

Summary of the Hirshberg Symposium at the 2024 American Pancreatic Association

Each year, the [APA](#) gathers a global community of researchers to explore the latest advancements and opportunities in clinical and basic science research focused on pancreatic diseases, with an emphasis on pancreatic cancer. As part of this collaboration, the Hirshberg Foundation hosts the annual Hirshberg Symposium, spotlighting cutting-edge topics. This year's symposium, *Targeting KRAS to Treat Pancreatic Cancer*, delved into the evolving therapeutic landscape of [KRAS](#) inhibitors and shared fresh perspectives on the biology and treatment strategies for pancreatic cancer.

Field and Historical Timelines

Channing Der, PhD
University of North Carolina, Chapel Hill

Dr. Der reviewed the seminal findings in the field of KRAS starting with the identification of this signaling protein and the central role it plays in cellular physiology. Dr. Der is an expert in KRAS, made many of the initial discoveries about KRAS and continues this research. Nearly all pancreatic cancers have a mutation in KRAS, and it is thought that this is an initiating factor in pancreatic carcinogenesis. KRAS may have the same impact on as many as 20% of all cancer types.

Current Therapeutic Landscape of KRAS

Inhibitors

Gabriela Chiorean, MD
Fred Hutchinson Cancer Center

Dr. Chiorean reviewed many of the clinical trials that have used KRAS inhibitors to treat cancer. Very recently, advances in the understanding of the structure and function of KRAS has allowed the ability to develop drugs that target this protein. Early trials with KRAS inhibitors like sotorasib (the first KRAS inhibitor approved by the FDA which targets the G12C mutation) and others indicate these drugs can have equal benefit to traditional chemotherapy in delaying cancer progression in patients with advanced disease. Now there is interest in combining KRAS inhibitors with other modalities like tumor vaccines and chemotherapy.

New Insights Into the Biology and Therapy Strategies for Pancreatic Cancer

Raghu Kalluri, MD, PhD
University of Texas MD Anderson Cancer Center

Dr. Kalluri reviewed the biology of KRAS inhibitors and how cancers can have variable KRAS mutations in tumor development. Importantly, it is possible to reverse the impact of KRAS on early changes in the pancreatic cancer development before the cancer is formed with KRAS inhibition in models. This demonstrates the importance of KRAS and how targeting this abnormally active protein is potentially very valuable for patient treatment.

Mechanisms of Resistance to KRAS Inhibitors

Andrew Aquirre MD, PhD

Dana-Farber Cancer Institute, Broad Institute at Harvard and MIT

Dr. Aquirre discussed the current status of KRAS drugs and relayed that there are as many as 100 new KRAS inhibitors in development to treat cancer. Each drug has a different mechanism of action and because pancreatic cancers can have variable expression of mutant KRAS throughout the tumor and over time, it will be important to understand the mechanisms of resistance to these new drugs so treatment can be revised for the patient as the tumor evolves.

The 2024 Hirshberg Symposium provided a comprehensive exploration of the latest advancements in [KRAS research](#), emphasizing its critical role in pancreatic cancer development and treatment. From historical milestones and groundbreaking therapeutic strategies to insights into resistance mechanisms and evolving clinical approaches, the panelists illuminated the promising future of targeting KRAS to improve patient outcomes.

As research continues to unlock new possibilities, collaboration and innovation are key to driving progress towards a cure for pancreatic cancer. The Hirshberg Foundation remains committed to supporting transformative research and sharing these critical updates with the community.

[Watch the full recording of the Hirshberg Symposium from the APA](#)

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What is Pancreatitis?

Pancreatitis is an inflammatory condition of the pancreas, with both acute (short-lived) and chronic forms, and a known risk

factor for developing pancreatic cancer, especially in cases of long-term chronic inflammation.

Inflammation is an important part of the body's response to infection or physical injury; it's the signal that brings in the immune cells to fight the infection or to start the healing process. Usually, when the infection or injury is resolved, inflammation stops, but sometimes, this does not happen. This is called chronic inflammation and can damage cells and tissues. While pancreatitis is rare, it is a risk factor for developing pancreatic cancer.

