

# 2017 NETRF Grant Funding Opportunities

## Request for Applications

### 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, bronchial, and other types of NETs.

Since its founding, NETRF has awarded more than \$18 million in research grants to researchers whose work can help provide insight into the causes of NETs and/or lead to improved treatments for patients. Although we have made significant progress, we still have too few NET investigators and an incomplete understanding of the unique characteristics of these tumors.

Made possible by the generous support of our donors and family foundation partners, including the Margie and Robert E. Petersen Foundation, we are pleased to announce the **2017 Request for Applications (RFAs)**, and we invite **Competitive Letters of Intent (LOIs)**. LOIs should outline research with the potential to transform our understanding of NETs and/or lead to improved treatments and diagnostics for patients. LOIs may focus on any type of NET and may propose basic, translational, or clinical cancer research. While we continue our interest in pancreatic and gastrointestinal tract NETs, this year we also seek proposals addressing other common but less well researched forms, such as bronchial NETs. Some areas of interest include but are not limited to: application of existing or new technologies to study, understand and target NETs – the immune microenvironment, nanotherapies, patient-derived xenografts – clinical, correlative, adaptive studies – nuclear medicine, theranostics, imaging – metastasis drivers, chemoresistance, biomarkers.

We expect to fund:

- At least one 4-year **Accelerator** award in the amount of \$1,200,000 (\$300K/year).
- At least one 2-year **Petersen Investigator** award in the amount of \$300,000 (\$150K/year).
- One to three 1-year **Pilot Project** awards not to exceed \$100,000 (\$50K-100K/year).

Submitted LOIs will be reviewed by the NETRF's Scientific Advisory Board, comprised of highly respected leaders in the field. The investigators with the most promising and transformative ideas will be invited to submit full applications.

Full applications will be *peer reviewed* by both external expert reviewers and by the NETRF's Scientific Advisory Board. 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.

NETRF's Board of Directors will select the grant recipients based on a) the recommendations of the Scientific Advisory Board, b) funds available, and c) impact of the research on the mission of NETRF.

## **KEY DEADLINES**

Deadlines are as follows:

RFA Release Date	July 5, 2017
Competitive Letter of Intent Deadline	September 5, 2017
Notification / Invitation to Submit Full Application Date	September 15, 2017
Application Receipt Deadline	October 31, 2017
Peer Review	November/December, 2017
Recommendations to Board of Directors	January, 2018
Award announcement	January, 2018
Earliest Anticipated Start	February/March, 2018

## **ELIGIBILITY**

We are seeking investigators and teams with the tools to study neuroendocrine cancers in innovative and transformative ways. 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.

Projects that bring together investigators from diverse scientific disciplines are highly encouraged. For team applications, a recipient principal investigator and recipient institution must be selected. International applications are welcome.

Candidates must demonstrate a commitment to continue with NET research and the potential for further development in this area. Please note that prior research in this field is not a prerequisite; in fact, the Foundation wishes to encourage expert scientists to enter the field. Applicants must, however, demonstrate a plan for continuing their research in NETs beyond the award period.

Awardees must agree to present updated progress throughout the life of their grant and at the annual NETRF research symposium held in the spring each year.

A detailed progress report summarizing research accomplishments and use of the funds is required biannually for the duration of the award. Future funding will be contingent upon review of progress and achievement of relevant milestones.

Eligible organizations include public or private institutions, such as universities, colleges, hospitals, and laboratories, both domestic and international. Grants will be paid in US dollars.

## **OBJECTIVE AND SCOPE**

This year's initiative is designed to promote innovative and transformative research in NETs that can bring the field closer to more effective therapies. We invite basic, translational and clinical research applications, and encourage collaborations between investigators with expertise in different fields, such as bioinformatics, engineering, nanotechnology or other suitable disciplines.

We continue to have an interest in a) understanding the molecular underpinnings of NETs and the mechanisms that drive initiation and progression, and b) immunotherapy, where we encourage the study and/or application of either novel or existing immunotherapies that may be transferable to NETs, including immunoengineering and other types of nanotherapies. Use of patient-derived xenografts might be applicable to these as well as other studies.

