

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.

School of Nursing Grant Focused on Emotional Wellness

A new study, funded through the Hirshberg Foundation's [Seed Grant program](#), will focus on the emotional wellbeing of patients and their caregivers as they face pancreatic cancer.

Through a new partnership with the clinical teams at the [UCLA Agi Hirshberg Center for Pancreatic Diseases](#) and the psychosocial clinicians at the [Simms/Mann-UCLA Center for Integrative Oncology](#), Dr. [Eden Brauer](#), Dr. Denice Economou, and Barbara Demman have developed a study to identify the optimal way to provide a mindfulness-based intervention to patients and caregivers facing pancreatic cancer. The team has devised an intervention plan to provide four pre-recorded, self-paced

modules that will focus on four aspects of the cancer journey and ways to be mindful. These include: 1. Introduction to Mindfulness, 2. Cultivating Self-Compassion, 3. Making the Most of the Moment, and 4. Life Review and Legacy Envisioning.

These modules, recorded by a nursing faculty member who is a mindfulness certified facilitator, will be available online through a study website so participants can engage with them in a flexible way. This will allow study participants to access the four modules when it is convenient for them and as often as they need over a six-week period. The team's primary objective will be to determine the best way to provide a web-based mindfulness practice and set of tools for those facing pancreatic cancer. Another objective of the study is to collect data on other aspects of the patient and caregiver emotional well-being throughout the cancer journey. This mindfulness intervention aims to track and improve self-reported symptoms of depression, anxiety, spiritual wellbeing, sleep, and quality of life for both the patients and caregivers.

The Hirshberg Foundation is honored and excited to partner with the UCLA School of Nursing to work towards understanding the ways to support and improve both patient and caregiver emotional well-being throughout the cancer journey. This research is made possible thanks to our community.

Research Publications from the

Sahin-Toth Laboratory in 2023

The [Sahin-Toth Laboratory](#) remains an important part of the Hirshberg Foundation's research program and is central to our efforts on UCLA's campus. Led by our Scientific Advisory Board Chair, Dr. Miklos Sahin-Toth, his lab is focused on hereditary chronic pancreatitis, a major risk factor for pancreatic cancer. Dr. Sahin-Toth's work is in partnership with Dr. Guido Eibl in our [Translational Laboratory](#). Their two teams are committed to better understanding genetics, obesity, diet, and inflammation and how they contribute to pancreatic cancer acceleration.

Dr. Sahin-Toth and his team continue to contribute to prestigious journals, participate in conferences across the globe, and secure funding from the NIH. We eagerly await more updates from Dr. Sahin-Toth and his research group in the future.

Publications from the Sahin-Toth Laboratory in 2023

1. [Modelling chronic pancreatitis as a complex genetic disease in mice](#). *Gut* 2023, 72:409-410. PMC9666703.

Jancsó Z, Demcsák A, Sahin-Tóth M.

The final published form of a remarkable paper from 2022. Chronic pancreatitis is a complex genetic disease, and patients often carry multiple genetic variants. Here we crossed mouse strains with different pancreatitis-associated gene variants to study their combined effect. Mice with single genetic changes showed no pancreas disease; however, mice with both gene variants developed severe chronic pancreatitis. *Gut* is a preeminent journal in gastroenterological sciences.

2. [Trypsin activity in secretagogue-induced murine pancreatitis is solely elicited by cathepsin B and does not mediate key pathologic responses.](#) **Gastroenterology** 2023, 164:684-687. PMC10441611.

Geisz A, Tran T, Orekhova A, Sahin-Tóth M.

Our flagship paper of 2023! Here we demonstrated that trypsin activity generated by cathepsin B during the early phase of pancreatitis is a marker rather than a driver of the disease. One important implication is that cathepsin B should not be considered as a therapeutic target in pancreatitis. Gastroenterology is the official journal of the American Gastroenterological Association (AGA), and the most prominent US publication in the gastroenterological sciences.

3. [No evidence for the benefit of PPIs in the treatment of acute pancreatitis: a systematic review and meta-analysis.](#) **Scientific Reports** 2023, 13:2791. PMC9935541.

Horváth IL, Bunduc S, Hankó B, Kleiner D, Demcsák A, Szabó B, Hegyi P, Csupor D.

[Alexandra Demcsak](#) (2022 Seed Grant recipient) contributed to this clinical paper showing that acid-reducer PPIs have no therapeutic benefit in acute pancreatitis. The Scientific Reports is an open-access journal publishing original research from all areas of life sciences. It is part of the prestigious Nature Research journal family.

4. [Mouse model of PRSS1 p.R122H-related hereditary pancreatitis highlights context-dependent effect of autolysis-site mutation.](#) **Pancreatology** 2023, 23:131-142. PMC10492521.

Jancsó Z, Morales Granda NC, Demcsák A, Sahin-Tóth M.

Modeling the pathogenic effect of the p.R122H cationic

trypsinogen mutation in mice has been a challenge since its discovery in 1996. Here we clarify why this mutation causes pancreatitis in humans but not in mice. *Pancreatology* is the official journal of the International Association of Pancreatology and the European Pancreatic Club.

5. [Substrate specificity of human chymotrypsin-like protease \(CTRL\) characterized by phage display-selected small-protein inhibitors.](#) *Pancreatology* 2023, 23:742-749. PMC10528761.

Németh BZ, Nagy ZA, Kiss B, Gellén G, Schlosser G, Demcsák A, Geisz A, Hegyi E, Sahin-Tóth M*, Pál G*. *contributed equally.

The most recent chapter of our long-running collaborative work with the Pál laboratory aimed at the characterization of the substrate specificity of human pancreatic chymotrypsins and elastases. It is hard to believe, but we published the first joint paper on this problem in 2011. *Pancreatology* is the official journal of the International Association of Pancreatology and the European Pancreatic Club.

6. [Risk of chronic pancreatitis in carriers of the c.180C>T \(p.Gly60=\) CTRC variant: case-control studies and meta-analysis.](#) *Pancreatology* 2023, 23:481-490. PMC10586708.

Berke G*, Beer S*, Gede N, Takáts A, Szentési A, Hegyi P, Rosendahl J, Sahin-Tóth M*, Németh BC*, Hegyi E*. *contributed equally.

This important addition to the literature on pancreatitis genetics provides a quantitative assessment of the effect of a common chymotrypsin C (CTRC) variant on the risk of chronic pancreatitis. *Pancreatology* is the official journal of the International Association of Pancreatology and the European Pancreatic Club.

7. [CFTR p.F508del mutation carrier status is not associated with biliary acute pancreatitis.](#) **Pancreas** 2023, 52:e256-e257.

Martonosi ÁR, Németh BC, Párniczky A, Vincze Á, Szentesi A, Erőss B, Sahin-Tóth M, Hegyi P, Hegyi E.

An intriguing hypothesis that turned out to be wrong. The risk of biliary pancreatitis is not increased by CFTR mutations. *Pancreas* is the official journal of the American Pancreatic Association.

8. [Functional predictors of pathogenicity of missense CPA1 variants in chronic pancreatitis.](#) **Gut** 2023

Sándor M, Sahin-Tóth M.

Another highlight of our 2023 publications! After functionally characterizing 50 carboxypeptidase A1 (CPA1) mutations, we found, to our surprise, that very few cause chronic pancreatitis and despite measurable functional defects, most CPA1 mutations are benign. *Gut* is a preeminent journal in the gastroenterological sciences.