Our UCLA Activity Summary Report is now Available

The Hirshberg Foundation maintains its longstanding partnership with UCLA and is a crucial source of support for a wide range of research programs, patient care initiatives, and faculty members in the UCLA Agi Hirshberg Center for Pancreatic Diseases. Despite the difficulties of 2020, our supporters help us provide the financial stability necessary to face challenges with the innovation, compassion, and ingenuity that are hallmarks of the Hirshberg Foundation and the UCLA Hirshberg Center.

Each year, UCLA provides the Hirshberg Foundation with a detailed report of the advances being made and what we are accomplishing together. Below are a few of the achievements taking place at UCLA thanks to your continued support.

UCLA Agi Hirshberg Center for Pancreatic Diseases

In March of 2020, as the pandemic reached the United States, UCLA Health and the David Geffen School of Medicine at UCLA worked to transition many activities to virtual platforms. Once safety protocols were in place, pancreatic cancer care and surgery continued. Hirshberg Center's pancreatic disease-focused integrated practice unit (IPU), which brings together surgeons, medical oncologists, radiation oncologists, pathologists, gastroenterologists, geneticists, and psychosocial care specialists, continued virtually to collaborate on care plans for individual patients. Amid the myriad challenges of 2020, delivering excellence in patient care remains a cornerstone for the Hirshberg Foundation and the Hirshberg Center.

Clinical Trials at UCLA

UCLA is currently participating in nine clinical trials aimed at improving treatment for pancreatic disease. One of these trials uses high-dose magnetic resonance imaging (MRI)-guided hypofractionated radiation therapy delivered using daily adaptive dose planning. This treatment model has been shown in a retrospective study to result in improved overall survival (relative to patients receiving lower radiation doses) in patients with locally advanced pancreatic cancer, without increasing the rate of serious gastrointestinal toxicity. Another high impact clinical trial is examining the effectiveness of nivolumab, a treatment combining immunotherapy with monoclonal antibodies, in conjunction with combination chemotherapy, which work synergistically to shrink tumors and stop the spread of cancer prior to surgery.

Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory

Under the direction of Guido Eibl, M.D., Professor, Department of Surgery, David Geffen School of Medicine at UCLA, the Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory is home to a robust research program focused on understanding the role of diet, obesity, and inflammation in pancreatic cancer. In May 2020, Dr. Eibl and his team were awarded a $5.75 million five-year grant from the National Cancer Institute to advance their pioneering work. The grant is funding an interconnected series of research projects with participating researchers from Cedars–Sinai Medical Center and the University of California, San Diego, collaborating with the team at UCLA. Dr. Eibl's project is examining inflammation associated with body fat and how the mechanisms of this chronic condition can

accelerate pancreatic cancer. This study is shedding new light on the mechanisms that influence the formation of pancreatic tumors and on ways to intervene and prevent cancer in people who have risk factors.

The Sahin-Toth Laboratory

The 2019 recruitment of Miklos Sahin-Toth, M.D., Ph.D., a leading pancreatic disease researcher and specialist in chronic pancreatitis and Garry Shandling Chair in Pancreatic Diseases, accelerated the center's world-class research program, resulting in numerous recent publications and discoveries. As part of his pioneering work investigating the genetic foundations of chronic pancreatitis, Dr. Sahin-Toth helped create international guidelines for risk factors in chronic pancreatitis, which were recently published in *Pancreatology*. These risk factors include alcohol consumption, smoking, and certain genetic alterations. In addition, Dr. Sahin-Toth recently published an article in *Gastroenterology* discussing the ways that COVID-19 multiorgan failure resembles lipotoxic organ failure during severe acute pancreatitis. In both diseases, interstitial leakage of pancreatic lipase may occur resulting in adipose lipolysis and increased levels of unsaturated fatty acids. These toxic fatty acids cause mitochondrial injury and stimulate the excessive production and release of proinflammatory immune mediators (cytokine storm) that can drive disease progression and eventual multiorgan failure, including acute respiratory distress syndrome, the leading cause of COVID-19-related mortality. In 2021, Dr. Sahin-Toth received a new grant from the National Institutes of Health (NIH) to explore how genetic risk factors affecting the digestive enzyme chymotrypsin cause pancreatitis.