We strongly encourage proposals on clinical and adaptive studies, therapeutic sequencing, as well as correlative studies that may build upon existing clinical trials, to enhance and transform current therapeutic approaches.

Other topics of intense interest include nuclear medicine, theranostics, imaging, drivers of metastasis, understanding chemotherapy resistance, and new approaches to the early diagnosis of NETs.

We also seek proposals that suggest innovative ways to study NETs in the absence of conventional models (cell lines, mice, etc.).

A variety of state-of-the-art technologies may be utilized. The creation and use of novel genetically modified animals, including transgenic or gene knockouts, or of reliable neuroendocrine cell lines, is also desirable.

## COMPETITIVE LETTER OF INTENT (LOI) – SUMMARY

The NETRF RFA model employs a 2-step process: the first step is the submission of a competitive LOI. One LOI per applicant may be submitted for any of the three funding categories. 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 LOI is deemed most meritorious will move to the second step, and will be invited to submit a full proposal.

LOIs for the **Accelerator** and **Petersen Investigator** awards must include the following information:

- **Scientific Abstract** – Limited to **300 words**.
- **Project Summary Statement** – Limited to **two** pages (not including references).
- **Key Literature References** – Not to exceed **two** pages.
- **Curriculum Vitae** – Including publication and funding history.
- **Collaboration Letter(s)** – If applicable.
- **Letter of Institutional Commitment** – The letter(s) must be written by the department head, dean, or other senior member of the institution on behalf of the applicant.

LOIs for a **Pilot Project** award must include the following information:

- **Scientific Abstract** – Limited to **150 words**.
- **Project Summary Statement** – Limited to **one** page (not including references).
- **Key Literature References** – Not to exceed **one** page.
- **Curriculum Vitae** – Including publication and funding history.
- **Collaboration Letter(s)** – If applicable.
- **Letter of Institutional Commitment** – The letter(s) must be written by the department head, dean, or other senior member of the institution on behalf of the applicant.

The deadline for submission of Competitive LOIs is **September 5th, 2017, by 11:59 pm, Eastern Daylight Time, US**.

Please submit your LOI by electronic mail to [effie.tzamei@netrf.org](mailto:effie.tzamei@netrf.org)

## **Competitive Letter of Intent for Accelerator and Petersen Investigator Awards**

### **Investigator Contact Information**

Investigator's Full Name:			
	<i>Last (Family)</i>	<i>First (Given)</i>	<i>Middle Initial</i>
Degree:	<input type="checkbox"/> MD <input type="checkbox"/> PhD <input type="checkbox"/> MD, PhD <input type="checkbox"/> PharmD <input type="checkbox"/> Other:		
Title/Position:			
Department:			
Institution:			
Mailing Address:			
	<i>City</i>	<i>State</i>	<i>Zip Code</i>
Country:			
Telephone:			
E-mail:			
Lab website URL			
Assistant's Name			
Assistant's E-mail			
<b>Title of Project:</b>			

