



FROM THE DIRECTORS

Dear Brenden-Colson Center Researchers and Supporters,

This spring the Brenden-Colson Center was focused on preparing and submitting collaborative research funding proposals. And already we have news of success!

- The BCCPC has been awarded a \$250,000 **Pancreatic Cancer Action Network Early Detection Targeted Grant** towards the assembly and maintenance of a new Oregon/California patient samples cohort and analysis of those samples using Immunovia's IMMray PanCan-d assay technology. The study will look specifically at new-onset diabetics, as part of the development of promising blood biomarkers for the early detection of pancreatic adenocarcinoma. This project will leverage the Center's ongoing partnership with Immunovia as well as our experience with multi-group collaborations.
- The Center's proposal in response to the **NIH U01 consortium for Biological Comparisons in Patient-Derived Models of Cancer (PDMCs)** draws on the diverse expertise of our collaborative OHSU research group, our OPTR tissue and blood specimen repository, and the BCCPC Atlas project that identifies the molecular and phenotypic features of primary tumors that can be recapitulated by various models – conditionally re-programmed cells, organoids, patient-derived xenografts and combinations of these – including their response to microenvironmental factors and therapy. The BCCPC's history of intra- and extra-mural interdisciplinary collaboration makes us a highly competitive candidate to join the NCI's PDMC consortium.
- The Center has also agreed to be co-leader of a proposal spearheaded by Steven Artandi, MD, PhD, of Stanford University, in response to the **SU2C-Lustgarten Foundation Pancreatic Cancer Interception Initiative**.

We are very pleased to announce that **Dr. Daniel Marks**, Professor of Pediatric Endocrinology at OHSU, has agreed to be a Program Leader for the Brenden-Colson Center. Dan studies cachexia (disease-associated wasting), which in pancreatic cancer may be the limiting determinant for quality of life and long-term survival. He has established a collaboration with Apple to distribute series 2 Apple watches to patients diagnosed with PDAC to prospectively record activity through the patient's course of chemotherapy. This activity monitor may serve as a surrogate to observe toxicity of therapy and/or progression of disease. We welcome Dr. Marks' leadership and mentorship of new investigators in developing the Center's quality of life programs.

To all of you working in pancreas research, and foremost from our patients and their families, we **thank you**.

Sincerely,

Brenden-Colson Center Co-Directors
Rosalie Sears, PhD
Brett Sheppard, MD

To make a donation in support of the Brenden-Colson Center's programs, please use this link to visit the [OHSU Foundation](#) site. Thank you.

RESEARCH UPDATES

Quantitative Multiplex Immunohistochemistry Reveals Myeloid-Inflamed Tumor-Immune Complexity Associated with Poor Prognosis

Lisa Coussens, PhD, and collaborators have developed a method to quantify multiple types of immune cells that are detected in tumor histology specimens, allowing evaluation of 12 biomarkers in a single section of tissue. They found that immune cell densities correspond with patient response to therapy and prognosis in multiple cancer types. Specifically in pancreatic ductal adenocarcinoma specimens from patients who had received neoadjuvant GVAX vaccination, tumors inflamed with a high density of myeloid immune cells and exhausted T cells correlated with shorter overall patient survival. (Tsujiikawa et al., 2017, *Cell Reports* 19, 203–217, April 4, 2017)

“Clinical trials must mandate the pre-treatment and post-treatment collection of tumor and blood for robust biomarker and bioresponse correlative studies that will inform the next generation of molecularly defined subgroup-driven trials. As our knowledge of pancreatic cancer biology grows, we owe it to patients to start applying that knowledge in novel clinical trial designs.”

Chemoradiation for Locally Advanced Unresectable Pancreatic Cancer—What Now?

Gina Vaccaro, MD, and **Charles D. Lopez, MD, PhD**, reviewed a clinical trial recently conducted in France involving patients with locally advanced pancreatic cancer whose results showed no significant difference in overall survival with chemoradiotherapy compared with chemotherapy alone and no significant difference in overall survival with gemcitabine compared with gemcitabine plus erlotinib. Vaccaro and Lopez concluded that the study “confirms and underscores the complex biology that we are discovering scientifically and that we observe clinically and challenges us to raise our game.” (*JAMA Oncology* Published online August 4, 2016; <http://oncology.jamanetwork.com/>)

Diabetes, Pancreatogenic Diabetes, and Pancreatic Cancer

Surprisingly, diabetes has been shown to be both a risk factor for and a result of pancreatic cancer.

