Understanding Early Tumor Progression Through Tuft Cells

One of the main ways to improve the outcomes for pancreatic cancer patients is early diagnosis and the way to better diagnostics is through a greater understanding of the initiating events in tumor progression. That is exactly what Kathleen DelGiorno, Ph.D. and her lab at Vanderbilt University are studying.

Dr. DelGiorno was a 2018 Seed Grant Awardee back when she was at The Salk Institute for Biological Studies in the Wahl Lab. Thanks to funding from the Hirshberg Foundation, she was able to publish her research, collaborate on other publications, and in her words, "become a much more attractive candidate for Assistant Professor positions." We were thrilled to hear that in July 2020 she was offered the position of Assistant Professor at Vanderbilt University in Nashville, TN. She wrote to Agi, "Your generous funding has allowed me to be very productive over the last year. Thank you so much for launching my career!" Dr. DelGiorno's success is emblematic of what our Seed Grant program aims to achieve.

Below, read more about Dr. Kathy DelGiorno's research and what she has been studying thanks to support from the Hirshberg Foundation.

Dr. DelGiorno's research is looking to uncover early changes in the pancreas that lead to tumor formation. Chronic pancreatitis is a known risk factor for pancreatic ductal adenocarcinoma (PDAC), which accounts for more than 90% of pancreas cancers,

and is characterized by inflammation, fibrosis and acinar to ductal metaplasia (ADM). ADM is a process where acinar cells (differentiated specialized cells in the pancreas) undergo remodeling back to ductal-like cells when the pancreas is injured. When oncogenic KRAS is present, ADM can be initiated, but the reversal of ADM does not happen, leading to metaplastic cells (less differentiated cells) that can then lead to precancerous lesions such as pancreatic intraepitheliel neoplasia (PanINs) or directly into PDAC. Dr. DelGiorno also studies tuft cells, which are solitary chemosensory cells seen throughout the hollow organs of the digestive tract and have been found to form spontaneously in the pancreas as the result of injury or tumorigenesis.

Research published by Dr. DelGiorno in *Frontiers in Physiology* details the landmark formation of tuft cells in the pancreas of wild-type mice, those with no genetic mutations, in the context of wound healing. This study linked tuft cell formation to ADM and shows that ADM takes place in the pancreas of mice after injury. This research demonstrates that wild-type mice can be used as a model and establishes a system to further study pancreatic tuft cells.

Subsequent research published in *Gastroenterology*, demonstrated that the formation of tuft cells originated during ADM, and that tuft cell generation may be a step in the process of tumorigenesis in the pancreas. The study found that when tuft cell formation was inhibited, pancreatic cancer development increased. They analyzed gene expression and found differences in the genes involved in inflammation, lipid (fat) synthesis, and metabolism. Prostaglandins, lipids that have hormone like functions, specifically prostaglandin D2, was shown to be lower when tuft cells were deleted. These lipids play an important role in keeping the pancreas from becoming inflamed and activating stromal cells, which contribute to pancreatic tumor

formation. This suggests that tuft cells may actually restrain early tumor progression by secreting lipids, which inhibit inflammation.

Recently, Dr. DelGiorno's lab at Vanderbilt released a pre-print (a research paper that is still under peer review) at bioRxiv using single cell sequencing to characterize all of the cell types that result from ADM and pancreatic injury. They found that, in addition to tuft cells, ADM is also characterized by enteroendocrine cell formation, cells that generate hormones with the potential to control information, tissue injury, and tumor formation. The DelGiorno lab is now studying how these cells control tumor formation and their potential to become tumors themselves.

Through her lab at Vanderbilt, Dr. DelGiorno's research continues studying how tuft cells inhibit tumors in the hopes that these pathways can be mimicked therapeutically. Her ultimate goal is to exploit anti-tumorigenic signaling or target pro-tumorigenic signaling pathways in the hopes of benefitting patients. We applaud the work of Dr. DelGiorno and her lab for their contributions to understanding the early mechanics of tumor formation.

These advances are made possible thanks to your support. Thank you for helping us fund this vital research.

New Podcast from Pancreatic

Cancer Survivor Offers Hope

Since her diagnosis with an inoperable pancreatic tumor in 2002, Roberta Luna has embarked on many new adventures. From her first half-marathon, to her first tattoo to her first of many sky diving trips, Roberta has embraced living life to its fullest. As she said, "we tend to put off doing things we want to… because we think there's plenty of time down the road." So when the opportunity to host a podcast radio show on OC Talk Radio presented itself, Roberta, along with her husband and caregiver, Vic, began yet another first.