**Applicant:**

\_\_\_\_\_

*(signature)*

Print Name: \_\_\_\_\_

Date: \_\_\_\_\_

**Department Chair, Division Head, or Dean:**

\_\_\_\_\_

*(signature)*

Print Name: \_\_\_\_\_

Title: \_\_\_\_\_

Date: \_\_\_\_\_

**Institutional Signing Official:**

\_\_\_\_\_

*(signature)*

Print Name: \_\_\_\_\_

Title: \_\_\_\_\_

Date: \_\_\_\_\_

## LETTER FORMAT

- **Title:**
- **Name of Principal Investigator and Co-Investigator(s):**
- **Scientific Abstract** – Limited to **300 words**, should provide a clear, concise overview of the proposed NET research project, objective, and significance.
- **Project Summary Statement** – Limited to **two** pages (not including references). Must describe the proposed NET research project and include:
  - Background
  - Specific Aims
  - Rationale
  - Study design
  - Novelty and Innovation
  - Plan for access to any necessary patient tumor samples, if applicable
  - Potential for translational application and patient benefit.
- **Key Literature References** – Full citations to publications supporting the proposed research should be included and may not exceed **two** pages.
- **Curriculum Vitae** – Applicant’s Curriculum Vitae including publication and funding history.
- **Collaboration Letter(s)** – If applicable, a letter from a collaborator outlining the type and duration of said collaboration, must be included.
- **Letter of Institutional Commitment** – The letter(s) must be written by the department head, dean, or other senior member of the institution on behalf of the applicant. The letter(s) should confirm that the applicant holds a tenure-track position. The letter(s) must critically address the scientific merit and novelty of the proposed research, the scientific independence demonstrated by the applicant in previous work, and the dedication of the applicant to NET research.

### **Formatting and Submission Instructions** – Applicants must adhere to the following instructions:

- Must use 12-point Times New Roman for the text, and no smaller than 9-point type for figures, legends, and tables.
- Single-spacing is acceptable, and space between paragraphs is recommended.
- The page margins must be no less than 0.75 inches on each side.
- The narrative must be numbered consecutively.
- All required sections must be combined into one PDF file and e-mailed to [effie.tzamei@netrf.org](mailto:effie.tzamei@netrf.org) by **September 5th, 2017, 11:59 pm, Eastern Daylight Time, US.**

*Early submission is encouraged*

## Competitive Letter of Intent for Pilot Awards

### Investigator Contact Information

Investigator's Full Name:			
	<i>Last (Family)</i>	<i>First (Given)</i>	<i>Middle Initial</i>
Degree:	<input type="checkbox"/> MD <input type="checkbox"/> PhD <input type="checkbox"/> MD, PhD <input type="checkbox"/> PharmD <input type="checkbox"/> Other:		
Title/Position:			
Department:			
Institution:			
Mailing Address:			
	<i>City</i>	<i>State</i>	<i>Zip Code</i>
Country:			
Telephone:			
E-mail:			
Lab website URL			
Assistant's Name			
Assistant's E-mail			
<b>Title of Project:</b>			

**Applicant:**

\_\_\_\_\_

*(signature)*

Print Name: \_\_\_\_\_

Date: \_\_\_\_\_

**Department Chair, Division Head, or Dean:**

\_\_\_\_\_

*(signature)*

Print Name: \_\_\_\_\_

Title: \_\_\_\_\_

Date: \_\_\_\_\_

**Institutional Signing Official:**

\_\_\_\_\_

*(signature)*

Print Name: \_\_\_\_\_

Title: \_\_\_\_\_

Date: \_\_\_\_\_

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- **Name of Principal Investigator and Co-Investigator(s):**
- **Scientific Abstract** – Limited to **150 words**, should provide a clear, concise overview of the proposed NET research project, objective, and significance.
- **Project Summary Statement** – Limited to **one** page (not including references). Must describe the proposed NET research project and include:
  - Background
  - Specific Aims
  - Rationale
  - Study design
  - Novelty / Innovation
  - Plan for access to any necessary patient tumor samples, if applicable
  - Potential for Translational Application and Patient Benefit.
- **Key Literature References** – Full citations to publications supporting the proposed research should be included and may not exceed **one** page.
- **Curriculum Vitae** – Applicant’s Curriculum Vitae including publication and funding history.
- **Collaboration Letter(s)** – If applicable, a letter from a collaborator outlining the type and duration of said collaboration, must be included.
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*Early submission is encouraged*



## FULL APPLICATIONS - SUMMARY AND GUIDELINES

### SUMMARY

The term neuroendocrine tumor (NET) is used broadly to define and group together highly heterogeneous neoplasms that derive from distinct neuroendocrine cell types in different organs. As such, neuroendocrine cancers are highly diverse, and a pancreatic NET is very different from a gastrointestinal tract or lung NET. Lack of a complete understanding of the genomic alterations in NETs, combined with a scarcity of reliable cell lines and animal models, has hindered progress in NET research. With the molecular pathogenesis of NETs still largely unknown, therapeutic management has been challenging.

