Seed Grant Research Update: Biomarkers for Early Detection

The Hirshberg Foundation's Seed Grant Program remains instrumental in funding pancreatic cancer research worldwide, spanning many critical areas. Although pancreatic cancer is difficult to detect early, the Foundation is committed to changing these outcomes through scientific advancement. With this goal in mind, in 2017, Nelson Yee, MD, PhD, RPh was awarded a Seed Grant to fund a project for early detection: *Extracellular Vesicles as Biomarkers for Early Detection of Recurrent Pancreatic Ductal Adenocarcinoma.* The aim of Dr. Yee's study is to determine whether Nanoscale extracellular vesicles cargo proteins and nucleic acids can sensitively detect early recurrence of pancreatic cancer. Early detection is a critical step to fighting pancreatic cancer. As he continues to make strides forward, we look forward to sharing more updates.

In 2022, Dr. Yee shared that ten (evaluable) enrolled patients had undergone surgical resection of pancreatic carcinoma. Each patient was followed up with surveillance and their blood specimens were to be collected and stored as described in the protocol. Dr. Yee and his team have been analyzing (using the proposed methodology and novel methodology) the blood specimens for extracellular vesicles and genetic mutations along with the clinicopathological data.

2023 Project Abstract:

The mortality rate of pancreatic cancer is among the highest among all human malignancies, and treatment is mostly palliative except for patients with localized tumor that can be resected with a curable intent. Even following surgical resection, the

rate of tumor recurrence either locally or as distant metastasis is frequently high. Molecular biomarkers for early detection of tumor recurrence following surgical resection will facilitate prompt treatment and improve patient survival. However, there is no sensitive and specific method or biomarkers for detecting tumor recurrence.

Nanoscale extracellular vesicles (nEVs), molecules in bodily fluids, contain proteins and nucleic acids, which can reflect disease status. Hence, we hypothesize nEV cargo proteins and nucleic acids could sensitively detect early recurrence of pancreatic cancer. In our previous study, we developed a lipid nanoprobe (LNP) system for rapid and efficient nEV isolation and performed subsequent nEV cargo analyses. The LNP system overcomes low throughput, low purity and other common shortcomings in nEV isolation, showing great potential for clinical use. This proposed research aims to use the LNP system to analyze several key proteins and genetic mutations, and to evaluate these molecules as biomarkers of pancreatic cancer recurrence.

The validation of this hypothesis will demonstrate the potential of nEV cargo as a promising tool to track evolution of pancreatic carcinoma and monitor tumor dynamics with the goal of improving survival of patients. We have completed collection of the blood specimens and molecular data as well as the clinicopathological data of the enrolled subjects. We have been analyzing the biospecimens along with the clinicopathological data, and we expect to report the study results in the year 2024.

To date, the Hirshberg Foundation has provided funding for more than 120 research projects in the following areas: treatment/therapy, patient care, early diagnosis, detection, cancer biology, basic science, prevention/metabolism and

research core facilities. Make a donation today in support of early detection research and cutting-edge science funded by the Hirshberg Foundation.

Momentum Newsletter: Winter 2023

As 2023 comes to a close, the Hirshberg Foundation reflects on another exciting year marked by achievements in scientific collaboration, patient support, and much more. Your ongoing support has been instrumental in fulfilling our goals every year. Together, we are fostering innovation, driving advancements in research, and creating a meaningful difference in the well-being of patients.

Seed Grant Announcement

In August, a remarkable 126 Seed Grant applications were received, setting a record for the Foundation. Submissions poured in from locations across the United States and internationally, with a notable emphasis on collaborative initiatives involving multiple research institutions. We are delighted to unveil the 2023 Seed Grant Cohort with projects spanning early detection, treatment, immunotherapy, and basic science. You can also watch our Seed Grant Program video.

