Marathon Goddess, Julie Weiss Raises One Million Dollars for Pancreatic Cancer Research

Ten years ago, Julie Weiss finished her journey of 52 marathons in 52 weeks, in a quest to raise one million dollars for pancreatic cancer research and became known as the *Marathon Goddess*. On Sunday, March 19th, Weiss will be celebrated by pancreatic cancer survivors and supporters everywhere as she crosses the Los Angeles Marathon finish line yet again, and at the Hirshberg Foundation's Purple People Party Cheer Station near Mile 21. The celebration will commemorate Weiss raising more than one million dollars for pancreatic cancer research over the past decade, and helping raise awareness about the disease that has the highest mortality rate of all major cancers.

MY BIGGEST FAN & INSPIRATION…

In 2010, following the death of her father to pancreatic cancer, Julie remained determined to make a difference, and running gave her a purpose. Just one week after he passed, she fulfilled their dream for her to qualify and run the Boston Marathon. He was, after all, her biggest fan. "I know he was there with me. He was the wind at my back and had the best seat in the house my heart after I ran the Boston Marathon in 2011," Julie shared. From there, she decided to turn her passion into a purpose and embarked on an incredible endeavor to raise hope, money and awareness for pancreatic cancer. In time, Julie chose the name Marathon Goddess, but is quick to point out its true meaning that it is not about her, it's a name that allows her to encourage others to embrace their passion and let it shine.

A $1 MILLION DOLLAR GOAL…

Since 2010, Julie has made many ties in the pancreatic cancer community. She has witnessed the ups and downs of statistics and gotten to know the faces and journeys of countless survivors whom she has run in honor of. Through the ups and downs, her focus hasn't waivered: "When I began this journey, my objective was to raise a million dollars to find a cure for pancreatic cancer, the disease that took my father away from me, and to help others affected by this insidious disease," said Weiss."Julie set out to achieve a lofty goal, at the grass roots level, and never wavered in her commitment to see it through," said Lisa Manheim, Executive Director of the Hirshberg Foundation. "In addition to being our partner in helping spotlight pancreatic cancer, the awareness and money she raised has helped fund much-needed research bringing us one step closer to finding a cure." Throughout the years, Weiss has received support and donations from corporate sponsors and running organizations, however, the majority of her fundraising has come from individuals and families that have been impacted by the disease and those she has inspired through her running.

PHILANTHROPIST & AMBASSADOR…

As a marathon runner, author, philanthropist, ambassador and advocate, Weiss keeps busy by sharing enduring stories of hope, empowerment, loss and resilience from patients and families fighting for their lives and the lives of their loved ones. She has remained a fervent supporter of the Hirshberg Foundation throughout her journey, motivating fellow runners on the Hirshberg Training Team each year, running the LA Cancer Challenge 5K and receiving the Never Give Up Award, leading a team at Tour de Pier, and inspiring communities across the country to Never Give Up hope. She has been a spokesperson for

the Hirshberg Foundation's successful fundraising campaign, *52 Races for 52 Faces*, a year-long, philanthropic crusade in which she competitively ran in marathons, half marathons, 10Ks and 5Ks in 52 cities throughout the U.S., and across the Pacific Ocean to shine a light on pancreatic cancer. The campaign started and ended with Weiss running the Los Angeles Marathon which also included the foundation's signature Halloween fundraiser, the L.A. Cancer Challenge.

Through running, Weiss hopes to show the world that pancreatic cancer is much more than devastating statistics. There is a name and a face behind every survivor, and she is running for them. "Over a decade later, my mission to fight the good fight against pancreatic cancer has evolved to not only fundraise, but to be a voice for patients and to create awareness about the risks." She added, "Although we have seen progress, more needs to be done, and together, we can find a cure. We got this!"

