23 Years of Faithful Support Leads to Results!

Dear Hirshberg Foundation Family,

Long ago, the Hirshberg Foundation selected Never Give Up as our mantra, expressing our dedication to patients and long-standing commitment to funding early research for a cure. The message continues to resonate with pancreatic cancer survivors, families and researchers. Our community doesn't give up! After 23 years of faithful support we have gained a better understanding of what causes this disease, we have a new standard of care, treatment options and clinical trials. This simply didn't exist before the Hirshberg Foundation was launched. **As you read about our recent accomplishments, I ask that you help us continue working towards a cancer-free future and make a much-needed donation today.**

Despite the COVID-19 pandemic, we've seen robust progress from our Seed Grant researchers. They have given us extraordinary forward momentum and the results speak for themselves.

- Dr. Tzatsos has received new funds from the National Institutes of Health to continue his Seed Grant project! He has identified a loss of the protein BAP1, linking chronic pancreatitis to pancreatic cancer may present a new tailored therapy.
- Our team of doctors at UCLA have been granted $5.75 million from the National Cancer Institute (NIH) to fund 3 collaborative Seed Grant projects studying the role of obesity & inflammation in the development of pancreatic cancer.
- Our labs at UCLA are prioritizing pancreatic cancer while also actively helping us all in the fight against

COVID-19.

Your vision for improved patient care, advances in science and medicine has allowed us to make extraordinary strides. Keeping survivors informed and empowered is a also personal priority of mine. Our new Patient & Family Webinar Series is one of many ways we're serving patients nationwide. Webinar topics include surgery, oncology, nutrition, genetics, clinical trials and 'a nurses guide' with more topics to come this year. We need your help as we make sure our patients are never left behind. Please give what you can today so we may continue to propel forward in 2020.

With Gratitude,

Agi Hirshberg
Founder

P.s. Register for our Nationwide Virtual LA Cancer Challenge Walk/Run today to support our efforts!

Chemotherapy for Pancreatic Cancer Patients: Less is More!

Our Patient & Family Webinar series continues with a presentation on chemotherapy for pancreatic cancer patients. Dr. Isacoff will present *Chemotherapy for Pancreatic Cancer Patients: Less is More!* We are excited to have him share his findings on why lower, more frequent doses of chemotherapy may be a more patient friendly treatment regimen, with fewer side effects and better survival rates.

Dr. William H. Isacoff, who leads the Pancreatic Cancer Center of Los Angeles, has earned a reputation as one of the foremost gastrointestinal oncologists within the United States. He has developed innovative treatments which have significantly extended the lives of pancreatic patients throughout the country. He has worked for decades to form better, safer and more effective treatments for patients battling pancreatic cancer and other gastrointestinal cancers.

With the use of low dose "metronomic" chemotherapy without radiation, Dr. Isacoff and the Pancreatic Surgical Team at UCLA have down staged more than 60 patients who upon initial diagnosis were felt to be inoperable. After successful "metronomic" treatment with a combination of chemotherapies, the patients were then able to become surgical candidates. Seventy-five percent of those patients were found to have lymph nodes that were uninvolved with metastatic disease as a result of the prolonged use of effective chemotherapy. Dr. Isacoff shares these promising results and more information on how lower, more frequent doses of chemotherapy may impact a patient's outcome.

Watch Webinar

Dr. Isacoff's Metronomic Manuscript can be seen here »
Learn more about Dr. Isacoff and schedule a phone consultation »

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Research Identifies Loss of Protein Linking Chronic Pancreatitis to Pancreatic

Cancer, May Present New Tailored Therapy

Chronic pancreatitis is a known risk factor for the development of pancreatic cancer. However, the genetic alterations that cause this chronic inflammation and therefore predispose the patient to malignant transformation of the pancreas remain unknown. However, newly published research in *Nature Communications* by two-time Seed Grant Awardee, Alexandros Tzatsos, MD, PhD, has identified a protein that links chronic pancreatitis to pancreatic cancer.