Dana Andersen, MD, FACS, discusses this complex relationship and the data presented at the American Diabetes Associations’ recent “Diabetes, Pancreatogenic Diabetes, and Pancreatic Cancer” symposium, describing the current understanding of the interrelationships between diabetes, diabetes management, and pancreatic cancer, and identifying areas where additional research is needed.

Diabetes 2017;66:1103–1110 | DOI: 10.2337/db16-1477

COLLABORATION UPDATES

- The Brenden-Colson Center has recently engaged with several outside groups for developing patient cohorts and studies, including **Sutter Health**, one of the nation’s largest private health care providers based in Northern California.
- New European partnerships include the **CRUK/MRC Oxford Institute for Radiation Oncology** (Dr. Eric O’Neill), and the Liverpool Pancreas Biomedical Research Unit in the Department of Clinical Cancer Medicine, **University of Liverpool** (Prof. Eithne Costello).
- The BCCPC has also established a collaboration with Dr. Jody Hooper of **Johns Hopkins University** to acquire tumor tissues collected at autopsy.
- Dr. Craig Dorrell (OHSU Stem Cell Ctr) has established conditions to utilize PDAC patient-derived organoid cultures in a high-throughput screening program run by Drs. Christopher Kemp and Carla Grandori at the **Fred Hutchinson Cancer Research Center**. Drs. Kemp and Grandori provided therapeutic compounds, including the NCI Cancer Target Development and Discovery drug panel, for screening the organoids.



Brenden-Colson Center leadership clean and happy as they view **Immunovia’s** chip fabricator in Sweden last fall. L to R: Brett Sheppard, Joseph Carroll, Andrea Yoshioka, Rosie Sears, Bree Mitchell, Chris Corless.

CLINICAL UPDATES

The BCCPC is expanding its **Science Tissue Donor** program. The goal of this program is to collect legacy tumor tissues to study samples that are known to be resistant to chemotherapies. The program is designed to efficiently collect tumor samples as soon as possible after death so as to prevent tissue breakdown. Patients and their next of kin specifically consent to this process, and a phone number has been set up for them to contact us directly to initiate the tissue collection. These types of samples will provide valuable insight as to why a therapy does not work and help us to create more effective therapies.

CONGRATULATIONS

Brenden-Colson Center Fellowships are designed to encourage researchers to launch new careers or new research directions and thereby advance the understanding of pancreatic biology, disease, and/or therapy. The first of these fellowships have been awarded to John Muschler, PhD, who will be designing research into the early-stage events of pre-malignant pancreas lesions, and to Stephanie Krasnow, PhD, who will be developing a clinical research program investigating cachexia biomarkers of pancreas cancer.



Meghan Joly, PhD (MMG, pictured left) received an **NCI F32 fellowship award** for her work examining the role of neuroendocrine transdifferentiation of pancreatic cancer cells on tumor progression and chemoresistance.

Brett Johnson, PhD (OCSSB) also received an **American Cancer Society Postdoctoral Fellowship** to study histologic and genetic heterogeneity in pancreatic cancer.

Daniel Marks, MD, PhD (Pediatrics) has been awarded funding from the **National Pancreas Foundation** for his collaboration with OSU researcher Oleh Taratula to study “Follistatin nanoparticle therapy for pancreatic cancer cachexia” – two researchers from different fields (nanoparticle chemistry, whole animal physiology) teaming up on a difficult clinical problem.

CEDAR Seed Grants were awarded to 3 Brenden-Colson collaborative projects!

Mara Sherman, PhD (CDCB), Ellen Langer, PhD (MMG) and Andrew Adey, PhD (MMG): “Defining early determinants of inflammation-driven pancreatic tumorigenesis” – will use innovative sequencing approaches to define genomic regions which may play a role in the early stages of pancreatic tumorigenesis, and will interrogate these regions to identify the critical factors driving this process.

