

Pivotal research on RNA splicing may hold key to treatment

As we celebrate summer and all that is blooming, we look back at seeds planted through our Seed Grant Program, and are optimistic about the progress being made in pancreatic cancer research. Our 2019 Seed Grant cohort faced a difficult year for conducting research, establishing their labs and providing updates. We are catching up with these great scientists to share their progress and advances in pancreatic cancer research.

When Luisa F Escobar-Hoyos, MSc, PhD, applied for a Seed Grant in 2019, she was a Senior Post-Doc at Memorial Sloan Kettering Cancer Center. Shortly after receiving her award, in February 2020, she became an Assistant Professor of Therapeutic Radiology and Molecular Biophysics and Biochemistry at Yale. Despite the pandemic severely impacting the establishment of her lab, she and her team continued to publish and their discoveries led to a new therapeutic modality for pancreatic cancer. Dr. Escobar-Hoyos is making great strides to cure pancreatic cancer, most notably through the discovery that pancreatic cancers are highly susceptible to a range of therapies directed at RNA splicing.

A majority of pancreatic ductal adenocarcinoma (PDAC) tumors are driven by mutations in the KRAS gene that increase the activity of KRAS driving cell growth and survival. A large subset of these tumors (70%) also have mutations in the TP53 gene but efforts to inhibit or drug these mutant proteins have largely failed. More recently, it has been shown that a specific group of mutations in TP53, called hotspot mutations, combined with high expression of genes involved in RNA splicing are markers of

aggressive PDAC. RNA splicing is a process where one gene can produce many different forms of a protein and involves a number of RNA splicing proteins. Dr. Escobar-Hoyos's recent work, published in [Cancer Cell](#), aimed to investigate if and how mutant TP53 and RNA splicing co-operate in pancreatic tumor cells. They found that mutant p53 hijacks RNA splicing to favor the production of proteins that stimulate KRAS to promote tumor growth and metastasis. Based on these findings, Dr. Escobar-Hoyos's lab developed and patented a new therapy for pancreatic cancers that harbor mutant KRAS and mutant p53, which corrects the RNA splicing errors, selectively killing pancreatic cancer cells in animal models.

This remarkable discovery, that oncogenic KRAS is susceptible to inactivation through the inhibition of RNA splicing, led Dr. Escobar-Hoyos to submit a patent for this type of therapy. The patent relates to a method for treatment administering an anti-sense oligonucleotides (a small piece of modified RNA) that block the splicing of cancer-related genes, thereby treating the cancer. This novel therapy, Splicing-Hit Oligonucleotide Therapy (SHOT), is currently being tested in Dr. Escobar-Hoyos's lab. As pancreatic tumors often don't respond to treatment, the hope that SHOT will be effective in tumors that are resistant to current therapies. Dr. Escobar-Hoyos is currently working with the Yale Cancer Center on a clinical trial to test this novel form of therapy for pancreatic cancers.

We applaud the work of Dr. Escobar-Hoyos and her lab and are hopeful that her discovery helps pave the way to a cure. As Dr. Escobar-Hoyos writes, "thank you for your support and I hope that [the Foundation] funds other pancreatic cancer scientists!" We are honored to fund Seed Grants and, thanks to your support, look forward to continuing our progress.

The 2021 UCLA Activity Summary Report

The Hirshberg Foundation remains a key partner in UCLA's pancreatic cancer program. The [UCLA Agi Hirshberg Center for Pancreatic Diseases](#) is a world-class integrated practice unit where researchers and physicians work together to advance the understanding and treatment of pancreatic cancer while being able to bring improved therapies directly to patients. Thanks to the generosity of the Hirshberg Foundation and our donors, [the UCLA Hirshberg Center](#) team was able to continue advancing research, share their discoveries with the scientific and patient communities, and make progress toward a world free from pancreatic cancer.

Each year, UCLA provides the Hirshberg Foundation with a [detailed report](#) of the progress that is possible thanks to our partnership. Below are updates on the important work taking place at UCLA.

UC Pancreatic Cancer Consortium

The UC Pancreatic Cancer Consortium ([UCPCC](#)) brings together the five UC campuses with medical schools – Davis, Irvine, Los Angeles, San Diego, and San Francisco – to unite pancreatic cancer scientists and clinicians in order to accelerate the progress and impact of their work. This highly collaborative model seeks to improve the lives of persons diagnosed with pancreatic cancer by translating innovative research into improved clinical care.

