

# Research Into The Pancreatic Cancer Microenvironment May Provide Novel Treatment Avenues

Pancreatic cancer is one of the most difficult cancers to treat in part because of the poorly understood and complex mechanisms of disease progression. Pancreatic cancer is characterized by the infiltration of multiple inflammatory cell types that surround the tumor, known as the tumor microenvironment. This microenvironment is harsh and nutrient-poor yet cancer cells continue to adapt and grow. Research by 2017 [Seed Grant](#) Awardee Mara Sherman, PhD seeks to better understand how the interaction of the tumor microenvironment and cancer cells fuels tumor growth in order to find better treatment options.

New research published in *Cancer Discovery* by Dr. Sherman, of Oregon Health & Science University, found that a specific cell type within the pancreatic tumor microenvironment known as stellate cells have evolved mechanisms to “feed” energy to cancer cells. These stellate cells simultaneously regulate the expression of cancer-supportive genes by tumor cells and secrete factors that promote the survival and growth of cancer cells.

Dr. Sherman’s research demonstrated that inhibition of this energy-providing mechanism drastically suppressed pancreatic tumor growth. This suggests that there are potential avenues for treatment through targeting the metabolic pathways of the stellate cells.

While further investigation is needed, this study is an important stepping stone in understanding the pancreatic cancer

microenvironment. Dr. Sherman's research suggests that despite the statistics, pancreatic cancer may have a novel metabolic vulnerability, which may be targetable for therapeutic benefit.

Read Dr. Sherman's full paper at [Cancer Discovery](#).

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Dr. Sherman and Jurre Kamphorst, PhD, a co-author on this study, were interviewed as part of the National Cancer Institute's [RAS Initiative](#). From their website:

More than 30 percent of all human cancers – including 95 percent of pancreatic cancers and 45 percent of colorectal cancers – are driven by mutations of the RAS family of genes. NCI established the RAS initiative in 2013 to explore innovative approaches for attacking the proteins encoded by mutant forms of RAS genes and to ultimately create effective, new therapies for RAS-related cancers.

You can read the interview with Drs. Sherman & Kamphorst on the NCI's [website](#).

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## **New research illuminates complex architecture of pancreatic cancer tumors**

Recently published research from [Seed Grant](#) recipient, Matteo Ligorio, MD, PhD, of Harvard Medical School has expanded our understanding of how the stromal microenvironment shapes a pancreas tumor and can impact clinical outcomes.

Dr. Ligorio and his team discovered that cancer associated fibroblasts (CAFs) profoundly alter the tumor microenvironment promoting an aggressive cancer phenotype with the ability to proliferate (PRO) and metastasize (EMT), called the Double Positive (DP) phenotype. With the use of cutting-edge technologies including single-cell RNA sequencing, phospho mass spectrometry and mass cytometry it was revealed that the co-activation of MAPK and STAT3 signaling pathways in these DP cells. This discovery may provide a new combination therapy strategy to target these specific cancer cells.

Most significantly, this research highlights the significance of the intra-tumor architecture, and links it to treatment responsiveness. The diversity within the tumor means that the cells do not behave uniformly but instead make up different tumor “glands” with their own proliferative and metastatic propensity. These eight different types of tumor “glands” were associated with differences in stromal abundance and correlate with patient survival and treatment response.

This study is an important step forward in understanding the complex biology of the tumor microenvironment and paves the way for novel therapeutic strategies for pancreatic cancer.

Dr. Ligorio and his team “would like to thank the Hirshberg Foundation for their generous support throughout the years...and especially express gratitude for being selected as a recipient of the 2017 Seed Grant.”

We congratulate Dr. Matteo Ligorio on this publication. The determination to understand the complex tumor microenvironment is providing the possibility of improved therapeutic options, and ultimately, increased survival rates.

Full article:  
[https://www.cell.com/cell/fulltext/S0092-8674\(19\)30510-0](https://www.cell.com/cell/fulltext/S0092-8674(19)30510-0)

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# New Publication by Seed Grant Awardees from UCLA

We are pleased to share that the January 2019 issue of [Pancreas](#) features an article titled “Emerging Evidence for the Clinical Relevance of Pancreatic Cancer Exosome,” written by the Director of the UCLA Agi Hirshberg Center for Pancreatic Diseases [O. Joe Hines](#), MD; Hirshberg Seed Grant Awardees [Jonathan C. King](#), MD and [Guido Eibl](#), MD; and Roxanne L. Massoumi, MD.

The article explains that over the last 5 years, exosome biology has gained increasing interest as a field of study. While much is still unknown about the role exosomes play in human health and disease, there is growing evidence that exosomes – nanovesicles produced by nearly all human cell types – may play a crucial role in cancer biology.

The team behind this publication focused on the currently available literature to review how exosomes have the potential to change the clinical management of pancreatic ductal adenocarcinoma, the most common form of pancreatic cancer. Pancreatic cancer is an aggressive malignancy that is often treatment-resistant yet there is a limited understanding of the molecular mechanisms that underlie this behavior. A growing body of literature points to exosomes as the mediators of numerous processes utilized by pancreatic cancer tumors to grow, invade and spread in the body while evading the body’s innate defenses.

Exosomes may also be valuable markers of disease and provide information on prognosis and treatment efficacy. There is still much work to be done to fully understand the role exosomes can

play in diseases processes but there is clear evidence of their importance. **In the future, further understanding of exosomes and the role(s) they play in the biology of pancreatic cancer may have significant impacts on the diagnosis and treatment of this deadly disease.**

We are proud of the team behind this paper. Publishing an article in a renowned medical journal is an important milestone for all scientists. We are hopeful that further research into exosome biology yields results for the treatment of pancreatic cancer.

