about Specific aim 1 & aim 2:

1) Validate the identified compounds on the 3D cNF cell culture models (Aim 1)
    - We will use two pairs of established cNF and immortalized cNF cells which are derived from human (female, male) cNF patients with NF1-/-
    - We will use two human cNF derived induced pluripotent stem cells (iPSCs) which are derived from human (female, male) cNF patients with NF1-/-.
    - Establish an optimized 3D model using at least three different coating substances
    - Cell viability assay will be by CellTiter-Glo 3D Cell Viability Assay
    - Image data analysis using image analysis software (Aim 1)
    - Select the most promising compound(s) based on therapeutic effect on cNF cells and normal cells for *in vivo* study
2) Receive XXX cNF mice from a collaborator and establish colony at XXX. (Aim 2)
3) identify the maximal beneficial dose (and minimal effective dose of selected compounds *in vivo* (Aim 2)
    - We will use 12-month-old male and female XXX cNF mice (n=8-10 per group)
    - There are four groups (vehicle treatment, three different doses of compound)
    - We will measure the volume of tumors using an imaging device (IVIS, ultrasound, caliper) as the outcome of the study
4) Submission of generated data to Synapse
    - Key raw data: Cell viability assay, tolerability and toxicity in xxx cNF mice, maximal beneficial dose and minimal effective dose across the cohort and by sex
    - Key protocol of the experiment

Deliverables:

- Results of in vitro validation study
- Results of in vivo study
- Upload key raw data to Synapse and annotate the uploaded data
- Upload key protocol to Synapse

Milestone 4 (18 months, September 30, 2027, $72,000)

This Milestone is about Specific aim 3:

1) Gene expression analysis of top compound *in vitro* cell culture (Aim 3)
    - We will use two pairs of established cNF and immortalized cNF cells which are derived from human (female, male) cNF patients with NF1-/-. The gene expression will be compared between compound treated cells and vehicle control treated cells. For comparison, we will use Schwann cells derived from NF1-/- as well.
    - The dose and duration of the top compound treatment will be based on the result of Aim 1 study
    - We will perform RNAseq and single-cell RNAseq
2) Analysis of the gene expression (Aim 3)
3) Validate several gene expressions altered by compound treatment in the established cNF and immortalized cNF cells which are derived from human (female, male) cNF patients with NF1-/- (Aim 3)
    - Quantification of pMEK and MEK expression in cNF and immortalized cNF cells with or without compound treated cells using pMEK antibody
4) Submission of generated data to Synapse
    - Key raw data: RNAseq, single RNAseq, qPCR
    - Key protocol of the experiment

Deliverables:

- Results of gene expression analysis
- Results of validation study
- Upload key raw data to Synapse and annotate the uploaded data
- Upload key protocol to Synapse

Milestone 5 (24 months, March 30, 2028, $72,000)

This Milestone is about Specific aim 3:

1) Gene expression analysis of top compound *in vitro* cell culture (Aim 3)
    - We will use two human cNF derived iPSCs which are derived from human (female, male) cNF patients with NF1-/-. The gene expression will be compared between compound treated cells and vehicle control treated cells.
    - The dose and duration of the top compound treatment will be based on the result of Aim 1 study
    - We will perform RNAseq and single-cell RNAseq
2) Analysis of the gene expression (Aim 3)
3) Validate several gene expressions altered by compound treatment in two human cNF derived iPSCs which are derived from human (female, male) cNF patients with NF1-/- (Aim 3)
    - Quantification of pMEK and MEK expression in cNF cells with or without compound treated cells using pMEK antibody
4) Submission of generated data to Synapse
    - Key raw data: RNAseq, single RNAseq, qPCR

- Key protocol of the experiment

5) Submission of Close-out documents (Final Scientific Summary, Final Financial Report) to NTAP

Deliverables:

- Results of gene expression analysis
- Results of validation study
- Submission of closeout documents
- Upload key raw data to Synapse and annotate the uploaded data
- Upload key protocol to Synapse

Exhibit C: Budget & Budget Justification

Please note, all of the text and estimated budget amounts in this example are imagined and designed to give a sense of structure and level of detail desired in the budget & budget justification. Investigators are asked to create budget amounts specific to their project. You can upload a budget table (1 page) as an excel file and budget justification (up to 3 pages) as a word document to the ProposalCentral.

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	$3,000
SUBTOTAL:	**$3,000**

Modified Total Direct Costs (MTDC):	**$35,632**
10% maximum indirect:	**$3,563.20**
GRAND TOTAL:	**$43,073.20**

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 ($3,000)

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

Indirect Costs ($3,563.20)

Maximum 10% of modified total direct costs per RFA guidelines.

Ps) Data Sharing Plan section

When a project is awarded for funding, the principal Investigator is asked to fill the Data Sharing Plan section, which is one of the components of the Exhibits document during the negotiation stage. The Data Sharing Plan will be finalized after a consultation with NTAP leadership and the NF-OSI team.