UCLA Scientists Meeting

This past October, we hosted a gathering of scientists and researchers working on pancreatic cancer at UCLA, highlighting some of our past Seed Grant awardees. With the goal of sharing innovative work across disciplines, connect researchers, and foster collaboration, it was an inspiring afternoon. Learn more about the presentations as their insights give hope for what's to come.

American Pancreatic Association Meeting

This year, we sponsored a groundbreaking symposium on Artificial Intelligence in Pancreatic Cancer at the American Pancreatic Association (APA) Annual Meeting. Moderated by our Scientific Advisory Board Chair, Miklos Sahin-Toth MD, PhD, the lectures were led by researchers from Mayo Clinic, Cedars Sinai, and MD Anderson Cancer Center each discussing innovation in the AI space as it relates to early detection and diagnostic tests. You can watch our APA Video on AI. With your support, we are empowering the medical community to pursue groundbreaking research and initiatives that make an impact across the globe.

Patient Support with CancerCare

Recently, we received our annual report from our esteemed financial aid partners at CancerCare. This enduring relationship has been pivotal to extending support to patients across the country through a modest one-time stipend. This assistance has provided funds to survivors for transportation, copays, treatment, and more. We can fund crucial patient programs like

this thanks to your commitment and generosity.

Genetic Counseling Webinar

As part of Pancreatic Cancer Awareness Month, the Foundation offered an interactive Zoom webinar Ask a Genetic Counselor: A Q&A to learn about testing and risks with UCLA's Wendy Conlon, MS, CGC. This event, perfect for those with a family history of pancreatic cancer or those who have questions for a genetic counselor, addressed how knowing your family history and your genetic makeup can affect medical care options for you and your loved ones. Watch the recorded webinar to learn more on this topic.

26th Annual LA CANCER CHALLENGE

October 23rd was a magical day for the LA Cancer Challenge as we celebrated great strides made in patient support and pancreatic cancer research. Coming together as a community to raise awareness and funds for research is one of the best days of the year for our community. Thanks to you, we raised over $547,000 as participants across 30 states and 3 countries shared our message of hope. Thank you for rallying with us as we Fight to the Finish. Rember to save the date for next year's LACC on Sunday, October 27th!

2024 Save the Dates

Symposium – Saturday, April 13, 2024
Hirshberg Training Team at the LA Marathon – Sunday, March 17, 2024
Purple People Party – Sunday, March 17, 2024

Tour de Pier – Sunday, May 19, 2024
LA Cancer Challenge – Sunday, October 27, 2024

The 2023 APA Meeting highlights the impact of AI in pancreatic cancer research

The partnership between The Hirshberg Foundation and the American Pancreatic Association (APA) continues to unite brilliant minds, showcases significant topics and keynote speakers, and highlights the contributions of researchers through an annual award. The APA meeting typically assembles a global community of scientists and clinicians each year who present and delve into the latest research findings on pancreatic diseases. This year, the Foundation sponsored a groundbreaking symposium on Artificial Intelligence in Pancreatic Cancer and presented two remarkable scientists with an award for the Best Abstract in Pancreatic Cancer.

Moderated by our Scientific Advisory Board Chair, Miklos Sahin-Toth MD, PhD, individual presentations were led by researchers from Mayo Clinic, Cedars Sinai, and MD Anderson Cancer Center, each discussing innovation in the AI space as it relates to early detection and diagnostics. The topics included:

- Harnessing Next Generation Imaging for Redefining Early Pancreas Cancer Detection, presented by Ajit Goenka MD, FSAR.
- PDAC Risk Prediction Using Artificial Intelligence

Analysis of Pre-Diagnostic Abdominal CT Scans, presented by Debiao Li PhD.
- Integrating Radiomics, AI, and Biomarkers into Early Detection Strategies, presented by Eugene Koay.

We invite you to watch a recording of these presentations and learn more about the impact of AI in pancreatic cancer research. The Foundation is dedicated to empowering an ever-growing research community by promoting the exploration of new and innovative approaches to combat this disease.