AN EXTRAORDINARY FINISH…

Throughout this extraordinary journey, Julie has shared enduring stories of hope, empowerment, loss and resilience from patients and families fighting for their lives and the lives of their loved ones. She has crossed over 1,000 finish lines, whether she was completing her 52 Races for 52 Faces campaign or her most recent 12 races in 12 months to raise awareness about the 5-year survival rate that has increased two years in a row. The stories she has helped share will never be forgotten and thanks to the one and only Marathon Goddess, we are $1 million dollars closer to a cure through research funding and patient programs. *"Running with a purpose to fight the good fight against pancreatic cancer has become my mission; I will not stop until we have found a cure."* We look forward to cheering her on as she leaps across her 116th marathon finish line!

National Cancer Prevention Month: How to Create Your Personal Cancer Prevention Plan

As the Hirshberg Foundation funds invaluable patient programs and research in prevention, early diagnosis, therapies and patient care, among these paths to eradicate pancreatic cancer, prevention is at the forefront. As shared by the CDC, preventative care options including blood tests, annual screenings, surveillance, and scans are all available for various cancers and diseases. The Hirshberg Foundation is eager to empower you and your loved ones with the tools you need to take control of your health and be proactive in your cancer prevention plan. As National Cancer Prevention Month comes to a close, we encourage you and your loved ones, especially if you are at high risk, to use the resources we've provided to create a prevention plan that will allow you to thrive.

Begin your prevention journey by taking a personal inventory of your health. In 2021, the National Institutes for Health, discussed the importance of *Pancreatic cancer epidemiology: understanding the role of lifestyle and inherited risk factors*. Rethinking certain lifestyle choices, documenting your family history, and assessing your risk factors could help set a foundation for a healthier future. Tackling modifiable risk factors (smoking, obesity, diabetes and pancreatitis) are just that, *modifiable*. Making the decision to quit smoking, maintaining or losing weight, preventing type 2 diabetes or

pancreatitis are significant steps. Speak with your doctor about how to begin addressing these important health issues.

Over time, we have found that some communities are disproportionately affected by pancreatic cancer while genetics play an important role for others. Both are at high-risk and raising awareness is only the first step in addressing the issue. Whether you are of Ashkenazi Jewish ancestry or have a family history of diabetes, pancreatitis, or pancreatic cancer, it's important that we address these diseases before they become life threatening. Progress continues to be made in the field of pancreatic cancer as diagnostic blood and saliva tests are in development, but our ultimate goal is to offer a cancer-free future. After 25 years of fighting this disease on many fronts and sharing the facts, we remain confident that we are getting closer and closer to reaching this goal.

Learn how you can support our efforts and make a donation for cancer prevention today!

PANCREATIC CANCER PREVENTION RESOURCES

MODIFIABLE RISK FACTORS

- Smoking
- Obesity, Nutrition and Exercise
- Stage-2 Diabetes
- High Risk Communities
- Risk Factors

GENETIC COUNSELING & TESTING

- Genetic Counseling
- Ashkenazi Jewish Ancestry

- BRCA1 & BRCA2 gene mutations
- Hereditary Pancreatitis

EDUCATIONAL VIDEOS

- Dr. Marcia Canto, Johns Hopkins: Pancreatic Cancer Screening and Surveillance in High-Risk Individuals
- Wendy Conlon, UCLA: Why Should I See a Genetic Counselor?
- Dr. Zhoaping Li, UCLA: Nutrition & Pancreatic Cancer – Food Matters!
- UCLA Center for Nutrition: Boosting your Immune System

Seventeenth Annual Symposium on Pancreatic Cancer

Held in collaboration with the UCLA Agi Hirshberg Center for Pancreatic Diseases at the Luskin Conference Center
March 11, 2023
8:30 am – 3:00 pm

Schedule

8:30 am – 9:00 am	Check-in
9:00 am – 9:20 am	Welcome and Opening Remarks
	Lisa Manheim, Executive Director
	Hirshberg Foundation for Pancreatic Cancer Re
	Agi Hirshberg, Founder & CEO

