NEUROENDOCRINE TUMOR RESEARCH FOUNDATION

DEDICATED TO CURING NEUROENDOCRINE CANCER

Research Grants 2005-2019

2019 GRANTS

Investigator Award: NETcure—Shine New Light on NET Therapy

Martin Gotthardt, PhD, Radboud University Medical Center, Nijmegen, Netherlands

An international collaboration in Spain and the Netherlands will explore photodynamic therapy. The team will develop a "photosensitizer," which is a molecule that upon activation with light induces cell death. The photosensitizer will be coupled with peptides that bind to neuroendocrine tumor cells. The therapy will then be tested and optimized in laboratory models.

2018 GRANTS

Accelerator Award: Multipronged Approaches to Develop Immunotherapy Targeting NETs

Xianxin Hua, MD, PhD, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

This 4-year study will develop nanobody-directed CAR T-cell therapy with various combinatory approaches in laboratory models to kill NET cells. The research will be carried out in collaboration with Dr. Carl June at the University of Pennsylvania, whose work was integrally involved with the approval of CAR T-cell therapy, a personalized, breakthrough immunotherapy for blood cancer. The multipronged approaches will significantly increase the opportunity to develop efficacious NET-specific immunotherapy.

Investigator Award: Understanding the Physiologically Relevant Functions of DAXX

Guillermina (Gigi) Lozano, PhD. The University of Texas MD Anderson Cancer Center, Houston, TX

To build upon an earlier discovery made by NETRF-funded research, Lozano and colleagues will explore the role of DAXX genomic mutations in pancreatic NETs. First, researchers will study the normal functions of the DAXX gene in laboratory models, then evaluate what happens when the gene is removed. This knowledge can help to identify therapeutic targets.

Investigator Award: New Strategies to Improve Drug Development for Carcinoid Tumors

Emily Bergsland, MD, University of California, San Francisco, CA

Incorporating serial blood samples and CT scan images from a recently clinical trial, a team of investigators from around the country will explore new approaches to monitoring response: evaluation of multiple proteins in circulating blood, and computational analysis of CT images. This very novel work could lead to the identification of better ways of assessing treatment effects, facilitating testing of the next generation of therapeutic agents in NETs.

Pilot Award: NET-Smart Chemotherapy: A Targeted Prodrug Strategy

Justin Annes, MD, PhD, Stanford University, Stanford, CA

By taking advantage of unique properties of NETs that are not found in healthy cells, researchers will try to target chemotherapy to attack only cancer cells, instead of all cells. Creating novel chemotherapeutic agents that will attack and kill only NET cells will help reduce the side effects of currently used systemic chemotherapy.

Pilot Award: Novel Radioligands to Improve Radiotherapy of NETs

Kuo-Shyan Lin, PhD, BC Cancer, Vancouver, Canada

Scientists will explore a novel, very stable compound that binds to NET cells' somatostatin receptors (SSTR2) more tightly than lutetium 177 (Lu-177) dotatate. This new radiopharmaceutical will be compared with Lu-177 dotatate in disease models. Researchers hope tighter binding of this radiotherapeutic agent to cancer cell receptors will lead to higher radiation accumulation and improved cancer response.

Pilot Award: Evaluation of 225Ac-Dotatate for Treatment of Lung Carcinoid Tumors

David Morse, PhD, Moffitt Cancer Center, Tampa, FL

Morse and colleagues will test a novel radiotherapy, 225Ac-dotatate, a derivative of lutetium 177 dotatate, in PRRT for lung NETs in laboratory models. This therapy emits alpha (α) particles instead of beta (β). Alpha particles are bigger, higher powered, with a shorter reach, which researchers hope will be more effective in killing lung NET cells with decreased toxicity in surrounding normal tissues. Laboratory tests will help evaluate the therapy's safety and efficacy to prepare for potential testing in humans.

Pilot Award: Phase 1 Study of SurVaxM™ in Survivin-Positive NETs

Renuka Iyer, MD, Roswell Park Comprehensive Cancer Center, Buffalo, NY

This study tests the immunotherapy SurVaxM in combination with a somatostatin analog in patients with survivin-expressing NETs. The vaccine targets survivin, a protein that's often highly expressed in lung, intestinal, and pancreatic NETs and associated with aggressive disease because of its ability to prevent tumor cell death. Many patients with incurable brain cancers on SurvaxM have shown better outcomes than would be expected with standard of care alone.