Clinical Trials for Treatment

Patients seen through the Hirshberg Center's Integrated Practice Unit (IPU) in Westwood have access to an array of treatment options including robust slate of 14 [clinical trials](#), 5 of which are currently enrolling patients. One such trial tests the [use of NGM120](#), a long-acting monoclonal antibody, in combination with other therapies in patients with metastatic pancreatic cancer. Another trial [evaluates GRT-C903 and GRT-R904](#), a neoantigen-based therapeutic cancer vaccine, in combination with immune checkpoint blockade, in patients with pancreatic and other cancers. [Living with Pancreatic Cancer](#), run by [Dr. Annette Stanton](#), seeks to identify the psychological and social factors that help people living with the disease and partners/primary caregivers maintain their quality of life. These clinical trials not only help advance understanding of this disease, but they also offer patients and their families hope for better treatment options.

Ronald S. Hirshberg Chair in Translational Pancreatic Cancer Research

Dr. J. Enrique Rozengurt holds the [Ronald S. Hirshberg Chair in Translational Pancreatic Cancer Research](#) and remains one of the globe's most vital medical researchers. He is Distinguished Professor of Medicine in the David Geffen School of Medicine at UCLA, Chief of Research in the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases, and a pioneer in the areas of signal transduction and cell growth regulation.

Over the past year, Dr. Rozengurt and his colleagues have found that statins potently block YAP-regulated genes in pancreatic

cells and that various statins inhibit the development of pancreatic ductal adenocarcinoma (PDAC) cells when acting synergistically with metformin, an FDA-approved medication for Type 2 diabetes, prediabetes and other conditions. Dr. Rozengurt's team is investigating whether a low-dose combination of metformin and statins can work in harmony to slow the production of pancreatic cancer cells, which may help to arrest the spread of pancreatic cancer. The use of metformin as a potential inhibitor of pancreas tumor growth has the possibility of rapid translation because of metformin's already widespread use.

UCLA Pancreas Tissue Bank

David Dawson, M.D., Ph.D., Associate Professor in the Department of Pathology and Laboratory Medicine, David Geffen School of Medicine at UCLA, continues to oversee the [UCLA Pancreas Tissue Bank](#). The Tissue Bank provides invaluable pathologic consultations to colleagues at UCLA, as well as collaborating with pancreatic researchers nationally and internationally. The bank continues to grow as Dr. Dawson accrues additional snap frozen and viable tissue samples from patients, archival clinical materials, and large tissue microarrays of pancreatic tumors. Support from the Hirshberg Foundation plays a key role in enabling Dr. Dawson to provide tissue samples and offer his expertise in pathology to his collaborators, creating a multiplier effect as resources and support at UCLA benefit the wider pancreatic research community. Dr. Dawson is also primary investigator for the pathology core of the [UC Pancreatic Cancer Consortium](#), which collaborates across five UC campuses to accelerate the progress and impact of pancreatic cancer.

Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory

The [Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory](#), helmed by Guido Eibl, M.D., Professor, Department of Surgery, David Geffen School of Medicine at UCLA, investigates the connection between inflammation, diet, and obesity in pancreatic cancer. Dr. Eibl and his team continue to make tremendous progress on their [\\$5.75 million five-year grant](#) from the National Cancer Institute (NCI) to study the impact of obesity on pancreatic cancer development, as well as the effect of treatment with statins, both alone and in combination with metformin. Drs. Eibl and Rozengurt continue to collaborate on additional projects as well, including a study investigating the role that the combination of obesity and stress have on pancreatic cancer development. As stress, particularly social stress, affects the lives of more and more individuals, it is vital to study its effects on pancreatic cancer risk. [Dr. Eibl](#) and his team continue to drive research towards a greater understanding of how this disease develops, with actionable ways to limit risk and slow the development of pancreatic cancer.

Psychosocial Care Via the Simms/Mann-UCLA Center for Integrative Oncology

Under the direction of Kauser Ahmed, Ph.D., Darcie Denkert Notkin Director of Psychosocial Oncology, the Simms/Mann-UCLA Center for Integrative Oncology remains a key part of UCLA Health's multifaceted approach to providing cancer patients with holistic care. When longtime clinical psychologist and pancreatic cancer patient liaison Elizabeth Cleary, Ph.D.,

transitioned into a remote role, Greg Flaxman, L.C.S.W., M.P.H., stepped in to ensure that pancreatic cancer patients continued to receive all the center's integrative care options. Mr. Flaxman has an active part in counseling patients after their diagnosis to help craft personalized psychosocial care plans as they prepare for surgery, chemotherapy, or other treatments. He helps patients with pancreatic cancer and their families navigate their care and connects them to resources that will ease the challenges of a pancreatic cancer diagnosis and treatment.

