Symposium Speaker Spotlight: Dr. Mark Girgis to share a Progress Report on Pancreatic Cancer

The Hirshberg Foundation is delighted that Dr. Mark Girgis will share the latest information in the field of pancreatic cancer detection and treatment at the 16th Annual Symposium on Pancreatic Cancer.

Dr. Girgis returns to our Symposium stage to present his report on the progress being made for the early detection and treatment of pancreatic cancer. Dr. Girgis is no stranger to our Symposium having presented, *Advances in Pancreatic Surgery* where he discussed the latest in robotic surgery. In addition, he participated in our Patient & Family Webinar Series with the talk, *Pancreatic Cancer: Advances in Research and Patient Care*. A surgeon as well as a researcher, we look forward to hearing the latest developments towards improving patient outcomes.

Dr. Mark Girgis is an Assistant Professor of Surgery at the David Geffen School of Medicine at UCLA. He also has a joint appointment at the Greater Los Angeles VA Medical Center. His interests include robotic and minimally invasive approaches to surgical oncology and more specifically on pancreatic diseases in his clinical practice as well as research endeavors. He received advanced training in robotic surgery and surgical oncology in his fellowship at the University of Pittsburgh. He is one member of the group of pancreas surgeons at UCLA that provide the highest level of care for their patients. He is committed to the improvement of cancer care through innovative technological advancements as well as ground breaking research.

His research endeavors focus on developing novel peptides targeting pancreas cancer for radioligand therapy and is part of a multidisciplinary group that collaborates on a variety of projects centered on developing new therapies for cancer patients.

A highly requested topic, we are grateful to have Dr. Girgis provide us with a *Pancreatic Cancer Progress Report* at the 16th Annual Symposium.

Symposium Speaker Spotlight: Judy Fortin to lead our Panel Discussion: Perspectives from Survivors and Caregivers

The Hirshberg Foundation is pleased to announce that Judy Fortin will moderate the uplifting and unique panel discussion portion of the 16th Annual Symposium on Pancreatic Cancer.

We are honored, each year, to share the stories of pancreatic cancer patients and caregivers. These honest and personal discussions give us all perspective, insight and sensitivity to the journey of both patients and loved ones once someone in the family is diagnosed with pancreatic cancer.

A veteran former broadcast journalist, Judy Fortin is Executive Director of Communications for UCLA Health and the David Geffen School of Medicine in Los Angeles, California. She leads a team that is responsible for all media relations and reputation

management at one of the top health systems in the United States.

Prior to joining UCLA in 2019, Judy served as Senior Director of Communications at Winship Cancer Institute of Emory University. Previously, she was National Director of Media Relations for the American Cancer Society. She spent 19 years as an anchor and correspondent at CNN and CNN Headline News in Atlanta. She won multiple national awards for her work as a CNN Medical Correspondent. Previously, she was a reporter for WCVB-TV in Boston and WMUR-TV in Manchester, New Hampshire.

Always an audience favorite, we are excited to have Judy Fortin joining us to moderate the *Panel Discussion: Perspectives from Survivors and Caregivers* at the 16th Annual Symposium.

Research Publications from the Hirshberg Translational Laboratory in 2021

Since its creation in 1998, the Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory has been at the forefront of pancreatic cancer research. Helmed by Dr. Guido Eibl, the lab is focused on understanding the intricate ways diet, obesity and inflammation can accelerate tumor development. Dr. Eibl and his research team have an accomplished track-record of NIH-funded projects. Despite the uncertainties in research due to COVID, Dr. Eibl and his team continues to publish in prominent journals and receive significant, multi-project

funding from NIH.

The Translational Lab has been a pioneer with collaborative projects and we look forward to sharing their progress.

Publications from the Translational Laboratory in 2021

1. *Direct Effects of Lipopolysaccharide on Human Pancreatic Cancer Cells.* ***Pancreas*** 2021;50(4):524-528 (PMCID: PMC8097724)

R.L.Massoumi, Y.Teper, S.Ako, L.Ye, E.Wang, O.J.Hines, **G.Eibl**.