Basic/Translational Science Investigator (BTSI) Award: Novel Antibody-Drug Conjugate for Pancreatic NET Targeted Therapy

Renata Jaskula-Sztul, PhD, University of Alabama at Birmingham School of Medicine, Birmingham, AL

This grant was issued in collaboration with NANETS.

Jaskula-Sztul will explore an antibody-drug conjugate, a novel delivery system for therapy, to increase precision and efficacy while reducing risks. She will be using a natural cytotoxic agent bound to an antibody that specifically targets the surface receptor SSTR2 on pancreatic NETs.

Next Generation Animal Models to Define Therapies for NETs

Pawel Mazur, PhD, MD Anderson Cancer Center, Houston, TX

This grant was issued in collaboration with AACR.

Mazur will explore an enzyme (KMT NSD3 or NSD3) in laboratory models of pNETs with genomic alterations in PTEN, MEN1, and ATRX to see if it helps pancreatic NETs. NSD3 may amplify the impact of these alterations, helping to give neuroendocrine cancer cells the "green light" to reproduce and grow.

Accelerator Award: An Integrated Preclinical and Clinical Evaluation of DNA-Repair Mechanisms in Determining Response to PRRT as a Guide to Patient Selection and for Development of Novel Combination Therapies*

Rodney Hicks, M.D., University of Melbourne, Melbourne, Australia

Hicks and colleagues will evaluate the impact of PRRT on tumor cells' ability to recognize and repair radiation damage. Laboratory studies will identify which targeted therapies "turn off" cellular repair mechanisms. Then, a pilot clinical trial will test the targeted therapies in combination with PRRT in patients.

Petersen Investigator: Simultaneous Auger-e- and β--Particle Therapy of Metastasized NET Using 161Tb-DOTATOC*

Roger Schibli, Ph.D., Paul Scherrer Institut, Zurich, Switzerland

Schibli and colleagues will develop a new therapy based on terbium radionuclides (161Tb), which have distinct radioactive properties, compared to Lu 177. The researchers will evaluate the ability of 161Tb-DOTATOC to kill single cancer cells and tiny metastases in a pre-clinical setting before they proceed with the first-in-man study.

Pilot Award: Exploring the Role of Epigenetic Dysregulation in PanNET Progression*

Sita Kugel, Ph.D., Fred Hutchinson Cancer Research Center, Seattle, WA

Kugel and colleagues have found that a protein called SIRT6 may affect metastatic progression in PanNETs. To test this, they will block SIRT6 to see if tumor cells grow faster in its absence, which would suggest that SIRT6 may block metastasis.

Pilot Award: Biomarkers of Response to Cabozantinib in Patients with NETs

Jennifer Chan, M.D., M.P.H., Dana-Farber Cancer Institute, Boston, MA

Chan and colleagues will analyze samples from a cabozantinib clinical trial to look for biomarkers that could predict response to cabozantinib. Their findings will be applied to a future investigation in a phase III clinical trial of cabozantinib.

Pilot Award: Development of Ex-vivo Models of Metastatic NETs*

Raj Srirajaskanthan, Ph.D., Kings College London, United Kingdom

Using precision cut slice technology, Srirajaskanthan and colleauges will cut and culture tissue slices from NET and adjacent healthy tissue in conditions that will maintain their original tissue properties. They will then be able to use this tool to test responses to various drugs.

Pilot Award: Models of NETs using 3D hydrogels

Charlotte Kuperwasser, Ph.D., Tufts University School of Medicine, Boston, MA

Kuperwasser and colleagues have developed 3D hydrogel technology that allows other tumors, isolated from patients to grow with > 90% success. They will apply this technique to grow ileum and appendix NET models to understand how NETs grow and to try to establish NET cell lines to assess therapeutic response.

2017 GRANTS

Enhancing Peptide Receptor Radionuclide Therapy in Well-Differentiated Pancreatic Neuroendocrine Tumors

Brian R. Untch, MD—Memorial Sloan Kettering Cancer Center, New York, NY

Issued in collaboration with NANETS: Basic/Translational Science Investigator Award.
Objective: To study PRRT alone and in combination with targeted therapies to identify optimal in vivo approaches for future PanNET clinical trials.

An Improved Approach for Detection and Therapeutic Monitoring of Neuroendocrine Tumors by PET

Babak Behnam Azad, PhD—Johns Hopkins School of Medicine, Baltimore, MD

Issued in collaboration with the Education and Research Foundation for Nuclear Medicine and Molecular Imaging.
The study evaluates a novel strategy for the direct, non-invasive imaging of NETS by PET to circumvent the limitations of [18F]Flouro-L-DOPA with the development of novel tracer element, (18F) FLuoro-D-DOPA.

