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 <u>risks & symptoms</u>, sharing <u>patient & family resources</u> for medical interventions and <u>uniting</u> 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 <u>Patient & Family Educational</u>
 Webinars
- American Cancer Society <u>Health Disparities Research</u>
- FDA Racial and Ethnic Minorities in Clinical Trials
- National Institutes of Health <u>Clinical Trial List</u>

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 <u>recently published</u> <u>research</u> 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 <u>UCLA Agi Hirshberg Center for Pancreatic Diseases</u>, this research builds on our years-long support of Dr. Donahue's research. As <u>Dr. Donahue</u> told us, "This project is an example of how continuing to understand the biology of this

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 <u>Patient & Family Resources</u> to provide the most up-to-date information possible. From our new <u>Caregivers</u> page to expanded information on <u>Genetic Counseling</u> to <u>Support Groups</u>, we continue to develop resources for our pancreatic cancer community. If you or a loved one needs assistance, we are here to help. Contact <u>Patient Support</u> today.

Our Patient & Family Webinar Series Continues

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 11th 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 <u>Hirshberg Training Team</u> 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 <u>Tour de Pier</u> 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 <u>Facebook fundraiser</u>, 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 <u>Viola Flora</u> 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, <u>Viola Flora</u>, and <u>Mayesh</u> 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 <u>Seed Grant Program</u> 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 <u>published</u> <u>IFN study</u> and primary investigator for the second NIH grant, is a Professor of Molecular and Medical Pharmacology and Co-Director of the <u>JCCC</u> 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 <u>Wainberg</u> 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 »

Celebrate Birthdays with a Facebook Fundraiser

Over the past year, many of us have celebrated *quarantine* birthdays by finding new and unique ways to share our special day with friends and family from afar. From car parades to sending balloon bouquets and Zoom parties, one way to celebrate a family member or friend's life is to support a cause close to their heart.

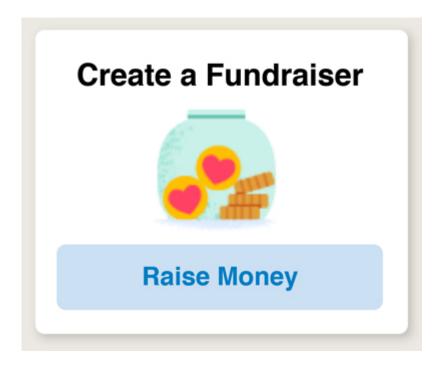
One of the easiest ways to share a cause that you care about is by setting up a Facebook fundraiser in celebration of your birthday or just because. Giving back is better when friends pitch in and that's exactly what happens when you create a Facebook Fundraiser. As we look forward to our own birthdays, as well as our friends' birthdays, celebrating with a Facebook Fundraiser for pancreatic cancer research is icing on the cake. Your support will raise awareness in the community and the generosity of friends and family will give us momentum to fight another day!

What is a Facebook Fundraiser?

Facebook Fundraisers are a feature on the social media platform that allows users to create and share a fundraising page with friends and family. The page helps supporters collect donations for a cause they care about in honor of their birthday or just because they want to give back. Users may add a photo or write a story to share why they are fundraising or keep it simple with the default text and image. Select the Hirshberg Foundation as a beneficiary and then post to your page. Fundraisers are easily shared with Facebook friends to help raise money. Give your birthday special meaning and make a difference in the fight to cure pancreatic cancer!

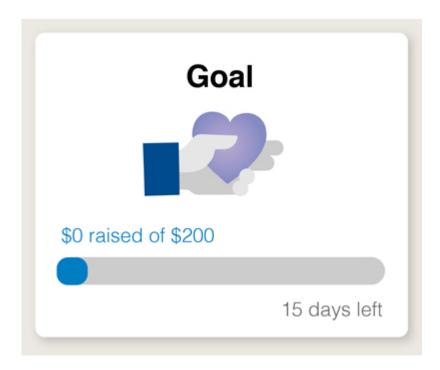
Get Started in 3 Easy Steps!

<u>Create a Facebook Fundraiser</u> with a few simple steps to create and launch your page. If you're curious what a Facebook Fundraiser looks like, preview these wonderful Facebook Fundraising pages for a <u>Birthday</u> and another to <u>Honor a Loved</u> One.