This paper provides evidence that lipopolysaccharide, a component of bacteria that is elevated during obesity, has direct effects on pancreatic cancer cells. This may explain why in the obese state pancreatic cancer cells seem to grow more quickly.

Pancreas *is a multidisciplinary, international journal involving both basic and clinical research on the exocrine and endocrine pancreas and their interrelationships and consequences in pancreatic diseases, including cancer.*

2. Metformin: *Review of Epidemiology and Mechanisms of Action in Pancreatic Cancer*. ***Cancer and Metastasis Reviews*** 2021,40(3):865-878 (PMCID: PMC8556217)

E.Rozengurt, **G.Eibl**.

The paper reviews the current literature on the role and actions of metformin, a widely used anti-diabetic drug, in pancreatic cancer. Our own data and evidence from epidemiologic and preclinical studies, show that the antidiabetic drug metformin **possesses beneficial effects** in pancreatic cancer, including reducing the risk of developing the disease and improving survival in patients with early-stage disease.

Cancer and Metastasis Reviews *is a quarterly peer-reviewed medical review journal covering oncology and the development of new cancer treatments.*

3. *Obesity and Pancreatic Cancer: Insight into Mechanisms*. ***Cancers*** 2021,13(20):5067 (PMCID: PMC8534007)

G.Eibl, E.Rozengurt.

This publication summarizes epidemiologic and preclinical evidence and novel concepts by which obesity promotes pancreatic cancer. Among various potential mechanisms linking obesity with pancreatic cancer, the adipose tissue and obesity-associated adipose tissue inflammation play a central role. This review paper discusses selected topics and mechanisms that attracted recent interest and that may underlie the promoting effects of obesity in pancreatic cancer.

Cancers *is a peer-reviewed, open access medical journal of the oncology field published semimonthly.*

4. *Crosstalk between KRAS, SRC and YAP Signaling in Pancreatic Cancer: Interactions Leading to Aggressive Disease and Drug Resistance*. ***Cancers*** 2021,13(20):5126 (PMCID: PMC8533944)

E.Rozengurt, **G.Eibl**.

This manuscript surveys the current literature on the role of SRC and YAP in pancreatic cancer. It postulates, supported by novel original data of our own, that a complex signaling network exists between SRC, YAP, and Kras, which emphasizes the therapeutic potential of a combination of SRC and MEK inhibitors.

With additional publications under review and grant proposals under consideration, we look forward to sharing updates from Dr. Eibl and his lab in the near future.

Research Publications from the Sahin-Toth Laboratory in 2021

The Sahin-Toth Laboratory focuses on hereditary chronic pancreatitis, a major risk factor for pancreatic cancer. Working in collaboration with the Dr. Guido Eibl's The Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory, they seek to better understand how diet, genetics, obesity, and inflammation contribute to pancreatic cancer acceleration.

As Dr. Sahin-Toth wrote in the lab report, "2021 was about re-building the lab after the devastation COVID inflicted on the research community." With four new researchers in the lab, there is a new energy and enthusiasm which is driving several exciting projects. Despite the altered landscape of research in the COVID era, the Sahin-Toth lab continues to publish in renowned journals, receive NIH funding, and advance our understanding of pancreatic cancer research. The lab faces 2022 with, "strong momentum" and we are hopeful for another productive and successful year to come.

Publications from the Sahin-Toth Laboratory in 2021

1. Defective binding of SPINK1 variants is an uncommon mechanism for impaired trypsin inhibition in chronic pancreatitis. ***J Biol Chem*** 2021, 296:100343. PMC7949130

Szabó A, Toldi V, Gazda LD, Demcsák A, Tőzsér J, **Sahin-Tóth M**.

This biochemical study demonstrated that pancreatitis-associated mutations in the SPINK1 gene rarely alter binding of the trypsin inhibitor to its target, trypsin. Instead, the vast majority of

mutations reduce expression of protective SPINK1.

The Journal of Biological Chemistry is the preeminent biochemical journal of the American Society for Biochemistry and Molecular Biology.

2. Mouse model suggests limited role for human mesotrypsin in pancreatitis. ***Pancreatology*** 2021, 21:342-352. PMC7969449

Mosztbacher D, **Sahin-Tóth M**.