Accelerator Award: Modeling NETs Using Adult Stem Cell-Derived Organoids*

Hans Clevers, MD, PhD—Hubrecht Institute, Netherlands

Objective: To engineer a "living biobank" of intestinal carcinoid and pancreatic NET tissue. Stem cells from healthy and tumor tissue specimens will be grown into organoids or "mini-organs" in a dish. The team will test whether certain genomic changes lead to the development of tumors, in healthy organoids. They will use the NET organoids to test sensitivity to various drug treatments.

Accelerator Award: Epigenetic Regulators of Intestinal Endocrine Cells and Carcinoid Tumors*

Qiao Zhou, PhD—Harvard University; Ramesh Shivdasani, MD, PhD—Dana-Farber Cancer Institute, Boston, MA

Objective: To understand how neuroendocrine stem cells, the original cells, can go awry and give rise to tumors, and how tumor cells are different, in terms of growth and function. They aim to identify mistakes in cellular proteins that can be corrected with targeted therapies.

Accelerator Award: Finding the Cause of Small Intestinal NETs*

Matthew Meyerson, MD, PhD— Dana-Farber Cancer Institute, Harvard Medical School; Eric Nakakura, MD, PhD—University of California, San Francisco; Chrissie Thirlwell, BSc, MD, PhD—University College London Cancer Institute

Objective: To analyze small intestinal NET specimens to look for inherited or acquired changes in the genome. The team will also sequence cells very close to the tumors to look for the earliest indications of cancer. Additional analyses will evaluate whether environmental or infectious agents can lead to genomic alterations.

Petersen Investigator: Role of ATRX/Daxx/H3.3 Chromatin Regulation in Pancreatic NETs*

Laura Banaszynski, PhD—UT Southwestern Medical Center, Dallas, TX

Objective: To study two key proteins involved in the development of NETs, which are found mutated in 43% of pancreatic NETs, to test the hypothesis that these proteins function to stabilize DNA and that the mutated proteins are not able to stabilize the genome, eventually leading to tumor formation.

Proteogenomic Analysis of Pancreatic NETs

Sharon Gorski, PhD, Genome Sciences Centre, Canada

This grant was issued in collaboration with the American Association for Cancer Research (AACR).
Objective: To develop molecular classifiers for pancreatic NETs and to comprehensively identify the molecular alterations associated with this rare disease.

Pilot Award: Mutational Landscape of Pancreatic NETs Using the "Liquid Biopsy"

Nitya Raj, MD; Diane Reidy-Lagunes, MD—Memorial Sloan Kettering Cancer Center, New York, NY

Objective: To evaluate how accurately analysis of cell-free DNA from blood samples can detect genetic changes in tumor DNA, as compared to those in tissue biopsies, which could help inform treatment options for patients.

Developing Novel Treatments for NETs using CAR T-Cell Technology*
Xianxin Hua, MD, PhD; Carl June, MD; David Metz, MD—Abramson Cancer Center, University of Pennsylvania
Objective: To develop new therapy for NETs via specifically killing cancer cells using CAR T-Cell Technology.

2016 GRANTS

Petersen Investigator: The Mechanistic Underpinnings of Pancreatic NETs*
Guillermina Lozano, PhD—MD Anderson Cancer Center
Objective: To generate and characterize mouse models to better understand pancreatic NETs and the events that contribute to tumor development, as well as identify the cellular changes that occur with loss of Daxx and determine how Daxx mutations can lead to tumor growth.

Petersen Investigator: Treating NETs via Synthetic Lethality*
Michael German, MD—University of California, San Francisco
Objective: To analyze how the UPR-MEN1-MAPK pathways interact to control neuroendocrine cell survival and death, and to evaluate synthetic lethal interactions in a patient-derived xenograft tumor model of pancreatic NETs.

Multidimensional Immune Profiling of Advanced Pancreatic NETs
Daniel M. Halperin, MD—MD Anderson Cancer Center
Objective: To examine the immune milieu in specimens of a heavily clinically and molecularly annotated population of patients with advanced pancreatic NETs, correlating with clinical outcome.

Systematic Evaluation of the Immune Environment of NETs
Tim Meyer, MD, PhD—UCL Cancer Institute, University College London
Objective: To characterise the immune landscape in NETs and investigate the effect of therapy on the immune cell tumour infiltration, and to determine which relevant immune-modulatory pathways control the function of tumour infiltrating lymphocytes.

