



# Research Grants

## 2005-2018

### 2018 GRANTS

#### **Accelerator Grant: 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 $\beta$ --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 Project: Exploring the Role of Epigenetic Dysregulation in PanNET Progression\***

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

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 Project: 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 Project: Development of Ex-vivo Models of Metastatic NETs\***

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

Using precision cut slice technology, Srirajaskanthan and colleagues 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 Project: 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**

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**

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 [<sup>18</sup>F]Flouro-L-DOPA with the development of novel tracer element, (<sup>18</sup>F) FLuoro-D-DOPA.

### **Accelerator Grant: 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 Grant: Epigenetic Regulators of Intestinal Endocrine Cells and Carcinoid Tumors\***

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

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 Grant: 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**

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 Project: Mutational Landscape of Pancreatic NETs Using the “Liquid Biopsy”**

**Nitya Raj, MD; Diane Reidy-Lagunes, MD—Memorial Sloan Kettering Cancer Center**

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

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