The Simms/Mann team is dedicated to providing guidance and support through the cancer journey, with pancreatic cancer patients averaging nearly nine interactions during the course of their treatment. The Simms/Mann Center experienced a nearly 13 percent increase in the number of pancreatic cancer patient encounters in 2021, further proof of the team's value to a vulnerable population. In addition, the growth of telehealth throughout the pandemic has coincided with the geographic growth of the Simms/Mann Center, which now offers services at 19 UCLA hematology/oncology clinics across Southern California, increasing opportunities for patients to easily access crucial psychosocial services at locations closer to home. Pancreatic cancer continues to be one of the most difficult diagnoses for patients to receive, and the generosity of the Hirshberg Foundation allows the Simms/Mann Center to keep these patients' particular needs at the forefront of the work they do.

The Hirshberg Foundation's partnership with UCLA has created a premiere pancreatic cancer center with cutting-edge research and world-class care that draws patients from across the country. Together we are making progress toward improved treatments, outcomes, and quality of life for patients with pancreatic

cancer. The past 25 years have laid the groundwork, now we are ready to watch research accelerate and discoveries compound to bring new hope to families and better outcomes to patients.

Read the full summary [here](#).

UCLA Agi Hirshberg Center for Pancreatic Diseases Earns National Pancreas Foundation Center of Excellence Designation

The UCLA Agi Hirshberg Center for Pancreatic Cancer Diseases has been nationally acknowledged as a Clinical and Academic Center of Excellence by the National Pancreas Foundation (NPF). This esteemed designation is awarded to premier healthcare facilities that focus on multidisciplinary treatment of pancreas disease, with specific attention to providing the best possible outcomes and improved quality of life for patients.

[Dr. Timothy Donahue](#), member of our Scientific Advisory Board, Chief of the Division of Surgical Oncology, and Vice Chair for Cancer Surgery in the Department of Surgery at UCLA, along with [Dr. V. Raman Muthusamy](#), Medical Director of Endoscopy at UCLA Health and Professor of Clinical Medicine at David Geffen School of Medicine at UCLA, spearheaded the efforts and extensive auditing process. An approved NPF Center of Excellence for Pancreatitis and Pancreatic Cancer must meet the criteria

developed by a task force made up of invited subject matter experts and patient advocates. The criteria includes having the required expert physician specialties such as gastroenterologists, medical and radiation oncologists, pancreas surgeons, and interventional radiologists, along with more patient-focused programs such as a pain management service, nutrition, and psychosocial support.

“It is an honor to have the Hirshberg Center for Pancreatic Diseases designated as an NPF Center of Excellence for pancreatic cancer,” said Dr. Timothy Donahue. “We are focused on providing innovative, whole-body care for our patients and the NPF Center designation will help further distinguish us as a location dedicated to the needs of those impacted by pancreas disease.”

Dr. Muthusamy added, “This designation not only identifies us as a leader in pancreatic cancer, but in all pancreatic diseases. The more we are able to deepen our understanding of the pancreas, the better equipped we are to provide care and treatment at the earliest stages, leading to better patient outcomes.”

The [National Pancreas Foundation](#) Center Program helps patients with pancreas disease find a vetted specialist at an institution that will provide a high-quality, multidisciplinary approach to their care. The over 140 Centers of Excellence also benefit from a partnership with the NPF. Founded in 1997, the National Pancreas Foundation provides hope for those suffering from pancreatitis and pancreatic cancer through funding cutting-edge research, advocating for new and better therapies and providing support and education for patients, caregivers and healthcare professionals.

“We are thrilled to expand our NPF Centers of Excellence Program

to better serve the needs of patients suffering from pancreas disease,” said David Bakelman, CEO of the National Pancreas Foundation. “The NPF Centers of Excellence Program is one of the pillars of NPF, and we are looking forward to working with our current and new Centers.”

“This award is a true achievement for our entire team, it represents the exceptional patient care we are delivering across the board,” said Dr. O. Joe Hines, Interim Chair of the Department of Surgery, UCLA Health Surgical Director for Perioperative Services, and Director of the UCLA Agi Hirshberg Center for Pancreatic Disease.