Profiling of Secreted Immune Mediators in NETs
Matthew Kulke, MD—Dana-Farber Cancer Institute
Objective: To characterize responses to PD-1 inhibition in an established patient-derived ex-vivo tissue slice model of small intestine NETs, as well as characterize secreted immune markers and cytokines in banked plasma of patients with advanced NETs, and assess if secretion patterns are associated with survival.

Development of a Mouse Model of Pancreatic NETs*
Eric Nakakura, PhD, MD—University of California, San Francisco
Objective: To characterize a xenograft mouse model of pancreatic NETs. This model will be useful to help develop and test potential new therapies for pancreatic NETs.

Targeting NETs by Suppressing a Cell-Surface Protease
Xianxin Hua, MD, PhD—Abramson Cancer Center, University of Pennsylvania
This grant was issued in collaboration with the AACR.
Objective: To elucidate the novel mechanisms accounting for the development of NETs and then develop new mechanism/target-based therapy to improve the treatment of NETs.

Intra-arterial Peptide Receptor Radionuclide Therapy (IA-PRRT) using 90Y-DOTA-TOC*
Thomas Hope, MD—University of California, San Francisco
This grant was issued in partnership with the Education and Research Foundation (ERF) for Nuclear Medicine and Molecular Imaging.
Objective: To evaluate possible 90Y-DOTA-TOC hepatic, marrow and renal toxicity and imaging of tumor response to hepatic arterial injection, three months post-therapy.

Targeting the Alternative Lengthening of Telomere (ALT) Pathway in Pancreatic NETs*
Christopher Heaphy, PhD—The Johns Hopkins University School of Medicine
This grant was issued in partnership with the North American Neuroendocrine Tumor Society (NANETS).
Objective: To test the hypothesis that the underlying molecular mechanisms specifically unique to the ALT pathway can be exploited therapeutically, for example by treatment with inhibitors of the DNA damage response pathway.

A Qualitative Study of Unmet NET Patient Needs*
International Neuroendocrine Cancer Tumor Alliance
Objective: To assess indicators of quality of life for patients to identify and rank unmet needs, including unmet research needs, using patient surveys, focus group, and stakeholder interviews and summarize in a white paper.

2015 GRANTS

Ex Vivo Compound Prioritization for Gastroenteropancreatic NETs
Andrea Califano, PhD—Columbia University
This grant was issued in partnership with the Falconwood Foundation.

Unfolded Protein Response in NETs
Scott André Oakes, MD—University of California, San Francisco
This grant was issued in collaboration with the AACR.

Defining the Immune Landscape of NETs—Towards Rational Combination Therapy
Professor Tim Meyer, MD, PhD—UCL Cancer Institute, University College London

Enlightenment of a New Era of Cancer Therapy: Prognostication, Target Selection, and Subsequent Therapy Determined by the Dual Tumor-Immune Phenotype
Holbrook Kohrt, MD, PhD; Pamela Kunz, MD—Stanford University Cancer Center

Molecular Analysis of the Immune Environment of NETs and Associations with Clinical Outcomes
Matthew H. Kulke, MD—Dana-Farber Cancer Institute

2014 GRANTS

Developing Novel Treatments for NETs using CAR T-Cell Technology
Carl June, MD; Xianxin Hua, MD, PhD; David Metz, MD—Abramson Cancer Center, University of Pennsylvania

Phase I/II Study of Intratumoral Ipilimumab with Anti-PD-L1 in Patients with Advanced, Progressive, Well-Differentiated NETs
Pamela Kunz, MD; Holbrook Kohrt, MD, PhD—Stanford University Cancer Center

Multifunctional Nanomedicine for Targeted Carcinoid Cancer Therapy
Herbert Chen, MD—University of Wisconsin-Madison
This grant was issued in collaboration with the AACR.

Treating NETs via Synthetic Lethality
Michael German, MD—University of California, San Francisco
This grant was issued in collaboration with the AACR.

2013 GRANTS

Implication of Heterogeneous Innate Immune Cells in Pancreatic NET Resistance
Gabriele Bergers, PhD—University of California, San Francisco
This grant was issued in collaboration with the AACR.