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

The COVID-19 health crisis has brought into sharp focus the necessity for world-class psychosocial support and integrative care, particularly for patients going through cancer treatment and the Simms/Mann-UCLA Center for Integrative Oncology has continued to serve those needs. The broad range of services offered by the center, including psychosocial and psychiatric support, workshops and groups, nutritional guidance, and spiritual care, can make the difference between a cancer treatment journey defined by pain or galvanized by hope. The Simms/Mann team rapidly implemented telehealth operations to continue treatment during the pandemic, an option made even more crucial because of the vulnerability of the patient population. Elizabeth Cleary, Ph.D., a licensed clinical psychologist, join our Patient and Family Webinar Series to present "Coping Skills for the Pancreatic Community: Tools and Tips during COVID-19" in April 2020.

Simms/Mann clinician Sydney Siegel initiated a new program for patients undergoing chemotherapy without the support of friends and family by their side that was featured in the *Los Angeles Times*. Cancer survivors wrote anonymous letters to newly diagnosed patients sharing their thoughts, insight, and encouragement. These letters were then compiled into a booklet, titled *From the Chemo Chair: My Heart to Yours*, and distributed to UCLA hematology/oncology clinics so patients could receive them on their first day of treatment, accompanied by a playlist of inspirational songs selected by survivors.

Listen to the playlist here. If you would like more information, please contact Amy.

Hirshberg Foundation Seed Grant Program

In 2020, the Hirshberg Foundation Seed Grant Program began a new initiative to encourage collaboration among researchers. The program invited groups of two or more UCLA investigators to apply for a cooperative grant of $100,000 each to develop collaborative research in pancreatic cancer. The Hirshberg Foundation Seed Grant Program received three joint applications from teams of UCLA researchers for the 2020-2021 seed grant cohort. One grant was awarded to a promising research project led by Dr. Guido Eibl and Zsanett Jancso, Ph.D., Assistant Project Scientist, to investigate whether hereditary pancreatitis accelerates pancreatic cancer development. The study will offer critical insight into how hereditary pancreatitis-associated pancreatic cancer develops and how chronic inflammation promotes tumor growth in the pancreas.

Through our partnership with UCLA, we are empowering clinicians and researchers to connect with one another and find inspiration in collaboration. Even in the era of social distancing, we continue to facilitate connection through our Patient and Caregiver Webinar Series, which was created in lieu of an in-person symposium in 2020. Each session covers topics relevant to patients and caregivers and enables experts to speak directly with the people who are benefiting from their work. In this way, the foundation continues to center on the experience of patients and ensure that their needs are met and their questions are answered.

United in purpose, the UCLA Agi Hirshberg Center for Pancreatic Diseases is making tremendous progress toward improved treatments, outcomes, and quality of life for patients with pancreatic cancer. Together, we continue to provide world-class

care and to seek improved standards of treatment through pioneering research.

Read the full summary here.

Advocating for Women Facing Pancreatic Cancer

This Mother's Day, as you celebrate, honor or remember the special women in your life, join us in taking action on behalf of the countless moms who have fought pancreatic cancer. Each year, too many women and mothers across the country face a pancreatic cancer diagnosis and must begin their treatment journey. The courage and resilience of these women inspires us to move mountains to save lives.

In celebration of Mother's Day, the Hirshberg Foundation is sharing the story of Purmine "Mine" Oksayan, a beautiful and vibrant representation of all the strong moms and survivors we're honoring. Diagnosed with pancreatic cancer in 2016, Mine is a mother and a wife, a friend and a hero. In Mine's story , her children Ani and Parsegh share a dedication.

"This strong, beautiful woman lived each day focused on taking care of her family, offering unwavering support and strength and functioning as the glue that held everything together. She's rolled up her sleeves, dove into her battle and the only option is recovery. And yes, that truly is her mindset – the only option is conquering the beast in her pancreas and getting on with her life. My brother and I hit the jackpot when we were chosen to be her children."