The Hirshberg Foundation is honored to receive this designation. One of the pillars of our mission is to “create a premier Pancreatic Cancer Center where all needs of pancreatic cancer patients can be met in one location with the most advanced treatment options.” Being recognized as an NPF Center of Excellence helps us achieve that goal and advances our quest towards a cure.

A Message of Gratitude for 25 Years of Support!

This summer, our Foundation commemorates 25 years of extraordinary scientific discoveries in the field of pancreatic cancer while providing support services for patients around the world. Thanks to our incredible community, the Hirshberg Foundation mission and our message of hope has reached thousands of families every year. Every milestone we surpass has led to

real-world results because of your generosity and dedication. We have checked off nearly every goal we set out to achieve when we first began this journey but that last piece of the puzzle, finding a cure, is why we will never give up.

[Watch Our 25th Anniversary Video →](#)

The mission statement and the vision of the Hirshberg Foundation remains the guiding light for all of the work we do. From the establishment of the [Agi Hirshberg Center for Pancreatic Diseases at UCLA](#) to becoming a [resource for patients](#) at the most critical time of their lives; our programs have given survivors a chance to thrive. Our goal was to build a community that could answer this pivotal call-to-action, and today, that very community is helping to fund [new and innovative research projects](#), [educational Symposiums](#), and patient [webinars](#). All of these accomplishments are steps towards our ultimate goal of finding a cure and eradicating this disease.

In 1997, when our Founder, [Agi Hirshberg](#), began paving a way forward for this organization, she knew that it would take collaboration and hard work, *“I wanted to help UCLA and their pancreatic program but they said they didn’t have one. Of course, my next sentence was, “you have one now, help me build it”*. She began this journey understanding just how relentless pancreatic cancer could be. It was a time when medicine offered the bare minimum; research was underfunded while patients’ lives were fated for an uphill battle with few resources. Today, the Agi Hirshberg Center for Pancreatic Diseases serves pancreatic cancer patients every day and a community of brilliant scientists and doctors are propelling research forward.

As we approach this remarkable milestone, we want to thank you and recognize all of the hard work that our supporters have contributed over the years. The vision for the Hirshberg

Foundation for Pancreatic Cancer Research may have begun with one family, but it has grown into a global community. 25 years later there's so much hope, there's so much work being done, there's so much progress that has been made and all of those things are things to celebrate!

With Gratitude,
Lisa Manheim
Executive Director

Learn more about what we've achieved over 25 years

[25th Anniversary →](#)

[Patient Support & Resources →](#)

[Seed Grant Program →](#)

[Hirshberg Community Events →](#)

UCLA awarded \$500,000 from the Canopy Cancer Collective for Patient Support

UCLA along with two other UCs, as part of the UC Pancreatic Cancer Consortium, has been awarded a total of \$1.5 million from the Canopy Cancer Collective to help improve patient outcomes. Canopy joins the long-standing efforts of the Hirshberg Foundation in advocating for and advancing patient care.

The [UC Pancreatic Cancer Consortium](#) (UCPCC) brings together the

five UC campuses with medical schools – Davis, Irvine, Los Angeles, San Diego, and San Francisco – to unite pancreatic cancer scientists and clinicians in order to accelerate the progress and impact of their work. The vision to improve the lives of persons diagnosed with pancreatic cancer by translating innovative research into improved clinical care dovetails with the Canopy’s goal to empower pancreatic cancer patients with new hope, treatments, and options. Agi Hirshberg, Founder and President of the Hirshberg Foundation, is honored to preside as the Chair of the Patient Advocacy Council for the UCPC.

UC Los Angeles, UC San Francisco and UC San Diego each received a \$500,000 three-year grant for the implementation of integrated multidisciplinary care to improve the outcomes and well-being for all patients with pancreatic cancer. Their additional support builds upon the Hirshberg Foundation’s work to center patient well-being as an integral part of the cancer treatment process, for without psychosocial care, true wellness cannot be achieved. Canopy Cancer Collective aims to provide the best available care for pancreatic cancer patients by connecting multiple institutions to foster collaboration among the top care-providers, coordinate impactful patient services and deliver innovative, comprehensive, and effective care to their patients.