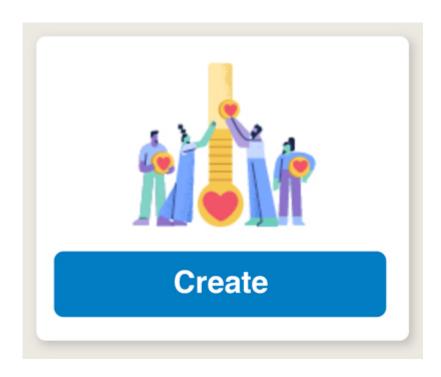
Step 1:

Click the link to open a new <a>Facebook <a>Fundraising <a>page



Step 2:

Add a Fundraising Goal. Text and a Photo are Optional.



Step 3:

Click the blue 'Create' button and your fundraiser will launch!

Hirshberg funded UCLA study finds combination therapy suppresses pancreatic tumor growth

UCLA Jonsson Comprehensive Cancer Center researchers, including our <u>Scientific Advisory Board</u> member and close <u>collaborator</u>, Dr. Timothy Donahue have uncovered a therapy that subdues tumor growth. The study, published in the prestigious *Proceedings of the National Academy of Sciences*, was funded by the Hirshberg Foundation the National Cancer Institute. As Dr. Donahue told us, "This project helps us to better understand the biology of pancreatic cancer and how to use that information to develop improved treatment strategies."

A hallmark of what makes pancreatic cancer so difficult to treat is the tumor's extensively reprogrammed metabolic network. All cells, including cancer cells, function by transforming nutrients into building blocks for cellular processes. Many of these processes require the critical cofactors NAD and its reduced form, NADH to carry out those processes.

The published research focuses on a subset of pancreatic tumors that express high intratumoral interferon signaling (IFN). The

team found that tumors with high type I IFN signaling, trigger a decrease in the level of NAD and NADH in pancreatic cancer cells. The study furthers our understanding of the biology of pancreatic cancer, including the mechanism by which NAD depletion occurs, a vulnerability that can be used in treatment. They showed that NAD and NADH can be further depleted by inhibition of a compensatory enzyme, NAMPT. These chemical cofactors are crucial for cell functions so reducing their availability can decrease tumor growth and disease progression.

The study demonstrated that cells with high type I IFN signaling were more sensitive to NAMPT inhibitors, which inhibit a major pathway in NAD synthesis. The use of NAMPT inhibitors paired with new systemic drugs, called STING agonists, which increase type I IFN signaling, showed not only decreased pancreatic tumor growth, but also resulted in fewer liver metastases.

The findings provide evidence that if tumors with high IFN signaling can be identified, or if IFN signaling can be amplified in tumor cells, those tumors may have greater sensitivity to treatment with NAMPT inhibitors. If so, the combination could provide greater treatment options for pancreatic cancer and improved outcomes. "This project is an example of how continuing to understand the biology of this disease will help us to improve the overall survival." Dr. Donahue told us.

Funded through the UCLA Agi Hirshberg Center for Pancreatic Diseases, this research builds on the Seed Grant relationship forged in 2009 when the Hirshberg Foundation first funded Dr. Donahue. Senior author of the study, Dr. Timothy Donahue, is the Chief of Surgical Oncology, Program Director of the General Surgery Residency Program and member of the UCLA Agi Hirshberg Center for Pancreatic Diseases. This research was a collaboration with senior author Dr. Caius Radu, Professor of

Molecular and Medical Pharmacology, first authors Dr. Alexandra Moore, resident physician in the department of surgery at the David Geffen School of Medicine at UCLA, and Dr. Lei Zhou, a visiting assistant project scientist in the department of surgery.

We applaud the researchers for deepening our understanding of pancreatic cancer biology and moving us another step closer to improved treatment options and ultimately a cure. These interdisciplinary collaborations are crucial for translating research from the bench to the bedside. As Dr. Donahue said, "I am optimistic that therapy for pancreatic cancer will markedly improve in the near future." Thanks to your support, our momentum is moving us closer to a cure.

Read the <u>UCLA news article</u> →

Read the original <u>research publication</u> →