Acute vs Chronic Pancreatitis

- **Acute Pancreatitis:** This is a sudden inflammation often caused by gallstones that physically block the vessels of the pancreas or with heavy alcohol consumption. The main symptom is severe abdominal pain. While it usually affects just the pancreas, it can sometimes be more widespread and life-threatening.
- **Chronic Pancreatitis:** This type involves long-term inflammation that damages the pancreas tissue over time and can decrease the ability of the pancreas to function. A mixture of risk factors includes chronic alcohol use, tobacco use, and inherited genetic mutations. As the pancreas gets damaged, it can lead to issues like weight loss, malnutrition, and diabetes, and it raises the risk of pancreatic cancer.

Pancreatitis is generally considered acute (short-lived) or chronic, but there is a spectrum of disease between these two designations. Patients can have one acute case over the course of their lives or multiple episodes, and acute pancreatitis, when not treated, can lead to chronic pancreatitis.

Chronic Pancreatitis & Substance Abuse

Alcohol abuse can cause chronic pancreatitis and increase the risk of developing pancreatic ductal adenocarcinoma (PDAC), the most common form of pancreatic cancer. The risk is further increased in those patients who also smoke. As the body breaks down alcohol, it generates byproducts that can be toxic to cells. If there is a buildup of these toxic byproducts, an increase in digestive enzymes can occur. An overproduction of these enzymes, meant to break down protein in our foods, can disrupt the cells of the pancreas and lead to further health problems.

While genetics and inherited conditions are beyond our control, we can limit inflammation and reduce risk factors. [Ongoing research](#) aims to find better treatments and improve outcomes for pancreatitis patients. If you or a loved one has pancreatitis and needs help, please contact [Patient Support](#).

Researchers receive \$4 million to advance immunotherapy treatment for pancreatic cancer

We are proud to share that our collaborative efforts with the UCLA Health Jonsson Comprehensive Cancer Center have led to a transformative \$4 million grant from the National Cancer Institute (NCI). This grant aims to advance immune-based

therapies for pancreatic ductal adenocarcinoma (PDAC) to improve treatment and patient outcomes.

Immunotherapy employs drugs to boost the immune system's ability to identify and attack cancer cells. Under the guidance of [Dr. Timothy Donahue](#), Director of the Agi Hirshberg Center for Pancreatic Diseases, [Dr. Zev Wainberg](#), co-director of the UCLA Health GI Oncology Program, and [Dr. Caius Radu](#), professor of molecular and medical pharmacology, a multidisciplinary team is delving deep into the role of adenosine in the immune suppression associated with pancreatic cancer. Their work seeks to understand how adenosine, a molecule in the body, affects the tumor environment and interactions between immune and cancer cells.

The grant will also fund a follow-up clinical trial examining a small molecule inhibitor combined with the existing combination of PD-1, an immunotherapy drug, and chemotherapy before surgery. Building on promising initial results, this trial seeks to diminish adenosine production within tumors, potentially boosting the immune system's ability to fight cancer more effectively. Previous Hirshberg Foundation [Seed Grant](#) Awardees, Dr. Thuc Le and Dr. Evan Abt, have also been working to study adenosine.

“By introducing a small molecule inhibitor to the existing chemotherapy and PD-1 inhibition regimen, we hope to limit adenosine production in the tumor microenvironment, thereby enhancing the immune response against the cancer,” said Donahue in the article published by UCLA Health. “We are hopeful this strategy will help the body's natural defenses fight the cancer more effectively, leading to better treatments for people with pancreatic cancer.”

This substantial grant is a beacon of hope. We are optimistic

that this research will uncover new therapeutic strategies that target adenosine, enhancing patient outcomes and leading to better treatments.

Our Summer Momentum Newsletter

As summer kicks into gear with family vacations, hot temps, and cool adventures, the Hirshberg Foundation looks forward to sharing the latest updates with our foundation family. Your efforts throughout the year, from fundraising to event participation, have ushered in another season of groundbreaking scientific advances and patient support. Soon researchers will submit proposals for our annual Seed Grant Program, as patients, caregivers, and families gather again for seasonal events that educate and energize our community. We thank you for your continued support as we raise awareness and Never Give Up in the fight for a cure!

A Pancreatic Cancer Progress Report

At our Annual Hirshberg Symposium on Pancreatic Cancer we had the pleasure of welcoming Dr. Eileen O'Reilly, a member of our [Scientific Advisory Board](#) from Memorial Sloan Kettering Cancer Center, to speak. She discussed the genetics of the disease and the latest developments in pancreatic cancer treatments, immunotherapy, and vaccine approaches currently in development. With a new FDA-approved drug for pancreatic cancer, targeted treatments, and other emerging approaches, Dr. O'Reilly shared, "You'll see that there's real progress happening, and we're on the cusp of important developments in this disease that

hopefully will translate to improved outcomes.”