	Hirshberg Foundation for Pancreatic Cancer Re
	O. Joe Hines, MD
	University of California, Los Angeles
9:20 am – 9:45 am	Turning Down the Volume on Worry: Managing C Related Anxiety
	Jenny Tran, PhD
	Simms/Mann – UCLA Center for Integrative Onc
9:45 am – 9:55 am	Q & A
9:55 am – 10:20 am	Dietary Management Post-Diagnosis
	Shelby Yaceczko, MS, RDN-AP, CNSC
	University of California, Los Angeles
10:20 am – 10:30 am	Q & A
10:30 am – 10:45 am	Break
10:45 am – 11:15 am	Pancreatic Cysts: Diagnosing and Treatment ir
	V. Raman Muthusamy, MD, MAS
	University of California, Los Angeles
11:15 am – 11:25 am	Q & A
11:25 am – 11:50 am	Integrative East-West Medicine to Optimize He Wellness
	KaKit P. Hui, MD
	University of California, Los Angeles

11:50 am – 12:00 pm	Q & A
12:00 pm – 12:10 pm	Survivor Photo
12:00 pm – 1:00 pm	Lunch
1:00 pm – 1:25 pm	Should I Participate in a Clinical Trial
	Randall Brand, MD
	University of Pittsburgh Medical Center
1:25 pm – 1:35 pm	Q & A
1:35 pm – 2:00 pm	Palliative Care – It's Not Hospice!
	Sandra H. Sacks, MD, MEd
	University of California, Los Angeles
2:00 pm – 2:10 pm	Q & A
2:10 pm – 3:00 pm	Panel Discussion: Perspectives from Survivors and
	Moderator: Jenny Tran, PhD
	Simms/Mann – UCLA Center for Integrative Onc

National Cancer Prevention Month: Taking a Proactive

Approach to Your Health

In recognition of National Cancer Prevention Month the Hirshberg Foundation is sharing important educational resources and steps you can take to live a healthier life. The goals of prevention are to help you and your loved ones remain cancer-free and to empower our community with the resources to keep you healthy. This month we will provide resources including a prevention worksheet, share the facts about risk factors, genetics, and the role of nutrition and exercise in your prevention plan. Pancreatic cancer prevention and awareness, especially for high-risk individuals, should be a priority for every family impacted by this disease. ***February 4th is also World Cancer Day, a reminder for all of us to raise awareness in our community, make an appointment for a cancer screening or genetic testing, and start a new healthy living plan.***

Your cancer prevention plan can become a year-round effort, however, as you start to check off your new year resolutions, this is the perfect time for a health check-in. Although pancreatic cancer remains the 3rd leading cause of cancer deaths in the U.S., taking steps to improve your health today can reduce your risk of being diagnosed. The key components to pancreatic cancer prevention include:

Know the inherited risk factors
Specific communities are disproportionately at higher risk for pancreatic cancer, learn whether you are in one of these groups.

Avoid the modifiable risk factors (obesity and smoking)
Choosing a nutritious diet, reducing stress and quitting habits including smoking and excessive drinking can extend your life.

Learn about pancreatic cancer testing and surveillance
Testing or surveillance may also be clinically recommended in

instances such as a new diagnosis of a pancreas cyst or lesion.

Seek genetic counseling
Meeting with a genetic counselor can help you determine your level of risk and how to tackle challenges.

In addition to personal pre-emptive steps you can take in your everyday life, the Foundation's Seed Grant Program continues to fund critical research and with the aim of pancreatic cancer prevention as well as therapeutics, diagnosis, immunology, and cancer biology. Thanks to these research projects, we are making strides forward everyday. Recently, the the 5-year survival rate for pancreatic cancer has increased to 12% putting it on an upward trajectory for the second year in a row. This news from the ACS (American Cancer Society) Cancer Facts & Figures Report gives survivors and families some additional hope as they navigate a diagnosis. We are headed in the right direction, but it is just as important that individual remain pro-active in our day-to-day lives.

Learn more about how to support our efforts and raise funds for cancer prevention.

[MAKE A DONATION]

Research Publications from the Sahin-Toth Laboratory in 2022

The most recent addition to our laboratories at UCLA, the Sahin-Toth Laboratory focuses on hereditary chronic pancreatitis, a major risk factor for pancreatic cancer. Dr. Miklos Sahin-Toth

joined UCLA to work in partnership with Dr. Guido Eibl in our Translational Laboratory to better understand how genetics, obesity, diet, and inflammation contribute to pancreatic cancer acceleration.