[Read the full article »](#)

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## **Symposium Speaker Spotlight: Wendy Conlon to discuss Genetic Counseling**

The Hirshberg Foundation is happy to announce that genetic counselor, Wendy Conlon, will be joining us at the 15th Annual Symposium on Pancreatic Cancer to discuss the importance of genetic counseling.

Wendy Conlon, MS, CGC, is a genetic counselor board certified by the American Board of Genetic Counseling and licensed in California. She received her MS in genetics from the University of Arizona's genetic counseling program in 2000, and received her BA from the University of Vermont in 1988. Before attending graduate school, she worked in a laboratory at the University of Vermont Cancer Center and performed genetic testing for

hereditary cancer predisposition for Lynch syndrome, retinoblastoma, Li-Fraumeni syndrome and others. Prior to coming to UCLA, her career as a genetic counselor has included over 12 years in the biotechnology industry working with physicians, scientists and patients in the development and provision of genetic testing, focusing on hereditary cancer and endocrinology. She has also worked as a clinical genetic counselor in varied settings, including adult cancer genetics, assisted reproductive technology and prenatal and preconception genetics.

Wendy is currently one of two genetic counselors that are part of the Integrated Practice Unit (IPU) at the [UCLA Agi Hirshberg Center for Pancreatic Diseases](#). With approximately 5 to 10 percent of pancreatic cancers linked to an inherited cancer predisposition, the IPU offers [genetic testing](#) and counseling. A genetic counselor can assess the likelihood that pancreatic cancer in a family is due to an inherited mutation and help to understand personal and family history with pancreatic, and all cancers. Results from genetic testing may also be used to devise tailored surveillance and risk reduction strategies for at-risk family members.

A highly requested topic, we are excited to have Wendy joining us to discuss the topic of *Why Should I See A Genetic Counselor?* at the 15th Annual Symposium.

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## **Symposium Speaker Spotlight:**

# Dr. Joe Hines to discuss Personalized Medicine & Tumor Testing

The Hirshberg Foundation is excited to have [Dr. Hines](#) joining us at the 15th Annual Symposium on Pancreatic Cancer to discuss personalized medicine and the importance of tumor testing.

Dr. O. Joe Hines is the Professor and Chief of the Division of General Surgery, Robert and Kelly Day Chair in General Surgery and the Vice Chair for Administration. He serves as the Director of the [UCLA Agi Hirshberg Center for Pancreatic Diseases](#). Dr. Hines attended the University of Oklahoma College of Medicine and was inducted into Alpha Omega Alpha Honor Society in 1989. He trained in general surgery at UCLA, including two years of research in gastrointestinal physiology, and was then recruited to the UCLA faculty in 1997. While at UCLA he has received the Department Golden Scalpel Award for teaching excellence 10 times and the UCLA School of Medicine Award for Excellence in Education.

His research has focused on angiogenesis, cytokines, and pancreatic carcinogenesis, including the role of diet in modulating these processes. Dr. Hines' research has been consistently funded by NIH, and he has served in the NIH Scientific Review Committee Tumor Progression and Metastasis. Dr. Hines is past-President of the Society of University Surgeons and has served as the Vice-President of the Pacific Coast Surgical Association, President of the Southern California Chapter of the American College of Surgeons, and now on the Board of Governors of the American College of Surgeons and as a Director of the American Board of Surgery. Dr. Hines was awarded

the American College of Surgeons Traveling Fellowship to Germany in 2005, and was a James IV Traveling Fellow in 2011.

Dr. Hines will speak on *Personalized Medicine and Tumor Testing* along with fellow [surgeon Dr. Timothy Donahue](#).

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## **Symposium Speaker Spotlight: Dr. Timothy Donahue to speak on Personalized Medicine & Tumor Testing**

The Hirshberg Foundation is excited to welcome Dr. Donahue to the 15th Annual Symposium on Pancreatic Cancer to discuss personalized medicine and tumor testing.

Dr. Timothy Donahue attended Northwestern University where he received both his Bachelor's degree and Medical degree. Upon completion, he continued his surgical and research training at UCLA. In 2009, he was appointed faculty and has made strides at UCLA ever since.

Dr. Donahue is a Professor of Surgery at the David Geffen School of Medicine at UCLA. He has a joint appointment in the Department of Molecular and Medical Pharmacology to facilitate his research program. Dr. Donahue is the Chief of the Division of Surgical Oncology and Vice Chair for Cancer Surgery in the Department of Surgery. In this role, he oversees all of cancer surgery including the pancreatic cancer program, which is one of the largest in the nation. Dr. Donahue is a valuable part of the



surgical team at the [UCLA Agi Hirshberg Center for Pancreatic Diseases](#). In addition, Dr. Donahue is also the Program Director of the General Surgery Residency Program at UCLA.

Dr. Donahue is a very busy pancreatic surgeon who works diligently performing up to three pancreatic surgeries per week. He is especially interested in caring for patients with pancreatic cancer. His clinical research is focused on improving the care of patients with borderline resectable or locally advanced disease. Dr. Donahue is a strong advocate of prolonged [preoperative chemo](#) or radiation therapy for this group of patients to optimally select for those who will benefit from a surgical resection. As a result of this approach, Dr. Donahue and his team have among the best survival rates that have been reported. In addition to his clinical work, Dr. Donahue is the Principal Investigator of a National Institutes of Health funded research laboratory. His scientific research focuses on developing improved treatment strategies and earlier diagnostic markers for patients with pancreatic cancer. He collaborates closely with other scientists across the UCLA campus, including faculty in the Ahmanson Translational Imaging Division and California Nanosystems Institute. He is optimistic that therapy for pancreatic cancer will markedly improve during his career.

Dr. Donahue will speak on *Personalized Medicine and Tumor Testing* along with fellow [surgeon Dr. Joe Hines](#).