[Read Progress Report →](#)

Supporting & Educating Patients in June

In June, we honored the courage of pancreatic cancer survivors around the world throughout National Cancer Survivors Month. Survivors, caregivers, and families impacted by this disease generously shared [messages of hope](#) and expressed support for patients and survivors setting out on a journey to wellness. This was on the heels of our spring Symposium and the release of educational videos that educate and empower both patients and caregivers. This year’s Symposium included important topics such as improving patient care through a partnership with [Canopy Cancer Collective](#), [genetic testing](#), [pancreatic enzyme education](#), [survivorship in pancreatic cancer](#) and [PRECEDE](#), the international collaborative study to improve early detection. We encourage everyone to check out the wide array of topics, especially our inspiring [panel discussion](#), where survivors and caregivers share their experiences, wisdom, and hope.

[Watch the videos now →](#)

Esteemed Journal Shares Agi Hirshberg’s Journey

In July, *Pancreas*, a scientific journal of pancreatic diseases, published a beautiful article spotlighting our founder Agi Hirshberg’s story, and her unwavering commitment to cure pancreatic cancer. It is a story that all of us can connect

with; every family's journey with pancreatic cancer is unique and yet so familiar. At the heart of these stories is a desire to empower loved ones, ensure that no one faces this disease alone, and ultimately, eradicate pancreatic cancer once and for all. In the article, titled [Our Lady of Hope](#), writer Shweta Lavania shares "a tale of compassion, inspiration, and true labor of love." This interview will resonate with you, and we hope you'll check it out.

[Read the Article →](#)

Registration is Open for the 27th Annual LA Cancer Challenge

Our signature event, the [LA Cancer Challenge](#) 5K Walk/Run is coming up on October 27th and registration is officially open. This incredible event unites families, survivors, and the medical community for an extraordinary day raising awareness. The LACC is more than a 5K, this event will inspire you! Come participate in our Fit Family Expo, Candyland Kids Zone, Halloween costume contests, and much more. Join us [in-person](#) at UCLA or [virtually](#) from wherever you are, and know that your participation brings us closer to a cure.

[Register Today →](#)

Make a Lasting Impact on Research for Make-A-Will Month

National Make-A-Will Month is coming up in August. In the spirit of supporting our mission and advancing pancreatic cancer research in the future, we invite you to learn more about estate

planning. A gift in your will has the power to change patient outcomes and drive cancer research forward beyond your lifetime. Through [FreeWill: a free online state planning tool](#), you can support your loved ones, protect your possessions, continue philanthropic efforts, and secure your legacy. We also encourage you to learn about other ways to give from [matching event gifts](#) to [Donor Advised Funds](#). Thank you for your shared commitment to cure pancreatic cancer!

[Learn About Planned Giving →](#)

Tour De Pier Rides for Love and Raises \$1.5 Million

In its 12th year, [Tour De Pier](#) offers the ride of your life and a unique experience for participants. This year, we embraced our theme of “Ride for Love,” and together, we packed more love into the day than we ever thought possible. Thanks to everyone who participated the outdoor stationary cycling fundraiser, our community raised a remarkable \$1.5 million and counting. TDP’s success and our ability to support research and patient services rely directly on supporters harnessing the power of their community. Together we ride for fun, ride for love, ride for hope, and ride to cure cancer. We can’t wait to see you on May 18, 2025 for year 13!

[Learn More →](#)

2024 Upcoming Events

[Hirshberg Training Team 2025](#): October 5, 2024 – March 16, 2025

[LA Cancer Challenge](#): Sunday, October 27, 2024

[Pancreatic Cancer Awareness Month](#): November 2024

[World Pancreatic Cancer Day](#): November 21, 2024

[Giving Tuesday](#): December 3, 2024<

Pancreatic Cancer Progress Report 2024

On April 13, 2024, the Hirshberg Foundation held the 18th Annual [Symposium on Pancreatic Cancer](#). It was an honor to welcome Scientific Advisory Board member, Dr. Eileen O'Reilly to share [a progress report](#) on the state of pancreatic cancer research. [Dr. O'Reilly](#) is a professor of medicine at the Weill Cornell College of Medicine, a medical oncologist at Memorial Sloan Kettering Cancer Center, a principal investigator of multiple phase one, two, and three clinical trials for pancreatic cancer, and an international leader in finding ways to better treat this disease.

