



NEUROENDOCRINE TUMOR RESEARCH FOUNDATION

DEDICATED TO CURING NEUROENDOCRINE CANCER

REQUEST FOR APPLICATIONS PROGRAM DESCRIPTION AND ELIGIBILITY

EXECUTIVE SUMMARY

The Neuroendocrine Tumor Research Foundation (NETRF) is the leading non-profit organization supporting basic, translational and clinical neuroendocrine tumor (NET) research. Our mission is to accelerate scientific discovery that will help create new and more effective therapies for carcinoid, pancreatic, adrenal and bronchial NETs.

Since its founding, NETRF has awarded nearly \$30 million in research grants to investigators whose work can help provide insight into the causes of NETs and/or lead to improved treatments for our patients. While we have made significant progress the past few years, we still do not have a complete understanding of the unique characteristics of these tumors.

OBJECTIVES AND CRITERIA

NETRF is seeking investigators and teams of investigators from around the world to study neuroendocrine cancers in new ways.

- NETRF seeks to support transformative basic, translational and clinical research studies that:
 - address critical questions or roadblocks to therapeutic development
 - exploit innovative technologies or strategies
 - are non-incremental
 - address funding gaps to advance the NET field
- NETRF encourages multidisciplinary collaborations between investigators with expertise in different fields, and prior research in NETs is not a prerequisite. The Foundation invites scientists with expertise in other areas to enter the NET field and to apply strategies and/or technologies to NETs that have proven successful for other types of cancers.

We seek proposals exploring the molecular and genetic underpinnings of NETs, and the mechanisms that drive initiation and tumor progression. We invite grants investigating novel therapeutic targets, metabolomics, the resistance to chemotherapy and theranostic treatments, new imaging, diagnostic and prognostic biomarkers and technologies. We continue to have an interest in innovative ways to study NETs, creating new or optimizing existing experimental models, and studies that exploit emerging NET model systems. We seek clinical and adaptive studies, therapeutic sequencing, and correlative studies building upon existing clinical trials. State-of-the-art research methodologies, appropriate NET models and appropriate statistical analyses should be applied.

NETRF has four grant programs and we anticipate at least one grant in each category:

- Accelerator award in the amount of \$1,200,000 (\$300K/year).

- Investigator award in the amount of \$300,000 (\$150K/year).
- Mentored Award in the amount of \$120,000 (\$60K/year)
- Pilot Project awards at \$100K/year.

Please see each program for more details.

ELIGIBILITY

Applicants must have a faculty appointment (instructor, assistant professor and above) for Accelerator, Investigator, or Pilot Awards. Applicants must have the skills, knowledge, and resources necessary to carry out the proposed research. An MD, PhD, MD/PhD or equivalent degree is required. Eligible organizations include public or private institutions, such as universities, colleges, hospitals, and laboratories, both domestic and international.

The Mentored Award is designed to encourage early-career investigators to pursue neuroendocrine research. Applicants must have a doctoral degree (PhD, MD, or equivalent degree) in a related field, and not currently be a candidate for a further doctoral or professional degree. Eligible applicants must hold a full-time, mentored research position with the title of postdoctoral fellow, clinical research fellow, or the equivalent. They must work under the auspices of a mentor at an academic, medical, or research institution and are dedicated to establishing themselves as experts in neuroendocrine tumor research. The award is transferable to the first year of a junior faculty position.

Applications from the biotech or pharmaceutical industries are not eligible.

SCOPE

Organ/Tissues of interest:

We invite proposals in pancreatic, bronchial, intestinal, and other NETs including:

- **GEP-NETs:**
All aspects of gastroenteropancreatic tumors including sites of metastasis.
- **Lung**
Well differentiated, low-grade typical carcinoids (TCs), well-differentiated, intermediate-grade atypical carcinoids (ACs), diffuse idiopathic neuroendocrine cell hyperplasia (DIPNECH).
- **Adrenal NETs:**
Pheochromocytoma and Paraganglioma.

We currently do not accept grants proposing to work on SCLC, LCLC, non-SCLC, squamous cell carcinomas, adenocarcinomas, mesotheliomas or poorly differentiated non-small cell lung carcinomas. Neuroendocrine prostate research is also out of scope. The Foundation may consider supporting work on other NET types based on allotted funding availability.

Eligible areas of interest include, but are not limited to:

- **Application of existing or new technologies to target NETs**
Designer or nano-based drugs to create targeted therapies/treatments, drug/biologic-targeted delivery to tumors, new tumor-specific targets, oncolytic viruses/cancer vaccines, nanoparticles that promote efficient drug delivery, AI-based strategies and novel therapeutic development.