Dr. Sahin-Toth and his researchers continue to publish extensively in renowned journals, present at conferences around the world and receive NIH funding. With additional publications forthcoming and grant proposals under consideration, we look forward to sharing updates from Dr. Sahin-Toth and his lab in the near future.

Publications from the Sahin-Toth Laboratory in 2022

1. *Chronic progression of cerulein-induced acute pancreatitis in trypsinogen mutant mice.* ***Pancreatology*** 2022, 22:248-257. PMC8941852
Jancsó Z, Sahin-Tóth M.

This is an important follow-up study on our high-impact 2020 Gastroenterology paper that described increased severity of acute pancreatitis in mice carrying a trypsinogen mutation. Here we demonstrated that this trypsinogen mutation also sensitizes mice to chronic pancreatitis. Pancreatology is the official journal of the International Association of Pancreatology and the European Pancreatic Club.

2. *Misfolding-induced chronic pancreatitis in CPA1 N256K mutant mice is unaffected by global deletion of Ddit3/Chop*. ***Scientific Reports*** 2022, 12:6357. PMC9012826
Németh BC, Demcsák A, Geisz A, Sahin-Tóth M.

In our seminal 2019 Gut paper, we found high levels of the signaling molecule CHOP in mice with chronic pancreatitis due to a mutation in the digestive enzyme carboxypeptidase A1 (CPA1). In this follow-up study, we demonstrated that CHOP plays no role

in disease initiation or progression. In other words, CHOP is a marker rather than a driver of chronic pancreatitis. The Scientific Reports is an open-access journal publishing original research from all areas of life sciences. It is part of the prestigious Nature Research journal family.

3. *Modelling chronic pancreatitis as a complex genetic disease in mice.* ***Gut*** 2022 May 16. Epub ahead of print. PMC9666703
Jancsó Z, Demcsák A, Sahin-Tóth M.

Chronic pancreatitis is a complex genetic disease, and patients often carry multiple genetic variants. Here we crossed mouse strains with different pancreatitis-associated gene variants to study their combined effect. This remarkable study showed that mice with single genetic changes showed no pancreas disease; however, mice with both gene variants developed severe chronic pancreatitis. Gut is a preeminent journal in the gastroenterological sciences, published in Europe by BMJ.

4. *Variants in the pancreatic CUB and zona pellucida-like domains 1 (CUZD1) gene in early-onset chronic pancreatitis – A possible new susceptibility gene*. ***Pancreatology*** 2022, 22:564-571. PMC9250292

Rygiel AM, Unger LS, Sörgel FL, Masson E, Matsumoto R, Ewers M, Chen JM, Bugert P, Buscail L, Gambin T, Oracz G, Winiewska-Szajewska M, Mianowska A, Poznanski J, Kosińska J, Stawinski P, Płoski R, Koziel D, Gluszek S, Laumen H, Lindgren F, Löhr JM, Orekhova A, Rebours V, Rosendahl J, Párniczky A, Hegyi P, Sasaki A, Kataoka F, Tanaka Y, Hamada S, Sahin-Tóth M, Hegyi E, Férec C, Masamune A, Witt H.

Discovery of new gene variants that increase risk for chronic pancreatitis is an ongoing collaborative effort. In this paper, we contributed biochemical experiments to demonstrate that mutations in the CUZD1 gene may act as risk factors for chronic

pancreatitis. CUZD1 is an abundant protein in the pancreas with unclear function. Pancreatology is the official journal of the International Association of Pancreatology and the European Pancreatic Club.

5. *Risk of chronic pancreatitis in carriers of loss-of-function CTRC variants: A meta-analysis.* ***PLoS One*** 2022, 17:e0268859. PMC9122191
Takáts A, Berke G, Gede N, Németh BC, Witt H, Głuszek S, Rygiel AM, Hegyi P, Sahin-Tóth M, Hegyi E.