Thanks to funding from the Hirshberg Foundation, Dr. Tzatsos's lab has identified that defective response to DNA damage stemming from the loss of BAP1 (BRCA1 associated protein-1) is a common denominator in pancreatic cancer patients with a history of chronic pancreatitis. Their research found that pancreas-specific deletion of BAP1 in models led to genomic instability, tissue damage, the development of chronic pancreatitis, and cooperates with oncogenic *KRAS* to promote pancreatic cancer.

In addition to genetic alterations, epigenetic mechanisms are central to the development of pancreatic cancer and contribute to shaping the immunosuppressive tumor microenvironment that hinders the therapeutic efforts to fight cancer growth. At the molecular level, BAP1 regulates genome stability. Their research also unveiled that BAP1-deficient pancreatic cancer showed sensitivity to platinum-based combination chemotherapy, such as those in FOLFIRINOX, and irradiation. This suggests that BAP1 loss can be used to identify patients who are likely to have a better response to these therapies.

Dr. Tzatsos's work is crucial to understanding the interplay of genetic and epigenetic alterations in pancreatic cancer while

seeking to develop patient tailored therapies. We are hopeful that this new research can begin to stratify patients to better predict their responsiveness to specific therapies. Dr. Tzatsos thanked the Hirshberg Foundation and its supporters for funding this critical work.

With support from the Hirshberg Foundation, over the past three years the Tzatsos Lab has been awarded R01 grants from the National Institutes of Health (NIH). Our early funding of innovative research projects has paid off and led to larger grants!

Dr. Tzatsos was awarded a Seed Grant in 2012 and again in 2018 to study the molecular foundations of pancreatic cancer to help develop tailored therapies. Dr. Tzatsos and the Tzatsos Lab at the Cancer Epigenetics Laboratory at George Washington University Cancer Center studies epigenetic programs and how they interact with genetic mutations to drive the development and spread of pancreatic cancer.

Read the original paper at https://www.nature.com/articles/s41467-020-16589-8

The ABC's of Finding A Clinical Trial with Dr. Anand

Clinical trials are scientific studies conducted to find better ways to prevent, screen for, diagnose, or treat disease. Clinical trials are used to study which medical approaches work best for certain illnesses or groups of people, with the goal to determine if a new treatment is safe and effective, often with

new medicines or protocols that the FDA has not yet approved. Clinical trials produce high-quality data for healthcare decision making, such as new ways to administer treatments, different doses, or using an approved drug on a different type of cancer. Clinical trials are a step in the long, careful research process, which may take many years.

It is up to the patient and their family to decide whether a clinical trial is the correct treatment option. There are hundreds of clinical trials happening across the globe as research institutions work towards improving treatment and finding a cure for cancer. If you've ever spent time researching clinical trials for you or a loved one diagnosed with pancreatic cancer, you know how challenging it can be. Although there are websites that share trial information with the list of qualifying criteria, it can still be quite daunting.

To help navigate the world of clinical trials, we asked Dr. Sidharth Anand, a medical oncologist and hematologist with UCLA, to share how to find a clinical trial and when it might be a prudent treatment option. Dr. Anand explains the phases of clinical trials as well as the various types of trials available, including randomized trials, double or single blind trials and single arm clinical trials. He discusses when to consider clinical trials as a sensible treatment option and how to maneuver the clinical trial database to be enrolled in a trial that will work for you or your loved one. Dr. Anand shared updates on current and hopeful pancreatic cancer clinical trials.

Dr. Sidharth Anand is a medical oncologist and hematologist who practices in Santa Monica and Westlake Village. He is a generalist with a specialized interest in gastrointestinal cancers, including pancreatic. He also has an interest in the application of integrative oncology, which means approaching

cancer care with traditional therapies, such as chemotherapy and immunotherapy, along with evidence-based integrative methods, including nutrition and exercise.

He received his medical degree from the USC Keck School of Medicine. Prior to that, he earned his MBA from Harvard Business School. He received his BA in Molecular Biology and a BS in Business Administration from UC Berkeley. Dr. Anand completed his internal medicine internship and residency at Cedars-Sinai Medical Center, where he was chief resident. He completed his hematology-oncology fellowship at UCLA. He is interested in technologies to help deliver higher quality care and access to clinical trials for patients.