Timothy Donahue, MD, chief of the Division of Surgical Oncology at UCLA’s Jonsson Comprehensive Cancer Center, is the Physician Champion leading the project through the [Hirshberg Center for Pancreatic Diseases](#), along with other great pancreas institutions across the country. This grant will expand upon and deliver more coordinated care in the Hirshberg Center for Pancreatic Diseases’ Westwood IPU clinic and ultimately throughout the entire UCLA Health network.

Through this initiative, UCLA plans to improve and standardize

pancreatic cancer care by focusing on nutrition, palliative care, genetic testing, clinical trial participation, quality of life, and patient education. One goal is to expand germline testing services to all pancreatic cancer patients in the UCLA Health Network, which has already seen a marked increase in referrals from 2019. Another area of interest is [nutrition](#), a topic we know is crucial and front-of-mind for patients and families. As part of the Canopy Cancer Collective, one goal is to provide nutrition support for all pancreatic cancer patients at UCLA. To that end, the IPU now includes a nutritionist on staff to provide nutrition assessment and intervention through the pre-operative and post-operative phases of surgery.

The other main objective of the Canopy Cancer Collective is to ensure that all pancreatic cancer patients in the UCLA Health Network, extending as far north as San Luis Obispo to Laguna Beach in the south, receive the same exceptional level of care established at the Hirshberg Center for Pancreatic Diseases. One aspect of this is the Clinical Quality Improvement Database, allowing doctors and staff to know in real-time every patient who is diagnosed with pancreatic cancer. This allows those patients to receive genetic testing, nutritional support, clinical trial information and more.

We are honored to have the Canopy Cancer Collective join the Hirshberg Foundation's work to improve patient care and are excited to see pancreatic cancer providers collaborating to give patient new hope. The Canopy Cancer Collective Pancreatic Learning Health Network, funded through the 1440 Foundation, aims to help cancer centers deliver comprehensive, coordinated care to people with pancreatic cancer. These exciting collaborative projects are creating improved treatment options and better patient outcomes for all.

New research on enzyme MMP-7 holds potential for drug development

As we celebrate spring and the blooms to come, we are looking back at seeds planted through our Seed Grant Program, and are optimistic about the progress being made in pancreatic cancer research. Our 2019 Seed Grant cohort faced a difficult year for conducting research, establishing their labs and providing updates. We are catching up with these great scientists to share their progress and advances in pancreatic cancer research.

Steven R. Van Doren, PhD, a 2019 Seed Grant recipient at the University of Missouri has provided an update on his research including a published review on the importance of drug development that targets the protein-cutting enzyme MMP-7.

Recently published in *Biochemical Society Transactions*, Dr. Van Doren's review explores the current research and understanding of the protease matrix metalloproteinase-7 (MMP-7). It is known that MMP-7 is secreted by tumor cells and that high levels in circulation correlate with poor prognosis and limited survival of patients with pancreatic ductal adenocarcinoma (PDAC). MMP-7 is required for the early [acinar-to-ductal switch](#) that leads to pancreatic tumorigenesis in mice, is present throughout tumor progression, and promotes tumor cell metastasis (spread of cancer to other areas of the body). In addition, high MMP-7 expression appears to be a marker of poor survival rates and may be predictive of unresectable tumors.

One area of research into treating pancreatic cancer is enhancing response to chemotherapies in order to increase surgical candidacy and prevent relapse post-surgical resection. MMP-7 protects cells from programmed cell death by targeting death signaling proteins from the surface of tumor cells. This appears to be one of the mechanisms by which pancreatic tumor cells are able to resist chemotherapy. Twenty years ago it was predicted that blocking MMP-7 could make pancreatic tumor cells more sensitive to chemotherapeutics. Recently, an anti-MMP-7 monoclonal antibody was [shown](#) to increase the susceptibility of several pancreatic cancer cell lines to chemotherapeutic drugs, by increasing their apoptosis (cell death) and decreasing migration.

Thanks to funding from the Hirshberg Foundation, Dr. Van Doren was also able to connect with Dr. Rolf Brekken at the University of Texas Southwestern Medical Center, a specialty center for investigations of pancreatic cancer using mouse models. Together, they have begun the early stages of drug screening and evaluation.

We are hopeful that this research brings progress to the treatment options available for pancreatic cancer. As Dr. Van Doren wrote, "I am grateful for the support from the Hirshberg Foundation to help enable this research. I am optimistic that targeting MMP-7 will advance treatment options" for all pancreatic cancer patients. It is thanks to your support that our momentum towards a cure continues.

[Read the complete article →](#)