Mine is more than a pancreatic cancer survivor. A dedicated supporter, Mine and her family make the long drive from San Diego to attend our LA area events and are ambassadors to the pancreatic cancer community. Her devoted husband and family encourage her light to shine, while her story, her smile and positivity inspire other survivors, patients, and families.

She has joined the Hirshberg Foundation year after year at the LA Cancer Challenge Walk/Run with her family and in 2020 she was our Honorary Starter. Attending Symposiums and Patient & Family Webinars, Mine understands how important it is for patients to have access to resources, support and research. She and her husband, children and grandchildren represent all of the families who deserve a better, brighter and healthier future together.

As we celebrate Mother's Day, help us get closer to discovering a cure so that more families can have a story like Mine's.

Paving the Way to Better Outcomes

The Hirshberg Foundation's pioneering research efforts in pancreatic cancer is driven by the countless families and faces in need of services and support everyday. When we evaluate the needs of our community from a scientific perspective or simply a place of compassion, one thing is evident: one group is disproportionaly affected by this disease. April, National Minority Health Month, is an opportunity to continue a dialogue on how we can better support Black Americans at highest risk for

pancreatic cancer.

Although Black Americans account for 13.4% of the U.S., the third largest population, it is still a community facing the greatest obstacles to prevent, detect, treat and survive pancreatic cancer. Risk factors from smoking, diabetes and weight are difficult hurdles for many Americans. However, socioeconomic factors can also impact a pancreatic cancer diagnosis and the reality that many Black Americans report racial discrimination at health provider visits makes those hurdles even higher.

Too often Black Americans are diagnosed at later stages, are underrepresented in clinical trials and even when pancreatic cancer is discovered early, patients are less likely to receive surgery than any other racial group in the U.S.

We strive to improve outcomes for these fathers and mothers, sons and daughters, cousins and grandparents, generations of families at high risk for this disease. The community has a 20% higher incidence of pancreatic cancer and faces a higher burden for overcoming chronic conditions that can lead to this disease. Communication and community are key to elevate awareness and reach families unaware of the risks. Talking about risks & symptoms, sharing patient & family resources for medical interventions and uniting our community are some of the steps we can take together.

To prevent this disease from rooting itself deeper, we must remain dedicated to increasing awareness across the country and the globe; share research progress and current medical treatments available; further diversify clinical trials through representation; educate patients and caregivers; and address the urgency for equity in the healthcare system.

The following are resources that could help save the lives of

family members, friends, neighbors and co-workers in the Black American community:

- Hirshberg Foundation – Patient & Family Educational Webinars
- American Cancer Society – Health Disparities Research
- FDA – Racial and Ethnic Minorities in Clinical Trials
- National Institutes of Health – Clinical Trial List

The United States is comprised of a blend of unique ancestry, ethnicities and cultures diverse in every way. Our approach to healthcare, prevention and community outreach is not one-size-fits-all. We will continue to advocate for all families, patients and high-risk communities so no one fights pancreatic cancer alone.

Momentum Newsletter: Spring 2021

Spring has officially begun and with it comes optimism, progress and good news! We began this year's Patient & Family Webinar series by celebrating long-term survivorship with participants from 3 continents! We are raising awareness for pancreatic cancer, and more importantly, connecting patients so that no one feels alone in their fight. We've witnessed research come to fruition in many ways this past year and are confident that our investigators are ready to change the course of pancreatic cancer. We look forward to sharing new research updates as our scientists collaborate and make leaps towards a cure.

Read on for the first exciting updates of 2021 in our Spring

Edition of Momentum!

UCLA Study Finds Potential Combination Therapy to Suppress Pancreatic Tumor Growth

Dr. Donahue and a collaborative team at UCLA recently published research on a novel way to target crucial metabolic processes in pancreatic cancer tumor cells. The team found that pancreatic tumors with high type I IFN signaling, trigger a decrease in crucial cofactors for many molecular processes. The study revealed the use of NAMPT inhibitors paired with an increase in type I IFN signaling, showed not only decreased pancreatic tumor growth, but also resulted in fewer liver metastases.

Funded through the UCLA Agi Hirshberg Center for Pancreatic Diseases, this research builds on our years-long support of Dr. Donahue's research. As Dr. Donahue told us, "This project is an example of how continuing to understand the biology of this disease will help us to improve the overall survival."