Appendix 4: Instructions for Milestones/Deliverables section

1. Defining project milestones
   a. A **milestone** is defined by a task or set of tasks or experiments that yield a specific outcome (i.e. generation of a specific dataset or receiving IRB approval for a protocol) related to the specific aims of the research plan.
   b. Applicants must propose one or more milestones for each Specific Aim.
   c. Milestones are associated with a specific schedule and budget.
      - As such the more detailed and achievable the milestone or set of milestones is in a specific time interval, the better. The totality of achievements across the milestones should equate to the successful completion to the specific aims of the research plan.
2. Defining deliverables: **Deliverables** are any project-related output during the milestone period. Basically, the deliverables are the data elements to be generated (the “work product”).
3. Using milestones to oversee research progress
   a. Both NTAP team members and the investigator team will reference the milestones throughout the life of the award to both release the funds owed to the investigator team and to enable changes that may be required as the project proceeds.
      - It is anticipated that certain tasks will be completed at different time periods in the life of the project as laid out in the original milestone schedule for a project. However, NTAP is aware that both milestones and timelines change as new information is gained and will use the investigator defined milestones to adjust the schedule as needed with the guidance of the investigator team.
      - The more clearly stated a milestone and its associated budget is, the more readily the timeline can be revised.
   b. Investigators should have well defined milestones every 6 months of the grant period.
4. Key points for milestones
   a. Should be stated clearly and be related to the specific aims.
   b. Specify the timeline for each milestone.
   c. Realistic to be accomplished within a given milestone interval.
   d. Milestones do not have to be completed for payment to be made, but progress toward milestone completion must be clear and definite.
   e. The total budget can be evenly divided or distributed accordingly for the project milestone(s)
   f. Each Milestone should have the following if the milestones are involved in a quantitative study such as an animal or human sample study:
      - Provide methods, outcomes, data analysis (if the results are quantitatively measured), and deliverables
      - Specify the cell system or species being used for the planned experiment
      - Specify sex, age and number of animals for the planned experiments
      - Specify age, sex, number, ethnicity and race for clinical studies
      - Specify the readout(s) of the planned experiments
   g. Quantitative criteria should be robust and consistent with the state-of-the-art in the field. Most of the time, the quantitative criteria for success in the milestones will also be used to make go/no-go decisions, which should be specified.
   h. For animal or human sample study, please consider an institutional approval time
   i. Include collaborator(s) information for each milestone if the study will be performed at subaward site
   j. Different specific aims can be performed during the same Milestone period
   k. When particularly critical milestones are missed and/or the work will not be completed as originally proposed, payment is adjusted accordingly until the milestone is met.

l. After a project is awarded and contract agreement is completed (fully executed), the agreed milestone/deliverable schedule can be modified during the project period. In that case, the investigator can request NTAP leadership approval for the modification with explanation before the due date of milestone/deliverable schedule.

5. **Key raw data** are shareable and useful data for secondary data analysis for you or other researchers in the future. Please include the data file type and file number for each key raw data.

Definition of key terms (from Sage Bionetworks/NF Data Portal) in the Milestones/Deliverables section:

Key data: Particular data sets selected from a statement of work which fulfill one or more of the following criteria: (1) Dataset contains more than 20 samples in the dataset or generated from patient samples (N > 5) (2) Dataset contains data generated using high-throughput methods that output raw data presented in a widely used systematic format (3) Omics data derived from unbiased techniques (4) Dataset considered to be validation data for a new method (5) Dataset considered to be of interest to the funding partner.

Metadata: Metadata is additional, standardized information included alongside the data to give it context—*data about the data*, if you will. Metadata is what allows data in the portal to be searchable, discoverable, accessible, re-usable, and understandable to others, including those who were not involved in the data generation process.

Raw Data: Raw data is the initial, unmodified information collected directly from sources, not yet processed or analyzed. For instance, in biological imaging, it's often in .ome-tiff format, preserving all details and metadata from microscopy. In genomics, it typically appears as .fastq files.

For example, if you are sharing RNA-seq information, **raw data** would be the raw, fastq.gz files, **processed data** would be the aligned reads (.bam) or gene counts data, and differential expression analysis and volcano plots would be considered **results**. A single Western blot image is typically not key data, because it can be used to answer just a handful of questions, typically all related to the protein that was assayed, and it is difficult to combine this information with lots of other Western blots to create a resource that can be mined. On the other hand, a collection of 5 whole slide images of patient tumor sections would likely be key data, because there are lots of questions that could potentially be asked of the data that were not examined in the study that generated in the data.

Annotation: Annotation is the process of labeling your data files with terms from the NF Open Science Initiative (NF-OSI) dictionary. By adding clinical or experimental annotations, you will help make the data easier for others to find and understand things like: what type of data it is, what sort of experiment was performed, what type of biological system it came from, and what format the data is. Metadata/annotation is not a substitute for sharing protocols or methodology; it won’t help someone reproduce an experiment from scratch, but it will help them get a basic understanding of the nature of the data, and can be very helpful to people who aim to reuse the data (or even future you)!

Appendix 5: 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.

Appendix 6: Checklist

Ensure that all required documents are posted or uploaded as attachments to ProposalCentral. Please review the checklist below to ensure the items are addressed in your application package.

Letter of Intent

☐ Research Areas of Interest - double-check the Open Proposal Program instructions

☐ cNF ☐ pNF ☐ aNF/ANNUBP

☐ Eligibility – double-check the full criteria, listed in the eligibility section, before applying

☐ LOI Document (maximum of 3 pages)

☐ Budget Summary (maximum of 1 page)

Full Proposal

☐ Research Areas of Interest - double-check the Open Proposal Program instructions

☐ cNF ☐ pNF ☐ aNF/ANNUBP

☐ Abstract (for a technical audience)

☐ Abstract (for a general audience)

☐ Key words

Attachments:

☐ Letter of introduction and summary of changes (only for resubmission – maximum 3 pages)

☐ 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. Rationale & Hypothesis
c. Gaps/Priority research areas
d. Project Goals
e. Significance
f. Specific Aims
g. Preliminary Data
h. Experimental Design
i. Anticipated Timeline

☐ Citations or References

☐ Exhibit A: Scope of Work

☐ Exhibit B: Milestones/Deliverable Schedule

☐ Exhibit C: Budget and Budget Justification (maximum 4 pages)

☐ Other support of the applicant

☐ Other support for all key personnel

- ☐ NIH Biosketch for primary investigator(s)
- ☐ NIH Biosketch for all key personnel
- ☐ Letters of support (as needed)