Join us in also celebrating the winners of the 2023 Best Abstract in Pancreatic Cancer Award. Michael Pfluger MD at Johns Hopkins University was presented with the award based on his work on Ductal Cancerization at the Pancreatic Neck Margin – Prevalence and Clinical Implications. In addition, Xiuhui Shi MD at the University of Oklahoma Health Sciences Center received the award for their work based on ZIP4 Promotes Anorexia and Cachexia Through Activating Tumor-Associated Macrophage Infiltration and GDF15 Secretion in Pancreatic Cancer Research.

Updates from our UCLA Seed Grant Recipients

In early October, we hosted a gathering of scientists and researchers working on pancreatic cancer at UCLA, highlighting some of our recent Seed Grant awardees. With the goal to share innovative work happening across disciplines, connect researchers, and foster collaboration, it was an inspiring afternoon.

We're excited to share some updates from past Seed Grant researchers that came from this gathering. We look forward to sharing more from these great minds as the afternoon sparked connections and potential future collaborations.

In 2019, Thuc Le, PhD, was awarded a Seed Grant for his project *Mapping and Targeting Nucleotide Biosynthetic Plasticity in Mutant KRAS Driven Pancreatic Cancer*. This research focuses on tackling mutant KRAS in pancreatic cancer and understanding its effects on cell signals and metabolism to influence the immune response. One important discovery that has been made to date is that blocking KRAS leads to higher levels of adenosine released by tumor cells, which can make the immune system less effective. Combining therapies that target both KRAS and adenosine shows promise in achieving stronger anti-cancer effects in this difficult-to-treat cancer.

Some pancreatic adenocarcinoma (PDAC) patients survive exceptionally long despite metastatic disease; these patients are able to generate effective, systemic immune responses against their tumors. Jason Link, PhD, a 2022 awardee, looked at the anti-tumor immune response that takes place in tertiary lymph structures to understand if these structures can be therapeutically ignited as a treatment avenue. Patients with poor outcomes fail to generate these immune responses due to ineffective signals between the tumor and immune cells, but these signals are therapeutically targetable.

KRAS mutations are the most common drivers of pancreatic ductal adenocarcinoma (PDAC). Recent clinical translation of mutant KRAS-specific inhibitors has reinvigorated hope for direct targeting; however, research has shown they need to be administered as combination therapies. Research from Evan Abt, PhD, a 2022 Seed Grant Awardee, uncovered new mechanisms that restrain anti-tumor immunity in pancreatic cancer. The

suppression of the immune response is partly due to unexpected crosstalk between metabolic and immune networks. These insights provide a rationale for new therapeutic interventions to unleash immune responses targeting pancreatic cancer.

2022 Seed Grant researcher, Alexandra Demcsak, MD, PhD, looked into hereditary pancreatitis, an early-onset form of chronic pancreatitis caused by mutations in the digestive proteases (enzymes that break down proteins). Her research investigated the effects of carboxypeptidase A1 (*CPA1*) gene mutations on pancreatic ductal adenocarcinoma development. Based on the results, the p.N256K mutation of the *CPA1* gene accelerates the development of precancerous lesions in the pancreas of *KrasG12D x p48-Cre* models. These findings provide support for the concept that misfolding *CPA1* mutants are risk factors for pancreatic ductal adenocarcinoma, deepening our understanding of how chronic inflammation promotes tumor growth in the pancreas.

An innovative 2021 Seed Grant project by Keisuke Iwamoto, PhD used weak magnetic fields to enhance treatment sensitivity of pancreatic cancer cells.

The projects presented at the UCLA gathering helped spark inspiration, collaboration, and connection across disciplines. We look forward to sharing future progress reports from these researchers as they continue their important work. It is because of your support that we can fund these crucial projects and help move science towards better diagnostic and treatment options, and ultimately, a cure.