This study tested the potential role of mesotrypsin in pancreatitis using a novel genetically modified mouse model. Mesotrypsin is a human digestive protease uniquely resistant to trypsin inhibitors and capable of degrading those. While our findings do not support a significant role for mesotrypsin in pancreatitis, the conclusions further strengthen the already established importance of the other trypsin isoforms.

Pancreatology is the official journal of the International Association of Pancreatology and the European Pancreatic Club.

3. Sentinel acute pancreatitis event increases severity of subsequent episodes in mice. ***Gastroenterology*** 2021, 161:1692-1694. PMC8545756

Geisz A, **Sahin-Tóth M**.

This paradigm-shifting study provided experimental evidence for the SAPE hypothesis which posits that the first episode of acute pancreatitis sensitizes patients for subsequent episodes and progression of their disease.

Gastroenterology is the official journal of the American Gastroenterological Association (AGA) and the most prominent US publication in the gastroenterological sciences.

4. Common calcium-sensing receptor (*CASR*) gene variants do not modify risk for chronic pancreatitis in a Hungarian cohort. ***Pancreatology*** 2021, 21:1305-1310. PMC8663126

Takáts A, Berke G, Szentesi A, Farkas G Jr, Izbéki F, Erőss B, Czakó L, Vincze Á, Hegyi P, **Sahin-Tóth M**, Hegyi E.

This study resolved the contentious issue whether common variants in the CASR gene increased risk for chronic pancreatitis. Our findings conclusively demonstrated that these gene variants should not be considered risk factors in the clinical setting.

Pancreatology is the official journal of the International Association of Pancreatology and the European Pancreatic Club.

5. Evolutionary expansion of polyaspartate motif in the activation peptide of mouse cationic trypsinogen limits autoactivation and protects against pancreatitis. ***Am J Physiol Gastrointest Liver Physiol*** 2021, 321:G719-G734. PMC8668397

Orekhova A, Németh BC, Jancsó Z, Geisz A, Mosztbacher D, Demcsák A, **Sahin-Tóth M**.

This interesting study utilized protease biochemistry and a new genetically engineered mouse model to demonstrate that mouse cationic trypsinogen evolved features that limit accidental activation and prevent pancreatitis. The findings confirm and extend the notion that unwanted intrapancreatic activity of the digestive protease trypsin plays a central role in pancreatitis development and progression.

The American Journal of Physiology – Gastrointestinal and Liver Physiology is an official journal of the American Physiological Society.

6. Mouse models of trypsin-dependent pancreatitis. ***Pancreapedia***:

Exocrine Pancreas Knowledge Base, DOI: 10.3998/panc.2021.11

Sahin-Tóth M.

This contribution reviews novel mouse models designed to understand how intrapancreatic trypsin activity causes pancreatitis and how these mice will be useful for preclinical testing of novel therapies targeting trypsin.

*The **Pancreapedia** is an open-access scientific information repository designed to expedite research on the exocrine pancreas.*

The 5-Year Survival Rate for Pancreatic Cancer Improves for All Stages

This week's release of the American Cancer Society (ACS) Cancer Facts & Figures Report shows an increase to 11% in the 5-year survival rate for all stages. Seeing this marked improvement in survival rates shows that we're headed in the right direction in making a difference for the pancreatic cancer community.

An increase in the overall 5-year survival rate* for pancreatic cancer means more time with loved ones, greater hope for patients, and shows that our work is truly moving the needle. "This is positive news and it's what we like to see. Statistics, however, can't be the only driving force in this fight," says Agi Hirshberg, the Foundation Founder. "Moms, dads, and loved ones who courageously fight to beat the odds – they are our

inspiration to find a cure. Our community is funding the best research in the world, and we're doing it in honor of the people we love."

Our recent funding of 8 new Seed Grants continues to drive research and advance our understanding of this disease, with over 105 grants to date. With projects focused on targeted therapy, early detection, and prevention for high-risk individuals, our teams are striving to improve patient outcomes. Learn more about these Seed Grant projects in the most recent edition of our Momentum Newsletter.