Early Research Pays Off Big with $6M in NIH Funding

Researchers at University of California, Los Angeles have received two grants from the National Institutes of Health (NIH) totaling over $6M to study the immunobiology of pancreatic tumors and develop an immunotherapy clinical trial. It was thanks to funding through the Hirshberg Foundation's Seed Grant Program, that compelling preliminary data was generated to help secure this substantial NIH funding. These NIH grants demonstrate how our early investments in research continue to pay off.

As research deepens our understanding of pancreatic tumor

development, novel strategies for prevention and treatment are possible.

Expanded Patient Resources Continue to Provide Hope & Strength

Over the past year, ensuring we continue to deliver outstanding patient and family support has been our top priority. It is thanks to your unwavering generosity that we have been able to strengthen our patient support program.

We've made updates to our website by focusing on our Patient & Family Resources to provide the most up-to-date information possible. From our new Caregivers page to expanded information on Genetic Counseling to Support Groups, we continue to develop resources for our pancreatic cancer community. If you or a loved one needs assistance, we are here to help. Contact Patient Support today.

Our Patient & Family Webinar Series Continues

We continue to provide our monthly Patient & Family Webinar Series library. In March, Dr. Jonathan King spoke about what happens in the pancreatic cancer operating room. He discussed what to prepare for before surgery, what to expect on the day of surgery and how to plan for the best post-surgical care. Later this month Dr. V. Raman Muthusamy will address the various types of pancreatic cysts, how they are diagnosed and treated, as well as what they mean for future pancreatic cancer risk. Plus, save the date for **May 14th when** Dr. McAllister will discuss the role of microbes in pancreatic cancer and **June 11**th when Dr. Suresh Chari will present his work on new-onset

diabetes and pancreatic cancer. We hope you'll join us on Zoom for these engaging topics.

The Hirshberg Training Team & LA Marathon are Back!

It's the announcement our Hirshberg Training Team has been waiting for: the LA Marathon will return on November 7, 2021. The Hirshberg Training Team running in a marathon while raising funds for research has been a tradition like no other. As the vaccination rollout continues, city and state guidelines are becoming less restrictive and allowing us to enjoy the outdoor activities we love once again. We will continue to share information as it is provided, but one thing seems certain, we're back!

Spring brings with it an excitement and eagerness to take action, to reunite with family and our communities, to return to the places and activities we have missed. The Hirshberg Foundation is optimistic to return to our vibrant in-person events this Fall, including both Tour de Pier and LA Cancer Challenge, while continuing to offer a virtual option for all.

We thank you for helping us make all these accomplishments possible. Every donation, every Facebook fundraiser, every social post and comment, every mention to a friend, all these small actions lead to making a difference for patients and families facing pancreatic cancer. We look forward to all we will be able to do together in 2021 and spring is just the start!

Healing Blooms, A New Partnership Grows with Viola Floral

The Hirshberg Foundation is honored to partner with Viola Flora for *Healing Bloom Zooms*, a no-cost flower arranging classes for cancer patients and survivors. The class aims to support patients on their healing journey, while raising awareness for pancreatic cancer.

The *Healing Bloom Zoom* was developed by Jelena Trifunovic, M.A., owner of Viola Floral, to help lower anxiety, reduce stress, improve mood, and enhance overall emotional wellness. Mayesh, the top national flower vendor, will be donating the florals and all classes will take place virtually via Zoom. Classes are taught by Trifunovic, a floral designer and seasoned K-12 science educator. Jelena brings her years of experience as an educator to provide informative classes that teach the fundamentals of floral design while providing a safe space for patients to relax, have fun and connect.

As a child growing up, Jelena was surrounded by the beauty of the natural world. In Serbia, later Southern California, holidays and family gatherings were spent in her family's kitchen arranging flowers with her mom, Luby, sharing stories, and laughing. When Luby was being treated for pancreatic cancer, Jelena remembers taking floral arranging classes and how much joy it brought them both. It is in Luby's memory that Jelena continues to give back and provide healing through floral therapy.