2023 CancerCare Summary on Financial Assistance for Patients

At the heart of the Hirshberg Foundation's mission is our commitment to provide support for pancreatic cancer patients and their families as they navigate this disease. In 1998, the Foundation established a partnership with CancerCare, a national organization providing free, professional support services to help manage the emotional, practical and financial challenges of cancer. This longstanding relationship has allowed our organization to provide low-income patients with a one-time grant. Thanks to community fundraising and the generosity of our supporters, we have made a positive impact on thousands of survivors and loved ones thanks to this grant.
Each year, CancerCare provides the Hirshberg Foundation with a report on how these funds have been used to support patients and families thanks to our partnership. Below are details on the services provided.

2023 PROGRAM SUMMARY

In 2023, through the Hirshberg Foundation's grant program with Cancer Care, nearly 150 financial assistance grants were provided to pancreatic cancer patients. This grant helps to alleviate some of the hardship that can come with a cancer diagnosis and the devastating impact it can have on a patient's life. CancerCare was able to serve a diverse group of individuals impacted by pancreatic cancer throughout the country.

This year, the program served 67 women and 78 men with resources provided across 33 states including Florida, New Jersey,

Georgia, Pennsylvania, and California. Funds to help cover the cost of transportation to and from treatment continue to be the highest need for CancerCare clients; approximately 43% of grant funds disbursed over the course of the 12-month period were allocated to transportation. Copayment charges and treatment expenses were the second most needed type of assistance, at 28% of grant funds. The remaining financial assistance grants contributed to insurance premiums, imaging tests, home care, massage/acupuncture treatments, biopsies, and childcare.

LEARN MORE ABOUT THE CANCERCARE GRANT

To date, the Hirshberg Foundation has provided over $1.2 million dollars for this patient program offering limited financial assistance associated with transportation to and from treatment, pain medication, childcare, home care, and beyond. Funds are provided to low-income patients for whom it has been a vital resource over the years. Patients and families can learn more about eligibility and program information today.

CancerCare Program
Medicaid Eligibility
CancerCare also offers a wealth of other resources free of charge including support groups, educational workshops, co-payment assistance, and case management. Counseling is available in English and Spanish and centers on the emotional and practical challenges that arise from cancer.

More CancerCare Services

HIRSHBERG FOUNDATION PATIENT

RESOURCES

Patients and families are not alone in this journey. We are here to help guide you through the initial steps of educating yourself and your family about this disease. Learn more about programs, events, and resources offered by the Hirshberg Foundation when you watch this video and review our patient and caregiver support services .

Learn More

Participate this November to Help Raise Pancreatic Cancer Awareness

“Participate” is one of our three key calls-to-action for November’s Pancreatic Cancer Awareness Month and a great way to get involved with making a difference. Join us to help raise awareness and funds for pancreatic cancer research and crucial patient & family support programs. Participation, by attending an event or hosting one yourself, by fundraising and giving, or by raising awareness allows us to help thousands of patients year-round while driving research towards a cure.

Get started by telling your family and friends how important our cause is to you. Hearing first-hand how this disease has affected you can make all the difference and inspire others to action. Whether you start a Facebook Fundraiser, create a You Can H.E.L.P. Fund or share how pancreatic cancer has touched your life, telling your story is the first step. Next, invite

your community to become a part of this journey towards curing cancer. Give your loved ones an opportunity to donate and show their support.

Find great ways to ***participate*** this November!

On November 8th, join us and Wendy Conlon to discuss the benefits and implications of genetic counseling and testing for you and your family. A great opportunity to educate yourself and loved ones.
Register Today →

Love a good party, 5K or yard sale as much as we do? Host your own in-person or virtual event. We've made it easy with guidance and ideas to get you started.
Be a Host →

Looking for an even bigger challenge? Register today to run a full or half-marathon with the Hirshberg Training Team! Wherever you are, you can sport your purple while running and get personalized coaching to help you cross the finish line.
[Hirshberg Training Team →]

However you choose to ***participate*** in Pancreatic Cancer Awareness Month, let’s make it fun and meaningful!