Identifying Altered Epigenetic States and Drivers in Intestinal Carcinoid and Pancreatic NETs
Bradley Bernstein, MD, PhD—Broad Institute, Massachusetts General Hospital; Daniel Chung, MD—Massachusetts General Hospital; Matthew Kulke, MD; Ramesh Shivdasani, MD, PhD—Dana-Farber Cancer Institute

Epigenomic Analysis of Intestinal Neuroendocrine Cells and the Epigenetic Basis of NETs
Ramesh Shivdasani, MD, PhD—Dana-Farber Cancer Institute
Pan-Mass Challenge Proceeds

Theragnostics of NETs with Somatostatin Antagonists
Wolfgang Weber, MD, PhD; Diane Reidy-Lagunes, MD—Memorial Sloan Kettering Cancer Center

2012 GRANTS

Understanding the Tumor Suppressor Activities of ATRX-Daxx through Epigenomic Profiling and Animal Models
Peter Lewis, PhD—University of Wisconsin-Madison (Previously C. David Allis, PhD, The Rockefeller University)

The Mechanistic Underpinnings of Pancreatic NETs
Guillermina Lozano, PhD—MD Anderson Cancer Center

Overcoming Resistance to mTOR Inhibition in Pancreatic NETs
Eric Nakakura, MD, PhD—University of California, San Francisco

Octreotide Targeted Treatment of Pancreatic NETs
Renata Pasqualini, PhD—MD Anderson Cancer Center
This grant was issued in collaboration with the AACR.

Mouse Model Project Using Forward Genetics
David Tuveson, MD, PhD—Cold Spring Harbor Laboratory

The Impact of MEN1, Daxx, ATRX, and PTEN in Pancreatic NET Pathogenesis
Kwok-Kin Wong, MD, PhD—Dana-Farber Cancer Institute

2011 GRANTS

Suppression of NETs via Epigenetic Regulation
Xianxin Hua, MD, PhD—Abramson Cancer Research Institute, University of Pennsylvania
This grant was issued in collaboration with the AACR.

Molecular Analysis of NET Survival
Matthew Kulke, MD—Dana-Farber Cancer Institute
Pan-Mass Challenge Proceeds

Transcriptome and Methylome of Pancreatic NETs with and without ATRX/Daxx Mutations
Nickolas Papadopoulos, PhD—Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University

Oncolytic Viral Therapy for NETs
Charles Rudin, MD, PhD—Johns Hopkins University School of Medicine
This grant was issued in collaboration with the AACR.

2010 GRANTS

Pancreatic NET Genome Project
Nickolas Papadopoulos, PhD—Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University

Mouse Model Project Using Forward Genetics
David Tuveson, MD, PhD—Cancer Research UK

2009 GRANTS

Caring for Carcinoid Foundation NET Bioconsortium
A collaboration among:
Dana-Farber Cancer Institute (Matthew Kulke, MD); MD Anderson Cancer Center (James Yao, MD); Massachusetts General Hospital Cancer Center (Daniel Chung, MD); Memorial Sloan Kettering Cancer Center (Diane Reidy-Lagunes, MD); Stanford University Cancer Center (Pamela Kunz, MD)
Pan-Mass Challenge Proceeds

Cellular Reprogramming of Enteroendocrine Cells and NETs
Michael Choi, MD—Massachusetts General Hospital

Carcinoid Cancer Genome Study
Matthew Meyerson, MD, PhD—Dana-Farber Cancer Institute
Pan-Mass Challenge Proceeds

2006 GRANTS

Identify and Validate Molecular Targets for Therapy in a Newly Developed Human Midgut Carcinoid Tumor Cell Line
Lee Ellis, MD—MD Anderson Cancer Center

Generate Mouse Models of Neuroendocrine Cancer
Seung Kim, MD, PhD—Stanford University School of Medicine

Origin and Differentiation of a New Class of Serotonin-Expressing Enteroendocrine Cells
Andrew Leiter, MD, PhD—University of Massachusetts Medical School

Elucidate the Role of the MEN1 Gene in Carcinoid Tumors and Determine a Functional Connection between the Genes MEN1, Rbp2 and p27
Matthew Meyerson, MD, PhD—Dana-Farber Cancer Institute

2005 GRANTS

Determining Unique Protein Expression Patterns in Gastrointestinal NETs
Daniel Chung, MD—Massachusetts General Hospital

Discover New Treatments for Carcinoid Cancer and Pancreatic NETs
Matthew Kulke, MD—Dana-Farber Cancer Institute

Understanding the Genetic and Cellular Origins of Carcinoid Cancer
Ramesh Shivdasani, MD, PhD—Dana-Farber Cancer Institute

*Studies made possible by the generosity of the Margie and Robert E. Petersen Foundation.

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