NTAP Cutaneous Neurofibroma Request for Applications (RFA):
Biology and Therapeutic Development for Cutaneous Neurofibromas

Background and Overview

Cutaneous neurofibromas (cNF) are multicellular tumors involving the skin that are the hallmark of the tumor predisposition syndrome neurofibromatosis type 1 (NF1). They affect >90% of adults with NF1 and are a major source of emotional and social distress as well as intermittent but chronic physical pain and itching. cNF typically appear in adolescence and commonly increase in number over time. Although cNF are not predisposed to malignant transformation and are rarely associated with functional limitations, they are highly damaging to people with NF1 via their disfigurement, pain and itching. In adults with NF1, perceived disease visibility is significantly associated with depression, psychosocial distress, quality of life impairment and negative body experience for attractiveness and self-confidence. There are no known ways to prevent cNF from developing and current treatments are limited to local or regional procedure based approaches.

Major advances in therapeutics for NF1 associated plexiform neurofibromas, new preclinical models for cNF, enhanced understanding about the relationship between *NF1* and Ras, and the biology underlying cNF set the stage for acceleration of the next phase of discovery, leading to effective strategies to prevent and treat (stabilize or reduce) cNF in people of all ages and skin types. Experts with diverse expertise met and reviewed all available data pertinent to cNF and generated a list of priority areas to be the focus of cNF funding to accelerate the next era of discovery and therapeutics for cNF.

The Neurofibromatosis Therapeutic Acceleration Program (NTAP) is investing in cNF research via funding grant proposals focused on NF1 associated cNF. Areas of special interest include:

1. Investigate the processes underlying the stages of cNF initiation, progression, maintenance and senescence in general and via the following specific topic areas:
    a. Integrate multi-omic approaches such as single cell (RNA, DNA, etc.); epigenetics (e.g. ATAC seq); phosphoproteomics; metabolomics; temporal-spatial assessment strategies and cell-cell signaling analyses in human and preclinical cNF samples.
    b. Validate existing preclinical models and explore novel models (including co-cultures, assembloids, organoids) that predict human cNF behavior, accounting for age, sex, ethnicity and race.
        i. Including clinicopathologic studies across humans and preclinical systems (*in vitro* and *in vivo* models).
    c. Assess tumor microenvironment including neuronal components that contribute to cNF pathogenesis at all stages of cNF development (initiation, progression, maintenance and senescence).
    d. Investigate the *NF1* gene (or other genes that effect *NF1* function), neurofibromin structure and function, and cNF biology, including non-RAS pathway related functions as specifically related to cNF initiation, progression, maintenance or senescence.
    e. Investigate the contributions of paracrine or autocrine factors, cytokines, chemokines, collagens, hormones and other proteins to cNF initiation, progression, maintenance or senescence.
2. Identify and validate therapeutic candidates across the various stages and expressions of cNF in preclinical or clinical systems, including strategies focused on prevention of cNF.
    a. Identify candidate therapy-matched biomarkers for cNF.
3. Identify or validate non-invasive approaches in humans and preclinical systems for detection and assessment of change (growth or response) of cNF.
4. Define or validate key variables (i.e. patient or tumor specific characteristics) and endpoints for cNF clinical trials, including but not limited to:
    a. Develop reliable and sensitive metrics for assessment of cNF appearance

    b. Identify and validate biomarkers of treatment response or toxicity, including but not limited to circulating and tumor-specific markers and patient-specific prognostic markers of cNF course.
5. Develop the infrastructure for patient-driven engagement programs to enable registries and rapid enrollment into clinical trials for cNF.

When responding to each of these priority areas, the following considerations must be addressed in the proposal:

1. The goal of NTAP funded research is to relieve the substantial burden of cNF on affected individuals; hence, the potential for clinical translation and clinical impact considering the perspective of the patient and caregiver should be addressed in all proposals.
2. The cell system or species being used for a given experiment should be justified based on the strengths and limitations of the model or system relative to the question being asked.
3. Specify the readout(s) of the planned experiments.
    a. Of note, all NTAP funded projects require that the data associated with key endpoints are uploaded to Synapse on Sage Bionetworks (see below)
4. Age of the tumor and/or patient being investigated should be stated when feasible.
5. Sex should be included as a variable in all experiments, given the data regarding sexual dimorphism for cNF in animal models and possibly, in humans.
6. To the extent possible, the stage of the cNF being studied (initiation, progression, maintenance and senescence), type of cNF or growth pattern of the cNF to be studied should be described.
7. For therapeutic discovery studies:
    a. Investigators should be explicit about plans (i.e. specific pharmacokinetic and pharmacodynamic studies) to identify the maximal beneficial dose (defined as the most efficacious dose for tumor prevention or shrinkage without causing intolerable side effects) and minimal effective dose (not the maximal tolerated dose).
    b. Investigators should be specific about the target profile of the treatment (e.g. halting initiation or proliferation; activating senescence or supporting stability).
        i. Efforts should be made to identify anatomical factors (skin regions and types) influencing cNF biology and response to treatment.
8. In clinical studies, age, sex, ethnicity and race should be addressed and diversity of participants should be promoted to better understand potential heterogeneity in cNF biology and response to treatment.

Award Details

NTAP anticipates funding up to 15 awards via this initiative. Awards are anticipated to be for projects lasting from 12-36 months, but with appropriate justification, projects can be outside of this timeframe. The anticipated funding is $300,000-$1,000,000 per project, but projects can require funding above or below this range with appropriate justification. Budgets must be precisely explained and match the scope and focus of the planned investigations. Investigators can be from academia, government, or private sector, and international candidates are welcomed. Applications that include investigators across multiple fields and specialties are especially encouraged. Indirect costs are not to exceed 10% of the total direct funds, consistent with NTAP's long-standing policy.

Some of the stated areas of focus are best suited by multi-principle investigator studies and initiatives that require multiple laboratories to collaborate to address comprehensive project goals. If an investigator team chooses to pursue a multiple principle investigator/laboratory approach, they are expected to demonstrate within the application the critical contributions of each participating laboratory, the ability to coordinate across institutions efficiently, and the capacity to lead a multiple-laboratory effort effectively. Budgets are expected to be higher for such efforts, but as above, must be explicitly justified.

Some of the areas of cNF special interest may encompass studies associated with larger research proposals that were not adequately funded to permit experiments focused on cNF (i.e. clinical trials for plexiform neurofibroma where there is an opportunity to add endpoints focused on cNF). NTAP does support "add-on" studies focused on cNF that would be associated with independent but related research efforts that may be underway. If an investigator has a study to propose that falls into this category, adequate description of the overall "parent" project as well as justification of the specific cNF experiments that were not funded or considered for funding previously should be specified in the proposal section of the application.

For all applications advanced for funding, a member of the investigator team will be required to participate in an in-person "kick-off meeting" and intermittent virtual science meetings with all of the other funded investigators to discuss the scope of their projects and overlap across proposed milestones for each project to identify areas of potential collaboration. NTAP will support efforts to establish communication and support synergy between all funded investigators. Support for the time required for this effort will be included in the project agreements.

Application Review and Award Review Process

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 by **8/5/2022** at midnight EST. The letter of intent is used only to identify reviewers needed to enable rapid response to investigators after submission. The full application must be submitted via the ProposalCentral portal (see Appendix 2 for instructions to create a login if you do not have this already) by **9/2/2022** at midnight EST.

2. Proposals will be reviewed by a minimum of three independent reviewers. The review panel will include experts from within and outside of the NF1 field. Applications will be scored based on:
    a. Responsiveness to the priority areas
    b. Innovation of the scientific strategy
    c. The quality and feasibility of the methods and research plan
    d. Clarity of the experimental endpoints and deliverables
    e. Diversity of investigator team and expressed commitment, research environment and expertise of the investigator team.
    f. Clarity and appropriateness of budget and clarity of budget justification

    Projects that highlight collaboration across multiple areas of expertise and proposals from investigators new to NF1 research are encouraged.

    All reviewers will be under a confidentiality agreement with NTAP to ensure the privacy of ideas and data within applications. Investigators will be informed of the final decision for acceptance and funding by 11/7/2022. Please note that revisions based on reviewer comments may be requested in order to proceed to funding (inclusive of the research plan, scope of work, timeline/deliverables, and budget/budget justification exhibits) as part of the process.

3. Proposal acceptance:
    If a proposal is advanced for funding, the primary investigator will be required to travel to Baltimore, Maryland, to participate in an investigators' meeting on **December 2, 2022 (please plan for 10:00 am - 4:00 pm)**. Members of NTAP Leadership, a representative from each investigator team whose proposals were advanced for funding, and experts who participated in the review will be present at this meeting to discuss the scope and proposed milestones for each project and the overall research program goals. The purpose of this meeting is to establish communication between all funded investigator teams for this announcement and provide expert

technical feedback with the goal of minimizing overlap and maximizing the chances for success in identifying and understanding biological factors underlying the initiation and pathogenesis of cNF. Participation in this meeting is required.