Young Hawn Chang, PhD (BME), Summer Gibbs, PhD (BME), Brett Sheppard, MD (Surgery), Tania Vu, PhD (BME) and Melissa Wong, PhD (CDCB): “Harnessing circulating hybrid cell biology and ultrasensitive single cell imaging technology for early detection of pancreatic cancer” – will develop a new platform technology to accurately fingerprint a new class of circulating tumor cells-circulating hybrid cells. These circulating cells will serve as improved biomarkers to stratify early pancreatic disease and pancreatic cancer using non-invasive blood sampling.

John Muschler, PhD (OCSSB) and Emek Demir, PhD (CompBio): “Target and biomarker identification through mapping of signaling networks that control the evolution of pre-malignant epithelial lesions” – will work to identify the molecular features and networks that control the evolution of pre-malignant lesion in the pancreas, to identify vulnerabilities in pre-malignant lesions that can be targeted for early intervention.

The Brenden-Colson Center will sponsor the attendance at the **Cold Spring Harbor Laboratory Workshop on Pancreatic Cancer**, June 6-11, 2017, for two graduate students who submitted competitive applications for this funding: Keith Earley (Sears lab) and Katherine Michaelis (Marks lab). Keith and Katie will each present a poster at the meeting, and, after they return, provide an overview to Brenden-Colson researchers on points of interest from the workshop.

UPCOMING SEMINARS



Dr. Angela Koehler, PhD

Biological Engineering, MIT; Koch Institute for Integrative Cancer Research
Thursday, May 11th 12:00pm Richard Jones Hall 4340

Chemical Probe Discovery for Transcription Factors

Hosted by BCCPC and Physiology & Pharmacology

Eric Barklis, PhD (MMBI)

Friday, May 12th 9:00am CHH 3181 (1B)

Analysis of K-Ras interactions by proximity-dependent biotinylation

BCCPC Pancreas Research Monthly Meeting

Philip Stork, MD (Vollum)

Friday, June 9th 9:00am CHH 3181 (1B)

New therapeutic targets for K-Ras signaling in PDAC cells

BCCPC Pancreas Research Monthly Meeting

Sara Courtneidge, PhD, DSc (CDCB), **Summer Gibbs, PhD** (BME), & **Danielle Jorgens, PhD** (BME)

Friday, July 14th 9:00am CHH 3181 (1B)

Invadopodia in PDAC and beyond

BCCPC Pancreas Research Monthly Meeting

Special guests **Steven Leach, MD** (Director, David M. Rubenstein Center for Pancreatic Cancer Research, Memorial Sloan Kettering Cancer Center) and **Andrew Rhim, MD** (UTMD Anderson Cancer Center) have also accepted invitations from BCCPC to visit this year; dates and locations TBA.

*Save the date for the Brenden-Colson Center clinical conference on the latest pancreatic disease research, clinical trials, and treatment options, scheduled for **October 6, 2017**.*

RECENT GUEST SPEAKERS

Gloria M. Petersen, PhD – Purvis and Roberta Tabor Professor of Epidemiology, Mayo Clinic College of Medicine, and Deputy Director for Population Sciences, Mayo Clinic Cancer Center

Genetic Predisposition to Pancreatic Cancer: New Implications for Risk Assessment and Testing

Hosted by BCCPC and MMG on November 30, 2016

Dr. Petersen also gave a talk on her study on the ethics and feasibility of returning genetic test results to tissue donors and their families.

Diane M. Simeone, MD – Associate Director for Translational Research Perlmutter Cancer Center and Director, Pancreatic Cancer Center, New York University Langone Medical Center

ATDC is Required for KRAS-induced Pancreatic Tumorigenesis

Hosted by the Knight and CDCB on January 9, 2017

Jurre Kamphorst, PhD – Cancer Research UK Beatson Institute and University of Glasgow

The Fats about Cancer: the Effect of the Tumor Microenvironment on Acetyl-CoA and Lipid Metabolism of PDAC Cells

Hosted by BCCPC and CDCB on March 3, 2017

Mandar Muzumdar, MD – Harvard Medical School, Dana-Farber Cancer Institute

Investigating Genetic and Environmental Contributors to Pancreatic Cancer Progression

Hosted by BCCPC, the Knight, and HemOnc on March 10, 2017

If you have ideas about topics or information you would like to see in the newsletter please email us at brendencolsoninfo@ohsu.edu.