Recognizing these research barriers, the NETRF has devoted much of its funding in years past to the interrogation of the genomic alterations in different types of NETs, to find driver mutations in genes that can provide predictive insights on treatment response. Our grant recipients have identified a number of mutations on key genes, opening new areas of inquiry with therapeutic potential. The NETRF has also funded the creation of molecular tools for an in-depth study of the disease in a laboratory setting, such as mouse models, patient-derived xenografts and most recently organoids. We have also invested in studies exploring the immune microenvironment, another challenging area of inquiry, as in many types of NETs, immune cell infiltration is minimal. Nevertheless, we believe that adaptation of technologies such as CAR T-cell therapy (which has shown to be promising in other types of cancers) to NETs, is of utmost importance, and we have taken a proactive and aggressive approach to funding such studies.

This year, NETRF seeks to expand its research portfolio to include more translational and clinical research. While we continue to invite, and fund basic research with the potential to improve our understanding of NETs, we welcome translational and clinical research grant proposals that will accelerate the development of diagnostic and therapeutic interventions for our patients. We also encourage applications from multidisciplinary groups combining not only expertise in basic, translational, or clinical research, but also in biotechnology and nanotechnology, or other relevant disciplines, as we believe that the most effective way to tackle our limited understanding of what drives the development of NETs, and the scarcity of experimental models available to us today, is to bring together diverse experts able to attack the problem from many different fronts, and to bypass existing experimental limitations. Proposals that cover promising and potentially transferable mechanisms and/or technologies, which have been applied successfully to other areas of cancer research, are highly desirable and will be evaluated based on their level of applicability to NETs.

### AREAS OF INTEREST

Areas of interest include but are *not* limited to:

1. **Application of existing or new technologies to study, understand, and target NETs** – Enhanced molecular analysis methodologies for the elucidation of basic mechanisms underlying NET initiation/progression and monitoring of NET stages; drug delivery to intended cancer targets *in vivo* / nano-delivery; patient-derived xenografts; chemotherapy resistance.
2. **The immune microenvironment** – Cold NETs versus hot NETs; immune effector functions and the metabolic landscape of the tumor microenvironment; reprogramming of the tumor metabolic pathways to improve immune response; adaptation or creation of methodologies to reprogram and leverage the immune system; immunoengineering; nanotechnologies.
3. **Clinical Research** - Clinical and correlative studies that may build upon existing clinical trials to enhance and transform current therapeutic approaches; proof-of-concept Phase I clinical trials; adaptive studies; combination and sequencing of therapies.
4. **Nuclear medicine, theranostics, imaging, molecular information** – Evaluation of imaging agents; image-guided surgery or therapies; assessment of imaging systems; predictive/prognostic clinical markers; delivery systems; novel biomarkers; new approaches to the early diagnosis of NETs.
5. **Metastasis** – Drivers of metastasis; anti-metastasis targets; small non-coding RNAs; adhesion molecules and epithelial-to-mesenchymal transition; metastasis-initiating or cancer stem cells; triggers that stimulate invasive behavior in an indolent tumor; biomarkers for metastasis and prognosis.

## USE OF FUNDS

Awarded funds are directed to the institution. Up to 10% in indirect costs may be requested *only* for grants over \$100K. 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 used to attend the annual NETRF symposium.

## SHARING RESEARCH RESOURCES

NETRF requires that grant recipients make unique research resources created by NETRF awards readily available for research purposes to qualified individuals within the scientific community, after publication. Investigators responding to this funding opportunity should include a sharing research resources plan to address how unique research resources will be shared, or explain why sharing is not possible.

## FULL APPLICATIONS - INSTRUCTIONS

On September 15, 2017, a limited number of applicants whose competitive LOI was deemed most meritorious will be invited to submit a full proposal. This section provides detailed instructions on how to prepare and submit a full proposal.

Please format your full proposal following the guidelines outlined below.