The final research plan (the scope of work, budget and timeline) incorporating the details agreed to at the investigators meeting will be requested to be sent to NTAP by December 16, 2022. If the research plan is complete, funds will be available for release immediately upon completion of contract agreements with the investigators' institutions. A signed contract agreement between the primary investigators' institutions and Johns Hopkins University are required prior to funds being released and completed. An additional material transfer agreement (MTA) required if data and materials are expected to be exchanged between the primary investigator's institution and Johns Hopkins University. Applications must meet all of the NTAP conditions for funding (www.n-tap.org; Research Opportunities). Applying to this RFA will not preclude an application to NTAP for other projects. However, duplicate funding (from NTAP or any other source) for the specific proposal submitted via this RFA is not permissible.

4. Overall Timeline:

RFA Release Date:	4/27/2022
Letter of Intent Submission Deadline (to assist in the identification of appropriate reviewers):	8/5/2022 Friday, at midnight EST
Proposal Submission Deadline:	9/2/2022 Friday, at midnight EST
Notification of award:	11/7/2022
Investigator Meeting Date:	12/2/2022
Final Research Plan Due:	12/16/2022
Funds Available:	TBD (pending contract and MTA; goal is no later than 1/13/2023)

5. For Questions or Concerns, please contact:

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www.n-tap.org

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/). As such, all NTAP funded investigators are required to identify and upload key raw 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 18 months from the end of project).

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.

Appendix 2: Application (Letter of Intent, Full Proposal)

Letter of Intent (LOI): A LOI is required and is intended to assist NTAP members in building an appropriate reviewer panel to enable rapid, expert review of submitted proposals. The submission of LOI and full application is done through the ProposalCentral (PC) portal.
If you do not have a ProposalCentral 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).

1. To start the LOI submission, please click HERE.
2. Please follow the PC directions for each six required sections.
    a. Project title
    b. Principal Investigator(s) (name, institution, role, email address, phone number)
    c. Lead institution (for potential contract negotiation)
    d. Key personnel (name, institution, role, email address, phone number)
    e. LOI section (Type up to 4,200 characters with spaces)
        i. The LOI consists of a statement that outlines the proposed scientific strategy for the study (or studies) of interest. Please include the following elements in the LOI:
        ii. Rationale
        iii. Primary goal(s) of the project
        iv. Outline of the specific question(s) to be addressed
        v. Broad schema of the experimental design including any special techniques
    f. Select keywords or type in keywords
    g. Validate
    h. Submit

    The letter of intent must be submitted by **midnight Eastern Standard Time on August 5, 2022**.

Full Proposal: The submission of full proposal is done through PC.

1. Once your Letter of Intent is Approved, please access the full proposal by clicking the identifier number on your Home tab on PC.
2. Please follow the PC directions for each section completing each as thoroughly as possible.
    a. Project title
    b. Download templates & Instructions
    c. Enable Other Users to Access this Proposal
    d. Principal Investigator(s) (name, institution, role, email address, phone number)
    e. Lead institution (for potential contract negotiation)
    f. Key personnel (name, institution, role, email address, phone number)
        i. NIH format biosketch(s) for all key personnel
        ii. Other support of all key personnel (see Appendix 5)
    g. Abstracts: One for a scientific audience and one for a lay audience. Each up to 3,000 characters with spaces.
    h. Keywords
    i. Proposal

        There are three attachments to be uploaded in this section:

The proposal. This is an outline of the scientific strategy. It is limited to 8 pages (typewritten, single-spaced in typeface no smaller than Arial 11-point and 0.5" margins) for sections a-g below. It should be uploaded as a PDF document. The proposal components are:

- Background/Rationale
- Specific aims
- Preliminary data
- Experimental design and methods
- Project goals and key deliverables
- Anticipated impact for people living with NF1 associated cNF
- Anticipated timeline for successful project completion and impact to be realized

References/bibliography for the proposal.