"Vic and I recently had the opportunity to take another leap of faith and embark on a new journey with OC Talk Radio. We have created the podcast and radio show, *Living Hope; Your Journey with Pancreatic Cancer*."

Through their podcast, Roberta and Vic hope to provide information and resources, share inspirational stories, give hope to those affected by pancreatic cancer. With new episodes available on Thursdays, Roberta is not only sharing her story, but stories from across the pancreatic cancer community. As she shared, "through my experience with this horrific disease, I believe I am here to help those who have also been affected by pancreatic cancer, to hopefully inspire them and give them much needed hope."

Roberta is a wife, mother, self-proclaimed thrill-seeker, tireless advocate and volunteer, and as of April 1, 2021, a 19-year pancreatic cancer survivor, with an inoperable tumor due to artery & vein involvement.

Vic and Roberta hope to share the journeys of various patients, caregivers and advocates, including the good, bad and ugly of facing this disease. They aim educate, raise awareness, provide

hope and spark inspiration in their audience. Together, the pancreatic cancer community can weather the storm with the support of loved ones, family, “the purple family” and the many people encountered along this often-difficult journey. We are happy to support Roberta and Vic on their latest endeavor!

Learn more and listen to their show → https://livinghopepc.com/
Follow along on their Facebook page → https://www.facebook.com/LivingHope2055

Pancreatic Cancer: Our Goals and How to Achieve Them!

We are excited to have Dr. William H. Isacoff return to our Patient & Family Webinar series with a follow-up to his previous webinar *Chemotherapy for Pancreatic Cancer Patients: Less is More!* Dr. Isacoff is a fan-favorite and we are happy to have him share, once again, with our community.

Dr. William H. Isacoff, who leads the Pancreatic Cancer Center of Los Angeles, has earned a reputation as one of the foremost gastrointestinal oncologists within the United States. He has developed treatment regimens which were not only more effective, but less toxic and extended the lives of pancreatic patients throughout the country. He continues to focus on the development of newer, more effective and less toxic treatments for patients with pancreatic cancer.

In July of 2020, Dr. Isacoff shared important information about his low dosage “metronomic” chemotherapy without radiation therapy. Dr. Isacoff and the Pancreatic Surgical Team at UCLA

have down staged more than 60 patients who upon initial diagnosis were felt to be inoperable. After successful “metronomic” treatment with a combination of chemotherapies, the patients were then able to become surgical candidates. In addition, as a result of the prolonged use of effective chemotherapy, 75% of the patients had lymph nodes that did not show metastatic disease. Dr. Isacoff shared these promising results and looks forward to continuing the conversation with his latest presentation.

William H. Isacoff, M.D., currently holds an academic appointment within the Department of Medicine at the David Geffen-UCLA School of Medicine. He serves on the Board of Directors of the Jonsson Comprehensive Cancer Foundation. He serves on the International Board of Governors of the Hebrew University of Jerusalem, and is a lifetime trustee of that university. He has designed clinical trials for and served as a consultant. He has worked for four decades to form better, safer and more effective treatments for patients battling pancreatic cancer and other gastrointestinal cancers.

Watch Webinar

The Financial Costs of Cancer

Cancer can be a very expensive illness. Even those with excellent insurance can face an array of new costs associated with their treatment. From transportation to hospital stays, prescriptions to medical devices, daily living expenses to

holistic care, there are a multitude of expenses to consider. Being organized and understanding your rights can give you a sense of control while helping prioritize.

Through our longstanding partnership with Cancer Care, patients are able to apply for a one-time grant to help cover the costs associated with cancer treatment. Cancer Care also provides an array of financial assistance resources to help cancer patients and their families better cope with financial concerns.

Below are some of the resources Cancer Care offers to help manage the financial costs of cancer.

- Managing The Cost of Cancer booklet. This guide will help you navigate what is covered by health insurance and what is not, as well as tools to help handle the cost of cancer.
- Tips for Managing the Cost of Cancer is a great overview of things to consider as you begin navigating a cancer diagnosis.
- Co-payment assistance is a program to help cancer patients overcome the financial barriers to prescribed treatment through co-payment aid.
- Understanding the Costs of Care and Your Health Care Coverage is a workshop that addresses the medical and indirect costs of treatment, benefits and limitations to health care plans, as well as advanced health care directives, led by a panel of experts.
- In addition to finances, there are legal considerations when facing cancer and Cancer Care offers legal assistance as well.
- A Helping Hand is a resource guide to help cancer patients and their families take control of their finances. This booklet can help you understand your options, know your rights and know where to turn for help. It will introduce

issues to consider such as government assistance, nonprofit hospitals and community programs near you that may help defer some of the costs.

