



INVESTIGATOR AWARD (IA) LETTER OF INTENT GENERAL GUIDELINES & INSTRUCTIONS

EXECUTIVE SUMMARY

The Neuroendocrine Tumor Research Foundation (NETRF) is the largest private global funder of 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 neuroendocrine cancers including gastrointestinal, pancreatic, bronchial, and adrenal-associated NETs.

Since its founding, NETRF has awarded more than \$36 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 to advance our understanding of tumor biology.
 - address roadblocks to therapeutic development.
 - exploit innovative technologies or strategies.
 - are non-incremental.
- **NETRF seeks proposals uncovering the molecular and genetic basis of NETs, and the underlying processes driving tumor initiation and progression.** We encourage mechanistic studies of NETs at multiple levels (genetic, epigenetic, proteomic, phosphoproteomic, kinomic, and/or metabolomic) and exploration / discovery of associated therapeutic opportunities. Emphasis on GI NETs is highly encouraged.
- **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. That said, NET biology is quite different than most other cancers; therefore, collaboration with a NET expert(s) is considered critical for PIs who are new to the NET field.
- **NETRF seeks innovative ways to study NETs.** Creating new or optimizing existing experimental models and studies that exploit emerging NET model systems are encouraged.

Other topics of interest include understanding chemotherapy resistance, interrogation of new therapeutic targets and strategies, early diagnostics, tumor heterogeneity and metastasis. We also consider exceptional clinical and adaptive studies, therapeutic sequencing, and translational studies building upon existing clinical trials. State-of-the-art research methodologies, appropriate NET models and proper statistical analyses should be applied.

Award decisions are expected to be completed by the end of 2023 with a funding start in early 2024. Please see each program for more details.

SCOPE

Organ/Tissues of interest:

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

We currently do **NOT** accept applications 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. The Foundation does not support research using human embryonic or fetal tissue.

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

- **Uncovering the molecular and genetic basis of NETs**

Elucidation of processes underlying NET initiation, progression, monitoring of NET stages.
Understanding the mechanistic rules for treatments to overcome therapeutic resistance and toxicity.
- **New/optimized experimental models:**

Cell lines, mouse models, optimized spheroids/organoids, patient-derived xenografts, and others.
Strategies to modify model proliferation and improve experimental utility.
- **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.
- **Cancer metabolism**

Understand and manipulate the way neuroendocrine cancer cells process energy in order to survive.
- **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.

- **Tumor microenvironment**
Immunologically “cold” 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, immune-oncology and contributing angiogenic processes.
- **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.
- **Clinical Research**
Exceptional clinical and correlative studies that may build upon existing clinical trials, proof-of-concept Phase I clinical trials, innovative combination therapies, adaptive and sequencing studies.
- **Nuclear medicine, theranostics, imaging**
Non-incremental, innovative, studies of novel imaging agents or therapies, new delivery/targeting systems, computational strategies.

CRITERIA

- Investigators from diverse scientific disciplines are highly encouraged to enter the NET research field, however, candidates must demonstrate the potential for further development in this area and provide a plan for continuing their NET research beyond the award period.
- Collaborative efforts are encouraged; however, a single principal investigator and institution must be selected to receive an award.
- 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 to attend and present at the annual NETRF Research Symposium whether in person, or virtual, for the duration of their grant and upon completion. NETRF grant monies are to be used to pay for NETRF conferences travel, if held in person.

ELIGIBILITY

Applicants must have a faculty appointment (assistant professor and above). 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.

Applications from the biotech, pharmaceutical industry, National Institutes of Health (NIH), or for-profit life sciences companies are **not** eligible.

LOI APPLICATION PROCESS

The NETRF RFA model employs a 2-step process. The first step is the submission of a competitive LOI. One LOI per applicant, per program, may be submitted. The purpose of the LOI is to identify projects with the greatest scientific potential without requiring applicants first to submit a full application. A limited number of applicants whose LOIs are deemed most meritorious will be invited to submit a full proposal. Investigator awards are medium size grants in terms of scope, length, and money. The Investigator Awards total \$270,000 and last for two years (\$135,000 per year).

These proposals typically have two aims for the two-year timeframe. They might have only one PI with or without collaborators. They are similar to an NIH R21 grant.

To start a Letter of Intent, go to the ProposalCentral website at <https://proposalcentral.com>. If you are a new user to ProposalCentral, follow the Create One Now link under Need an Account? and complete the registration process. If you are already a registered user, login at <https://proposalcentral.com> with your username and password. If you have forgotten your password, click Forgot your Password? Link.

Once logged in, select the Grant Opportunities tab and a list of applications will be displayed. Find Neuroendocrine Tumor Research Foundation and click the Apply Now link next to the Investigator Award to create your Letter of Intent.

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.

LOIs will be rated on scientific merit and potential impact. Full applications will be evaluated against five criteria, in accordance with NIH guidelines:

- Significance
- Approach
- Innovation
- Investigators
- Environment

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. **For Investigator Awards, up to 10% in indirect costs may be requested.** 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 from the awarded grant should be allocated to attend the Annual NETRF Symposium.

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. Sharing is expected to be an open process after publication of findings, although it is encouraged prior to publication if possible. Investigators responding to this funding opportunity must provide a research resource sharing plan in the full application.

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.

LOI INSTRUCTIONS

Please include the following information:

- I. TITLE PAGE
- II. ENABLE OTHER USERS TO ACCESS THIS PROPOSAL – Optional. Enter an email address for an individual if you would like to grant them access to your LOI.
- III. APPLICANT/PI INFORMATION
- IV. ORGANIZATION/INSTITUTION INFORMATION
- V. CO-PI/COLLABORATORS
- VI. ABSTRACT & KEYWORDS
 - a. SCIENTIFIC/CLINICAL IMPACT STATEMENT (1,500 CHARACTERS MAXIMUM)
 - b. SCIENTIFIC ABSTRACT (3,000 CHARACTERS MAXIMUM)
 - c. LAY SUMMARY (2,000 CHARACTERS MAXIMUM)
 - d. SELECTED FOCUS AREA (UP TO 3 SELECTIONS)
 - e. SPECIFIC AREA OF PROPOSAL FOCUS (UP TO 3 SELECTIONS)
 - f. AREA OF INTEREST (1 SELECTION)
 - g. PROPOSED RESEARCH TYPE (1 SELECTION)
 - h. NET ORGAN/TISSUE OF INTEREST (1 SELECTION)

LOI Submission Deadline is Monday, April 24, 2023, at 5PM ET.

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