We are excited to partner with Jelena, Viola Flora, and Mayesh to bring our pancreatic cancer community these complimentary

flower arranging classes! Our aim is to provide resource and support for all, and we hope the *Healing Bloom Zooms* will help patients on their healing journey and support positive mental health, while we raise awareness of pancreatic cancer.

Learn more and sign up for a *Healing Bloom Zoom* »

UCLA Researchers Receive Over $6M from NIH to Study Potential Immunotherapies for Pancreatic Cancer

Research teams at UCLA have received two grants from the National Institutes of Health (NIH), totaling over $6 million dollars to study the immunobiology of pancreatic tumors and develop a series of immunotherapy clinical trials. Our Seed Grant Program funded the early stages of these research projects and provided the preliminary data used to secure this substantial NIH funding.

One of the studies, led by Dr. Timothy Donahue will further the recently published research into interferon (IFN) signaling that triggers a decrease in the level of NAD and NADH in pancreatic cancer cells, crucial cofactors for cell function. Dr. Donahue's NIH project titled *Leveraging vulnerabilities induced by interferon signaling in pancreatic cancer*, also builds on earlier IFN and NAD metabolism research from 2018 Seed Grant recipient Shili Xu, PhD.

The complicated nature of the pancreatic cancer microenvironment has led to difficulties in treatment options but Stimulator of interferon genes (STING) agonists are a promising new avenue being explored in this study. This multiyear research seeks to understand the interplay between STING signaling, nucleotide/NAD metabolism and replication stress response in pancreatic ductal adenocarcinoma (PDAC) with the ultimate goal of developing new therapeutic treatments.

Through collaborative research, Dr. Donahue's team continues to investigate the targetable vulnerabilities in pancreatic tumors to develop novel immunotherapy treatments for this disease. Dr. Donahue wrote us to say, "We are thrilled that the Hirshberg Foundation has supported both of our laboratories with Seed Grants that generated data specifically for these awards."

Dr. Caius Radu, fellow senior author on the recently published IFN study and primary investigator for the second NIH grant, is a Professor of Molecular and Medical Pharmacology and Co-Director of the JCCC Cancer Molecular Imaging, Nanotechnology and Theranostics Program. Dr. Radu's NIH grant, titled *Targeting KRAS and adenosine mediated immunosuppression in pancreatic cancer* will work in collaboration with Drs. Donahue and Wainberg to better understand the immunobiology of pancreatic tumors.

Immunotherapy has had great success for the treatment of other tumors such as melanoma and lung cancer but pancreatic tumors show an intrinsic resistance to immunotherapy. This immunosuppressive tumor microenvironment, along with KRAS mutations and altered metabolism, are all hallmarks that make pancreatic ductal adenocarcinoma (PDAC) so difficult to treat.

Research by 2019 Seed Grant award recipient, Thuc Le, PhD, furthered understanding of how mutant KRAS impacts nucleotide metabolism, as nucleotides play a critical role in tumor cell

growth. The recent groundbreaking discovery of KRASG12C-specific inhibitors has proved hopeful for KRAS targeted therapies and open further exploration of immunotherapy for pancreatic tumors. There is also mounting evidence that the therapeutic potential of mutant KRAS inhibitors can only be fully realized when administered with immune-priming combination therapies. Dr. Radu's project seeks to understand the interrelationships between KRASG12C inhibition, nucleotide metabolism, adenosine signaling, and immunosuppression in order to bring to clinical trial a new immunotherapeutic strategy that combines drugs across several therapeutic classes.

As Dr. Radu wrote to us, "funding from the Hirshberg Foundation enabled us to generate compelling preliminary data that were critical to the success of our [NIH] grant applications. We strongly believe that the studies proposed in these two grants will yield new fundamental knowledge about pancreatic cancer and help further clinical trials for novel immunotherapies."

The success of these NIH grants demonstrate how our early investments in researchers continues to pay off. As research deepens our understanding of the mechanisms that drive pancreatic tumor development, we are better able to devise novel strategies for prevention and treatment of this disease.

Learn more about Dr. Timothy Donahue's NIH project »

Learn more about Dr. Caius Radu's NIH project »