The ACS report shares that 62,210 people in the US will be diagnosed with pancreatic cancer in 2022, a 2.8% increase from last year and a steadfast reminder of how important it is for each of us to take action today. Make 2022 the year to establish a personal cancer prevention plan for 2022 by learning the risk factors and facts about pancreatic cancer. If you or someone you know has been diagnosed with pancreatic cancer, contact us today.

Resources for Patients, Preventions, and Education

One-on-One Support

Patient & Family Webinars

Clinical Trials

As this new data is reviewed, we encourage you to be proactive and utilize the many resources available to our community. “We empower our community with resources, support, and education to fight for a cancer-free life,” shares Executive Director, Lisa Manheim. The actions we take for our own health and the health of our loved ones will help us beat the statistics.

* *The five-year survival rate, for the sake of this report, was determined by stage at diagnosis from 2011-2017 in the US.*

Momentum Newsletter: Winter

As this year comes to close, there is so much that we are thankful for, from reuniting in person at our Fall events, to our full roster of Seed Grants to a new year of possibility. It has been a busy and fulfilling year, and we are so grateful for our pancreatic cancer community.

The American Pancreatic Association (APA) Meeting

As a longtime supporter of the American Pancreatic Association (APA), we are honored to host the Hirshberg Opening Symposium

each year, and especially grateful to return to Miami this November to attend in person. This annual meeting brings together an international group of clinicians and scientists to discuss the latest research results and the best standards for treatment of pancreatic diseases. Each year we award the best abstracts, which are then published in the journal Pancreas. This year's awardees are Marta Sans, PhD, for her work to understand the progression on pancreatic cysts, and Gregor Werba MD, for his research into chemotherapy and T-cells. We applaud these young researchers and know that their efforts are driving us towards better treatment options.

Read more about the APA →

Seed Grants

We have returned to a full roster of Seed Grant awardees for 2021 and these 8 projects are working to advance pancreatic cancer research and improve patient outcomes. This year's projects range from understanding the tumor stroma in order to better design targeted treatment options, to analyzing how obesity impacts the development of pancreatic cancer in acinar and ductal cell derived tumors. One award will connect research from Oregon and Israel to form a consortium, allowing institutions to share data, create multi-institutional clinical trials and collectively learn how best to treat this disease. Collaboration and cooperation is the key to helping us conquer this disease, and that is what we are funding.

It is thanks to your support that we are able to make these advancements.

An Amazing Events Season!

The Fall was filled with excitement, and two events back-to-back! We united generations across the nation to make a difference, raise awareness and fund pancreatic cancer research.

Halloween marked the 24th Annual LA Cancer Challenge Walk/Run at UCLA and across the nation. Thanks to our community of patients, families, friends, and sponsors, we have raised over $522,000. We had participants from 33 states and 4 countries! Every dollar raised will advance research, and every step taken to cross the finish line is a step closer to a cure. We look forward to another extraordinary year as we celebrate 25 years of the LA Cancer Challenge in 2022!

The weekend after the LACC, our Hirshberg Training Team took to the streets to run the LA Marathon. On Sunday, November 7th, after a year of delays, every single one of our 27 HTT members crossed the finish line and helped raise over $125,000! We had 10 runners complete their very first marathon.

Want to cross the finish line yourself? Our Hirshberg Training Team is already gearing up for the 2022 LA Marathon and you can join them! Register today for personalized training from wherever you are, Put your sweat, your time and your dollars towards making a difference for all those facing pancreatic cancer.

Run the 2022 LA Marathon with the Hirshberg Training Team, Sunday, March 20, 2022

Register Today →

Our Patient & Family Education Symposium Returns in 2022

As we look toward the year to come, we are optimistic that we will be able to safely gather again for our Symposium at UCLA on April 23, 2022. Providing both an in-person and virtual opportunity to gather, learn from one another and create bonds through a shared experience, our Symposium is a keystone of the work we do. Connecting patients, families and researchers is an honor, we hope that you'll join us on April 23rd.

Save the Date →

Together we are driving research towards a cure while supporting all patients and families facing pancreatic cancer. The work we do is made possible thanks to your support.