>We are here to help, contact Patient Support today to receive additional information and resources.

Summertime Purple Ribbon Events are Making a Comeback!

Returning to in-person activities is becoming a reality for many across the country and we're excited about the countless reunions that await! As we begin dreaming up plans to re-unite with friends and family, we're inviting you to turn this reunion into a Purple Ribbon Event. Start a new tradition marking the occasion of a post-pandemic world or celebrate a birthday, anniversary or an upcoming holiday while supporting the fight against pancreatic cancer!

We're providing Purple Ribbon Event ideas and themes to get you excited, a planning checklist and event tips to help you get creative. Follow 5 simple steps to get started: choose a virtual event idea, ask a friend to help plan & co-host, create a fundraising page, select a location or online video platform, follow our checklist. Contact us at sbanks@pancreatic.org if you have questions about hosting an event or fundraising- we're happy to assist.

The Hirshberg Foundation is eager to launch new research in 2021 and offer more programs to patients and you can be a huge part of that!

Host an In-Person Event

Our in-person Purple Ribbon Event checklist and tips will help you get started, show you how to make a plan and how to use this fun opportunity to fundraise for cancer research too!

- Birthday Dinner
- Backyard BBQ
- Golf Tournament

- MudRun

…and more!

Host a Virtual Event

Connect virtually for a socially distanced event and we'll provide ideas and tools & tips on how to take an event online or virtual.

- Game/trivia night
- At-home scavenger hunt
- Cocktail making party
- Remote Walk/run

…and more!

Clinical Trial Awareness

Clinical trials are a crucial tool for advancing medical knowledge and patients who participate can benefit from these new and emerging treatments. Understanding the clinical trial process and how to find a trial can empowers patients to make informed treatment choices from day one. Today, the NIH website lists more than 280 pancreatic cancer clinical trials actively recruiting in the United States. Whether the trial is for adenocarcinoma (PDAC) or neuroendocrine tumors (NETs), the goal of a pancreatic cancer clinical trial is to improve patient outcomes and save lives.

The Clinical Trial Process

The complex nature of pancreatic cancer requires attacking the disease from all directions. Clinical trial research is designed to analyze and question the benefits and risks of a promising new treatment before it can be approved for patients. Emerging cancer treatments include, but are not limited to, new drugs, drug combinations, targeted therapy, immunotherapy, radiation and chemotherapy. Over the course of months or years, a promising pre-clinical study advances into a human clinical trial that builds from phase I to phase IV. Trials are developed for all stages of pancreatic cancer and may recruit participants

in phases I-IV. If each phase demonstrates success, the therapy is approved by the FDA and made available to public.

Clearing Up Misconceptions

Experimental treatments developed in clinical trials can offer a lifeline for patients and families. That is why it is critical that patients' concerns and questions are addressed. One common misconception is that clinical trials are a last resort. New drugs and treatments can actually be beneficial early-on in a treatment plan rather than waiting until options are exhausted.

Another common roadblock for patients is an initial apprehension as to how safe a clinical trial is because of its experimental nature. Clinical trials have some risk, however, from start-to-finish specific practices are put in motion to ensure patient safety. Patients must give informed consent and researchers develop clinical trial protocols, follow FDA regulations, are monitored and scrutinized by an Institutional Review Board and Data & Safety Monitoring Board. World-class scientists are committed to unlocking the answers to pancreatic cancer through clinical trials and accomplishing the task safely. <

Finally, it is important that the people who are eligible and will benefit from the research are represented in clinical trials. In 2018, an FDA Clinical Trial Snapshot disclosed that 48% of all adult clinical trials missed their target recruitment goal for minorities. Balanced representation can only be achieved if patients, doctors and clinical trial recruiting processes share this goal.

Finding a Clinical Trial

Clinical trials are helping to transform medicine, personalize treatment and expand our medical knowledge for generations to

come. If you are interested in exploring a clinical trial, discuss this option with your oncologist or physician. The following resources can help you or a loved one find a clinical trial that is right for you.

We are here to help, contact Patient Support today to speak with our Patient & Family Coordinator.

- Hirshberg Foundation video A-B-C's of Clinical Trials
- National Institutes of Health NIH) clinical trial database
- National Cancer Institute (NCI) search tool
- MassiveBio's SYNERGY search platform
- EmergingMed's clinical trial navigator service
- Let's Win PC video on How to Find a Clinical Trial
- UCLA clinical trial search tool