- **Deciphering the molecular underpinnings of NETs**
Elucidation of basic mechanisms underlying NET initiation, progression, monitoring of NET stages. Understanding the mechanistic rules for combinatorial treatments to overcome chemotherapy and PRRT resistance, and the causes of therapeutic toxicity.
- **Cell invasion and metastasis**
Drivers of metastasis, anti-metastasis targets, small non-coding RNAs, adhesion molecules and epithelial-to-mesenchymal transition, metastasis-initiating or cancer stem cells, metastatic organotropism, triggers that stimulate invasive behavior in an indolent tumor.
- **The tumor microenvironment**
Cold NETs versus hot NETs, immune effector functions and the metabolic landscape of the tumor microenvironment, novel types of CAR T-cell therapy for solid tumors, adaptation or creation of methodologies to reprogram and activate the immune system, immune-engineering, antibody-drug conjugates. Role of angiogenesis and immune compartment landscape.
- **Diagnostics/Biomarkers**
Predictive/prognostic clinical markers, biomarkers for metastasis, imaging biomarkers, new approaches to the early diagnosis of NETs, circulating tumor cells/cell free DNA/exosomes.
- **Cancer metabolism**
Understand and manipulate the way neuroendocrine cancer cells process energy in order to survive.
- **New/optimized experimental models:**
Cell lines, mouse models, optimized spheroids/organoids, patient-derived xenografts, and others.
- **Clinical Research**
Clinical and correlative studies that may build upon existing clinical trials, proof-of-concept Phase I clinical trials, adaptive studies, combination and sequencing of therapies.
- **Nuclear medicine, theranostics, imaging**
Evaluation of imaging agents, image-guided surgery or therapies, new delivery systems, radiomics, AI, individualization, combination.

CRITERIA

- Candidates must demonstrate a commitment to NET research, and the potential for further development in this area. Applicants must, demonstrate a plan for continuing their research in NETs beyond the award period.
- NETRF grantees are required to submit progress and financial reports twice per year throughout the duration of their grant. The progress reports track milestone and project benchmarks, summarize research accomplishments, and use of the funds for each six-month period. Future funding is contingent upon review of progress and achievement of benchmarks and will be paid in six-month installments, in US dollars.
- Post-award outcomes of the funded research are required to be reported at one, three and five years following the completion of funding.

- It is mandatory for Awardees attend and present at the annual NETRF Research Symposium whether in person, or virtual for the duration of their grant and upon completion. Applicants should use their NETRF grant monies to pay for their travel to NETRF conferences held in person.
- Projects that bring together investigators from diverse scientific disciplines are highly encouraged. For team applications, one recipient principal investigator and one recipient institution must be selected.

PROCESS

The NETRF RFA employs a 2-step process. The 1st step is the submission of a Competitive Letter of Intent (LOI). The purpose of the LOI is to identify projects with the greatest scientific potential without requiring applicants to first submit a full application. A limited number of applicants whose LOI that are deemed most meritorious will move to the 2nd step and will be invited to submit a full proposal.

One LOI / applicant / program may be submitted. An applicant may submit more than one LOIs, as long as the other LOIs are submitted to a different program, and there is no scientific overlap between them.

LOIs should outline research with the potential to transform our understanding of NETs and/or lead to improved treatments for patients. LOIs may focus on any type of NET and may propose basic, translational, or clinical cancer research. Submitted LOIs will be reviewed by the NETRF's Scientific Advisory Board and other leaders in the field. Investigators with the most promising and transformative ideas will be invited to submit full applications.

Full applications will be peer-reviewed by the NETRF's Scientific Advisory Board and external expert reviewers. Members of the Scientific Advisory Board will be recused if investigators from their institutions apply, or if there is another direct or perceived conflict of interest. The review process—including all meeting deliberations, scores and written critiques of applications, as well as other materials provided for the review of applications—is confidential. A confidentiality and conflict of interest statement must be signed by each reviewer. Applicants who wish to make reasonable requests to oppose reviewers may do so, explaining the nature of the conflict of interest.

Applications will be evaluated against five criteria, in accordance with NIH guidelines:

- Significance
- Approach
- Innovation
- Investigators
- Environment

A statement of institutional commitment, including any tangible support that the institution is willing to commit to the project, is required. When applicable, consideration of ethnic and/or socioeconomic diversity in studies involving patients or patient data must be addressed.

Biosketches must be in English and provide all relevant publication and funding records of the Principal Investigator. The NIH Biographical Sketch Form OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023) should be used and the appropriate form to download and instructions can be found using following NIH link: <https://grants.nih.gov/grants/forms/biosketch.htm>

Important: Any pending and/or funded projects that may overlap with the current proposal must be disclosed and any overlap must be addressed. Such projects must be highlighted in the Biosketch by formatting the grant name in **BOLD**.

NETRF's Board of Directors will select the grant recipients based on:

- The recommendations of the Scientific Advisory Board.
- Impact of the research on the mission of NETRF
- Available funds.

USE OF FUNDS

Awarded funds are directed to the institution. **Up to 10% in indirect costs may be requested only for Accelerator and Investigator Awards. We do not cover indirect costs for the smaller Pilot or Mentored Awards.** Funds may be used for personnel salaries, supplies, small equipment, and/or research-related services only. Funds must not be used entirely for salaries and may not be applied to costs covered by other sources. Funds may be allocated to attend the Annual NETRF Symposium if held in person.

SHARING RESEARCH RESOURCES

Grant recipients that have created unique research resources using NETRF funds, are required to make them readily available to qualified individuals within the scientific community, after publication. Investigators responding to this funding opportunity must include a sharing research resources plan to address how unique research resources will be shared or explain why sharing is not possible.

Investigators that have created new plasmids or viruses are encouraged to submit them to Addgene.

Investigators that have created new cell lines are required to submit them to ATCC. NETRF will facilitate submission to ATCC.

For any questions regarding this RFA, please email us at grants@netrf.org