**A. Principal Investigator** (including Co-Principal Investigators, if applicable):

1. Name
2. Position/title
3. Affiliation
4. Address
5. Phone number
6. Fax number
7. E-mail

**B. Sponsoring Institution** (in the case of Co-Principal Investigators, Recipient Institution)

1. Name, title, and contact information (address, telephone, fax, e-mail)

**C. Description of Project**

1. Title
2. Objectives, as they relate to the goals of the NETRF mission
3. Abstract (scientific version)
4. Abstract (lay version)
5. Performance metrics to track rapid progress
6. List and roles of all involved personnel and collaborators
7. Funding requested
8. Duration requested

**D. Detailed Research Proposal** (NIH format, not to exceed **eight** pages for Accelerator, **four** pages for Petersen Investigator, or **two** pages for Pilot project award applications)

1. Hypothesis and specific aims
2. Research strategy
  - a. Significance
  - b. Innovation
  - c. Experimental approach
    - i. Preliminary studies
    - ii. Anticipated results, potential pitfalls, and alternative approaches

**E. Appendix I** (no page limit)

1. Literature cited

2. Detailed budget, including other sources of support
  - a. Senior/key person
  - b. Other personnel
  - c. Equipment description
  - d. Material and supplies
  - e. Travel
  - f. Direct costs
  - g. Indirect costs
  - h. Total expenses
3. Plan for sharing research data and resources with other scientists/institutions
4. Plan for access to any necessary patient tumor samples, if applicable
5. Potential for translational application and patient benefit
6. Bio sketch (NIH format) of the Principal Investigator and key collaborators
7. List of all sources of funding (current and pending) for the Principal Investigator, including the specific aims associated with each source
8. Reprints and/or letters of collaboration, if applicable

#### **F. Appendix II - Formatting Instructions and Submission Process**

Applicants must adhere to the following instructions:

1. Must use 12-point Times New Roman for the text, and no smaller than 9-point type for figures, legends, and tables
2. Single-spacing is acceptable, and space between paragraphs is recommended
3. The page margins must be no less than 0.75 inches on each side
4. The Narrative must be numbered consecutively

#### Submission Process

1. Applications cannot be changed after submission. Incomplete applications will not be reviewed
2. All required sections must be combined into a single PDF file
3. Please use the type of proposal you are submitting (Accelerator, Petersen Investigator, or Pilot project award application) in your e-mail subject line
4. NETRF will e-mail applicants to confirm receipt of application within five business days
5. NETRF will disclose the application only to individuals directly involved in our process to award research grants

#### **G. Appendix III – Required Signatures**

Please complete and include the section in next page with your application.

The deadline for submission is **October 31, 2017, by 11:59 pm, Eastern Daylight Time, US**. Please submit the proposal packet by e-mail to [effie.tzameli@netrf.org](mailto:effie.tzameli@netrf.org)

*Early submission is encouraged*

**G. Appendix III – Required Signatures**

The Principal Investigator must acknowledge, agree, sign, and date the following statement.

*“I certify that the statements herein are true, complete, and accurate to the best of my knowledge. Any false or fraudulent statements or claims may subject me to criminal, civil, and/or administrative penalties. I have read and agree to be bound by the Neuroendocrine Tumor Research Foundation’s Research Grant Policies and Procedures.”*

**Applicant:**

\_\_\_\_\_  
(Signature)

Print Name: \_\_\_\_\_

Date: \_\_\_\_\_

The Department Chair and Institutional Official must acknowledge, agree, sign and date the following statements.

*“I certify that the statements herein are true, complete, and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, and/or administrative penalties. \_\_\_\_\_ has read and agrees to be bound by the Neuroendocrine Tumor Research Foundation’s Research Grant Policies and Procedures.”*

**Department Chair, Division Head, or Dean:**

**Institutional Signing Official:**

\_\_\_\_\_  
(Signature)

\_\_\_\_\_  
(Signature)

Print Name: \_\_\_\_\_

Print Name: \_\_\_\_\_

Title: \_\_\_\_\_

Title: \_\_\_\_\_

Date: \_\_\_\_\_

Date: \_\_\_\_\_