Watch Webinar

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UCLA’s 2019 Hirshberg Activity Summary Report Released

The 2019 Activity Summary from UCLA, a report that outlines the work we’ve funded on campus and evaluates the remarkable advances made in research and patient care, is now available. The Hirshberg Foundation continues to position the UCLA Agi

Hirshberg Center for Pancreatic Diseases as a hub for leading-edge investigations and a beacon of hope for patients and their families. During the past year, this focus on innovation and exploration continued to draw patients from all over the country to UCLA for consultation, treatment, and support.

The Center's Integrated Practice Unit (IPU) focuses on pancreatic diseases and brings together surgeons, medical oncologists, radiation oncologists, pathologists, gastroenterologists, geneticists, and psychosocial care specialists. The collaborative approach enables them to work together on comprehensive and personalized care plans for individual patients. Patients also have access to pioneering clinical trials. In addition to the IPU, where patients with pancreatic adenocarcinoma cancer are being treated, patients that are diagnosed with pancreatic neuroendocrine cancer can be brought before the UCLA neuroendocrine tumor board. This board was created to better address the specific needs of patients with tumors that originate in hormone-producing cells, including pancreatic tissue and helps evaluate which protocols will be most beneficial for individual patients. The Center's patients also have access to pioneering clinical trials.

The 2019 Summary also includes updates on the Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory, UCLA Pancreas Tissue Bank, Psychosocial Care via the Simms/Mann – UCLA Center for Integrative Oncology and our Seed Grant Program.

Read the full summary here.

$5.75 Million Grant to Help Researchers Study Obesity, Inflammation and Pancreatic Cancer

A combined team of Hirshberg Foundation-affiliated researchers from UCLA has been awarded a grant for $5.75 million to study the effects of obesity on pancreatic cancer formation. This grant will build upon work that the Hirshberg Foundation has been funding since it began in 1997.

“We know that the biological mechanisms of obesity, such as inflammation, can lead to the development of pancreatic cancer,” Dr. Guido Eibl, Laboratory Director of the Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory and a UCLA Jonsson Comprehensive Cancer Center researcher, told UCLA. This study will look at the mechanisms that drive the formation of pancreas tumors with the goal of preventions strategies for those at higher risk.

The National Cancer Institute’s P01 grant will fund three distinct projects over a five-year period. This collaborative approach will include Dr. Eibl from UCLA, Dr. Enrique Rozengurt, Ronald S. Hirshberg Memorial Chair in Pancreatic Cancer Research at UCLA, and Dr. Stephen Pandol, long-time collaborator and member of the Hirshberg Foundation Scientific Advisory Board with Cedars-Sinai.

The first project, led by Dr. Guido Eibl, will investigate the links between diet, obesity, inflammation and pancreatic cancer while looking to evaluate potentially preventive strategies. The second project, spearheaded by Dr. Rozengurt, will investigate

the potential for using statins and metformin, FDA-approved drugs to treat elevated cholesterol levels and diabetes, to prevent pancreatic cancer in high-risk individuals. The final project, coordinated by Dr. Pandol, will address the pancreatic microenvironment to better understand how obesity and inflammation impact the tumor and surrounding tissues. These highly synergistic and integrative projects are led by experienced pancreatic cancer researchers with a proven track record of successful collaboration over the past 12 years.

This pancreatic cancer research partnership includes input from the Hirshberg Foundation's long-time researchers and doctors, including Dr. David Dawson, Director of the UCLA Pancreas Tissue Bank; Dr. Vay Liang Go, Chief of the Hirshberg Scientific Advisory Board; Dr. O. Joe Hines, frequent Symposium presenter; and Dr. Gang Li, professor of Biostatistics.

We are honored that so many Hirshberg researchers are part of this amazing team working towards prevention and increased treatment options. The collaborative effort of this project is at the heart of the Hirshberg Foundation's mission of a cancer-free future. Our early Seed Grants are now bearing fruitful results and this great accomplishment is just another stepping-stone towards a cure. Thank you to our donors, your support helped make this possible.

Read the entire UCLA press release