Dr. O'Reilly provides an overview of pancreatic ductal adenocarcinoma (PDAC), the current treatment landscape, and the shifting epidemiology of the disease. She focuses on the current and evolving treatments for advanced-stage pancreas cancer, DNA-damage-directed therapies, KRAS-directed therapies, and new emerging approaches.

A decade ago, the primary form of treatment for pancreatic cancer was limited to chemotherapy based on our understanding of the disease. Now, pancreas cancer is approached as a KRAS-altered disease, which provides a few more avenues for treatment. The current standard therapy includes three main chemotherapy options: mFOLFIRINOX, Gemcitabine with nab-

paclitaxel, and NALIRIFOX. There is also emerging evidence for more use of maintenance therapy or a [de-escalated chemotherapy](#). For certain patients, there is also the option for integration of local therapies such as radiation, surgery, or ablation.

One main area of research for pancreas cancer treatment is KRAS, as about 88 to 90% of people with pancreas cancer will have an alteration in KRAS. KRAS, an important signaling pathway in pancreas cancer, is involved in the growth and metastatic potential of this disease, and it comes in various flavors. Most common in pancreas cancer is something called KRAS G12D, followed by G12V, followed by G12R. One KRAS alteration to highlight is G12C because current regulatory approvals and drugs are available for use in the clinic to treat the small subset of individuals with this specific mutation. Targeting KRAS directly or indirectly, tackling the protein, working on the gene itself, looking to different versions of the gene, and combining it with other things are avenues of current investigation for pancreatic cancer.

Genetic targeting, in terms of BRCA1, BRCA2, and PALB2, is another important topic for pancreatic cancer treatment. Although these cases comprise 5 to 8% of this disease, they're a very important subset that can benefit from specific treatments. These treatment options include platinum-based therapy and PARP inhibitors. Genetic targeting also influences future treatment directions, and some very interesting areas are being studied.

A great deal is happening around the globe to advance research and treatment options for pancreatic cancer. As Dr. O'Reilly said, "you'll see that there's real progress happening and we're just on the cusp of I think very important developments in this disease that hopefully will translate into improvements and outcomes for people." We thank Dr. O'Reilly for her presentation and look forward to sharing more as these treatment options

develop.

Watch the [full presentation](#) →

Celebrate National Research Month in May

In recognition of National Research Month, we're shining a light on extraordinary scientific advances gaining momentum in pancreatic cancer. To date, the Hirshberg Foundation has funded over 120 Seed Grant projects leading to significant [NIH funding](#), clinical trials, and [improved patient outcomes](#). Groundbreaking ideas are coming to fruition, including the use of [artificial intelligence to analyze CT scans](#) for pancreatic cancer patients and an [mRNA vaccine](#) in the pipeline to prevent disease recurrence. The greater pancreatic cancer research community remains committed to discovering answers and we are watching them turn an exciting corner.

This month and throughout the year, we look forward to sharing news from our [UCLA laboratories](#), [Seed Grant projects](#), and updates directly from the headlines. Your generous support has allowed us to increase our research efforts worldwide and we look forward to announcing the results of their efforts!

ACTIVITY SUMMARY REPORT

The UCLA Activity Summary Report includes a comprehensive overview of advancements in research and patient care. From [66](#)

[open clinical trials](#) to individual Seed Grant updates, and news from the [Agi Hirshberg Center for Pancreatic Diseases](#) – the latest report details this progress over the past year.

[Read the Report](#)

RESEARCH LABORATORIES

The Hirshberg Foundation's UCLA laboratories have propelled research forward in the global medical community. The collaboration between the [Hirshberg Translation Laboratory](#) and the [Sahin-Toth Laboratory](#) is central to our work on campus as they make great strides forward.

[Learn More](#)

NCCN GUIDELINES

The Hirshberg Foundation is a sponsor of the [NCCN Guidelines for Patients: Pancreatic Cancer](#). These extensive guidelines include clinical trials and studies, care options, treatment protocols, and much more.

[Learn More](#)

ARTIFICIAL INTELLIGENCE

At the latest APA meeting, 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. [Take a look at our APA Video on AI](#), a symposium funded by the Hirshberg Foundation.

With your support, we are empowering the medical community to pursue groundbreaking research and initiatives that make an impact across the globe.