Meta-analysis of published studies is an important tool to define the extent of risk associated with various genetic variants in chronic pancreatitis. In this collaborative paper, we analyzed variants in the chymotrypsin C (CTRC) gene, which encodes a pancreatic digestive protease that protects the pancreas against harmful trypsin activity and pancreatitis. The journal PLoS One is published by the Public Library of Science as a peer-reviewed, open-access forum for a broad spectrum of scientific results.

6. *Rate of autoactivation determines pancreatitis phenotype in trypsinogen mutant mice.* ***Gastroenterology*** 2022, 163:761-763. PMC9398983
Demcsák A, Sahin-Tóth M.

Our flagship paper for the year! Here we demonstrated that the propensity of mutant trypsinogen to become active determines the severity of pancreatitis in mice, and by extension, in humans. Gastroenterology is the official journal of the American Gastroenterological Association (AGA), and the most prominent US publication in the gastroenterological sciences.

7. *Loss-of-function variant in chymotrypsin like elastase 3B (CELA3B) is associated with non-alcoholic chronic pancreatitis.* ***Pancreatology*** 2022, 22:713-718. PMC9474678

Tóth A, Demcsák A, Zankl F, Oracz G, Unger LS, Bugert P, Laumen H, Párniczky A, Hegyi P, Rosendahl J, Gambin T, Płoski R, Koziel D, Gluszek S, Lindgren F, Löhr JM, Sahin-Tóth M, Witt H, Rygiel AM, Ewers M, Hegyi E.

Discovery of new gene variants that increase risk for chronic pancreatitis is an ongoing collaborative effort. In this paper, we contributed biochemical experiments to demonstrate that a mutation in the CELA3B gene acts as a risk factor for chronic pancreatitis. The CELA3B gene encodes a pancreatic digestive protease called elastase 3B. Pancreatology is the official journal of the International Association of Pancreatology and the European Pancreatic Club.

8. *Hereditary pancreatitis-25 years of an evolving paradigm: Frank Brooks Memorial Lecture 2021.* ***Pancreas*** 2022, 51:297-301. PMC9348779
Sahin-Tóth M.

On November 4, 2021, Dr. Sahin-Tóth had the special honor of delivering the Frank Brooks Memorial Lecture at the Annual Meeting of the American Pancreatic Association. This article summarizes key points of the lecture, and the milestones of the past 25 years spent on researching hereditary pancreatitis. Pancreas is the official journal of the American Pancreatic Association (APA).

9. *Arg236 in human chymotrypsin B2 (CTRB2) is a key determinant of high enzyme activity, trypsinogen degradation capacity, and protection against pancreatitis*. ***Biochimica et Biophysica Acta – Proteins and Proteomics*** 2022, 1870:140831. PMC9426946.

Németh BZ, Demcsák A, Micsonai A, Kiss B, Schlosser G, Geisz A, Hegyi E, Sahin-Tóth M, Pál G.

As part of a large international collaboration, previously we

identified a common genetic change in the chymotrypsin B1-B2 genes (CTRB1-CTRB2) that protects against chronic pancreatitis (Gut 2018). In this elegant follow-up study, we collaborated with Dr. Gabor Pal's group to provide biochemical data that further clarified the mechanism by which chymotrypsins protect against pancreatitis. Biochimica et Biophysica Acta is one of the oldest scientific journals in the field of biochemistry, published by Elsevier.

10. *Preclinical testing of dabigatran in trypsin-dependent pancreatitis*. ***Journal of Clinical Investigation Insight*** 2022, 7:e161145. PMC9675574
Pesei ZG, Jancsó Z, Demcsák A, Németh BC, Vajda S, Sahin-Tóth M.

A compelling story offering hope for the development of a drug treatment for chronic pancreatitis! Here we used mice with a trypsinogen mutation to demonstrate that the anticoagulant drug dabigatran etexilate (brand name Pradaxa) had good therapeutic efficacy in pancreatitis. JCI Insight is the open-access sister journal of the distinguished Journal of Clinical Investigation (JCI), which publishes high-quality studies that provide meaningful contributions to the understanding of the biology and treatment of disease.