Proposed Milestones/Deliverable Schedule relative to the requested Budget. NTAP uses a milestone and deliverable based funding model. 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 reviewer 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. This schedule is also used to identify key data elements to be uploaded to the NF Data Portal (a required element of NTAP funding). At the time of application, the investigator team is asked to provide a draft milestone/deliverable schedule relative to the requested budget and timeline provided in the Budget Period Detail (section 9) and the Budget Justification. An example of a milestone/deliverable schedule is provided in the Proposal Guidelines, Appendix 4.

j. Budget Period Detail: this is a line item budget of personnel and specific research costs
k. Budget Summary and Justification

The budget justification should provide a narrative explaining why all elements in the budget are requirement 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.

There is no required budget range, but the requested budget and budget elements should 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) before and after funding a proposal.

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 RFA and any other projects active during the period of the award.

l. Organization Assurances
m. Letters of Reference/Support
n. Validate
o. Signature Page(s)
p. Submit

It is possible that additional details, clarifications or edits will be requested by reviewers for the full proposal will be conveyed to the investigator(s) during the review, decision and project finalization 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@ntap.org) to the NTAP.

The full proposal is due at midnight Eastern Standard Time on **September 2, 2022**.

Appendix 3: Instruction for Milestone Driven Budget

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. 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.

3. 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.

Appendix 4: Example of Milestone/Deliverable Schedule relative to Timeline and Budget.

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.

Project period: 1/1/2023 – 12/31/2024

Specific aims

Specific aim 1: Perform a screening assay of 200 compounds (selected and provided by institution X) against cNF cells in a 96-well format.
Specific aim 2: Validate the top-performing compounds in *in vivo* models of cNF.
Specific aim 3: Investigate the mechanism of action of the top-performing compound *in vitro* cNF models to determine the optimal timing of dosing.

Milestones/Deliverables

Milestone 1 (0 months, January 30, 2023, $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, June 30, 2023, $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

Milestone 3 (12 months, December 31, 2023, $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

Milestone 4 (18 months, June 30, 2024, $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

Milestone 5 (24 months, December 31, 2024, $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

Appendix 5: Instruction for Other Support of lead investigator(s) 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.

Samples

DOE, JANE

ACTIVE

2 R01 NC 00000-13 (Doe) 03/01/2010 – 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) 07/01/2022 – 11/30/2023 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: Definition of the role of team members

NTAP defines the role of the team (Principal Investigator, Co-Principal Investigator, Multiple Principal Investigators, Co-Investigator, Collaborator, Consultant) as listed below and according to the NIH guideline. The roles of key personnel and collaborator should be stated in Letters of Support. If you are using Subawards, the applicants should create a formal agreement as well.

Program Director/Principal Investigator (PD/PI)
The individual(s) designated by the applicant organization to have the appropriate level of authority and responsibility to direct the project or program to be supported by the award. The applicant organization may designate multiple individuals as PD/PIs who share the authority and responsibility for leading and directing the project, intellectually and logistically.

Multiple Program Director/Principal Investigator
Multiple Program Director/Principal Investigator (multiple PD/PI) awards are an opportunity for multidisciplinary efforts and collaboration through a team of scientists under a single grant award. All PD/PIs share equally the authority and responsibility for leading and directing the project, intellectually and logistically. Each PD/PI is responsible and accountable to the applicant organization, or as appropriate to a collaborating organization, for the proper conduct of the project or program, including the submission of all required reports. The presence of more than one PD/PI on an application or award diminishes neither the responsibility nor the accountability of any individual PD/PI.

Co-Investigator(s)
An individual involved with the PD/PI in the scientific development or execution of a project. The Co-Investigator may be employed by, or be affiliated with, the applicant/recipient organization or another organization participating in the project under a consortium agreement. A Co-investigator typically devotes a specified percentage of time to the project and is considered senior/key personnel.

Collaborator(s)
Collaborators play an active role in the research, and they provide distinct expertise to complement the project but are not committing any specified measurable effort (person-months or percent effort) to the project. A collaborator is considered “other personnel”.

Consultant(s)
Consultants provide advice or services and may participate significantly in the research. They often help fill in smaller gaps by, for example, supplying software, providing technical assistance or training, or setting up equipment. List consultants as senior/key personnel only if they will contribute substantively and measurably to the scientific development or execution of a project.
Consultants do not receive a salary from the grant but may receive a fee.

Other significant contributors
Other significant contributors commit to contributing to the scientific development or execution of the project but are not committing any specified measurable effort (person-months or percent effort) to the project. Other significant contributors are typically listed in the application with "effort of zero person months" or "as needed."