11. *Bicarbonate defective CFTR variants increase risk for chronic pancreatitis: A meta-analysis*. ***PLoS One*** 2022, 17:e0276397. PMC9584382.
Berke G, Gede N, Szadai L, Ocskay K, Hegyi P, Sahin-Tóth M, Hegyi E.

Meta-analysis of published studies is an important tool to define the extent of risk associated with various genetic variants in chronic pancreatitis. In this collaborative study, we analyzed the association of variants in the cystic fibrosis transmembrane conductance regulator (CFTR) gene and chronic

pancreatitis. The journal PLoS One is published by the Public Library of Science as a peer-reviewed, open-access forum for a broad spectrum of scientific results.

12. *Novel p.G250A mutation associated with chronic pancreatitis highlights misfolding-prone region in carboxypeptidase A1 (CPA1).* ***International Journal of Molecular Sciences*** 2022, 23:15463. PMC9779553

Sándor M, Thiel FG, Schmid M, Demcsák A, Morales Granda NC, Németh BC, Vajda S, Hoerning A, Sahin-Tóth M.

Characterization of novel gene mutations found in patients with chronic pancreatitis is an ongoing project in our laboratory. Here we described functional properties of a newly identified gene variant in the digestive enzyme carboxypeptidase A1 (CPA1). Mutations in this enzyme have been known to cause hereditary pancreatitis in humans. The International Journal of Molecular Sciences is an open-access journal providing an advanced forum for a large variety of research projects, including biochemistry.

Research Publications from the Hirshberg Translation Laboratory in 2022

This February marks 25 years since the creation of the Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory. A cornerstone of our research program, this lab was the first at UCLA to be solely dedicated to investigating the driving forces

and biology of pancreatic cancer. Dr. Guido Eibl's research program is consistently funded by the National Institutes of Health (NIH) and continues to deepen our understanding of the intricate ways that diet, obesity and inflammation can accelerate tumor development.

We applaud Dr. Eibl and his lab and look forward to sharing more of the progress being made through their projects.

Publications from the Translational Laboratory in 2022

1. *Statins inhibit inflammatory cytokine production by macrophages and acinar to ductal metaplasia of pancreatic cells.* ***Gastro Hep Advances*** 2022; 1:640-651 (PMCID: PMC9615480)
S. Ako*, Y. Teper*, L. Ye, J. Sinnett-Smith, O.J. Hines, E. Rozengurt, G. Eibl. (* dual first authorship)

This original research paper reported that statins, FDA-approved drugs to treat hypercholesteremia, inhibited early pancreatic cancer development in cell culture and animal models. At least some of the effects were mediated by inhibiting macrophages, important inflammatory cells in the pancreatic microenvironment. This study supports the notion that statins may be beneficial in reducing the risk of pancreatic cancer.

2. *Opposite effects of Src family kinases on YAP and ERK activation in pancreatic cancer cells: Implications for targeted therapy.* ***Molecular Cancer Therapeutics*** 2022;21(11):1652-1662 (PMCID: PMC9630827)
J. Sinnett-Smith, T. Anwar, E.F. Reed, Y. Teper, G.Eibl, E. Rozengurt.

This paper described a novel signaling crosstalk in pancreatic cancer cells. In addition, the combination of SRC inhibitor and MEK inhibitor, FDA-approved drugs to treat certain types of human cancers, very strongly inhibited pancreatic cancer growth

in mice. This novel finding indicates a potential role of these drugs for a combination therapy in pancreatic cancer.

3. *Body Mass Index Trajectories Across the Adult Life Course and Pancreatic Cancer Risk.* ***Journal of the National Cancer Institute: Cancer Spectrum*** 2022;6(6) (PMCID: PMC9651977)

S. Arjani, P.F. Saint-Maurice , S. Julián-Serrano, G. Eibl, R. Stolzenberg-Solomon.

In collaboration with an epidemiology group at the NCI, this manuscript described the risk of developing pancreatic cancer in humans with various body mass index (BMI) trajectories across their adult life. It unequivocally shows that subjects that were overweight and/or obese as young adults and stayed in the overweight/obese category later in life carry the greatest risk of developing pancreatic cancer. The risk was greater in males than in females.