## Cannabis Components and Cancer: What We Know and Where We're Headed

Dr. Ziva Cooper, Director of the UCLA Cannabis Research Initiative, will join our <u>Patient and Family Webinar Series</u> to talk about the history of <u>cannabis</u> and what has been established with respect to cannabis and cancer. Dr. Cooper will discuss the origins of cannabis, its various cannabinoid components, current research and an exciting new study that may help cancer patients.

Dr. Cooper will spotlight a new study on the pain relief and appetite stimulating effects of cannabigerol (CBG), a minor cannabinoid that seems to lack the psychoactive side effects of THC. This research could provide a new tool to help manage the side effects of cancer treatment, such as loss of appetite and pain. The study will investigate whether CBG, alone or in synergistic combination with low doses of THC, can provide analgesic (pain relief) and appetite-stimulating properties in humans. It is particularly exciting as this will be the <u>first</u> <u>study of CBG</u> in humans.

Please join us for an hour of interesting conversation with Dr. Ziva Cooper on Friday, February 26th, 2021 at 1pm (PST). The presentation will be followed by a Q & A and our new **Survivor Chat**. During this time of isolation we continue to do what we can to bring our pancreatic cancer community together. Our **Survivor Chat**, is a space for patients and loved ones to have an opportunity to spend time talking amongst each other once the webinar is over. Share stories, information and ask questions of your fellow participants from the comfort of your living room! As the Director of the UCLA Cannabis Research Initiative, Dr. Cooper strives to incorporate a translational approach to understating both the potential therapeutic and adverse effects associated with cannabis and cannabinoids. Dr. Cooper is also Associate Professor-in-Residence in the Department of Psychiatry and Biobehavioral Sciences at David Geffen School of Medicine. Her current research involves understanding variables that influence both the therapeutic potential and adverse effects of cannabis and cannabinoids.

## More about UCLA's Cannabis Research Initiative:

The UCLA Cannabis Research Initiative (CRI) is a strategic initiative out of the UCLA Jane and Terry Semel Institute for Neuroscience and Human Behavior. As one of the first university programs focused on the multidisciplinary study of cannabis, they aim to bring together experts from diverse fields to advance the understanding the plant's impact on body, brain, and Despite unprecedented access, nearly a century of society. research restrictions and funding barriers have contributed to a lack of scientific knowledge about cannabis and hemp, particularly in regards to the therapeutic potential and the industrial applications. Their mission is to address the most pressing questions related to the impact of cannabis legalization through rigorous scientific study and discourse across disciplines.

## Watch Webinar

## February is National Cancer Prevention Month: Lifestyle

Throughout National Cancer Prevention Month we'll share risk factors, scientific research, webinars on topics touching on prevention and facts about how you can make an impact.

The choices we make and avoid when it comes to our personal health can have a ripple effect throughout the body. Research has shown that certain lifestyle choices, such as smoking, can damage cells and create a domino effect throughout our DNA. When cells become damaged, there is a risk of gene mutations that can cause cells to divide at unprecedented rates and grow exponentially. When cells grow rapidly, out of control or do not die off at the appropriate time, they cause tumors. In most pancreatic cancer cases, <u>risk factors</u> such as smoking, obesity, stage-2 diabetes and chronic pancreatitis can cause these DNA mutations. The first steps on the path to prevention are to adopt a healthy lifestyle and lower your modifiable risk factors.

Our <u>Path to Prevention</u> worksheet outlines risk factors to avoid and steps you can take to get on track towards wellness. While the scientific community is investigating possible methods for prevention and early screening, it is up to us to stay vigilant about our health. If you smoke make a <u>plan to quit</u>, reduce your alcohol intake and remember that your food choices matter. Build a lifestyle around <u>nutritious food</u>, find ways to <u>boost the</u> <u>immune system</u>, take care to <u>reduce stress</u> and <u>kick bad habits</u> as these changes may even save your life. Speak with your doctor on the best course of action to reduce inflammation, prevent insulin-resistance and lower stress. The path to prevention starts with a healthy lifestyle that can help lower your risk for cancer.

Share our Path to Prevention worksheet with your community »

## **Prevention Research**

In 2020, a team of UCLA researchers were awarded an NIH grant for \$5.75 million to study the roles diet, obesity and inflammation play in the development of pancreatic cancer. "We know that the biological mechanisms of obesity, such as inflammation, can lead to the development of pancreatic cancer," said Dr. Guido Eibl, Laboratory Director of the Hirshberg Translational Pancreatic Cancer Research Laboratory. This study will look at the mechanisms that drive the formation of pancreas tumors with the goal of prevention strategies for those at higher risk. Dr. Eibl included, "Several known and modifiable risk factors can increase the risk for pancreatic cancer, including obesity, smoking, and alcohol. In addition, chronic pancreatitis and genetic factors can enhance the risk for pancreatic cancer. It is paramount to avoid or lower known risk factors, manage chronic pancreatitis, and get genetic counseling (if pancreatic cancer runs in the family) to reduce the risk of and prevent pancreatic cancer."

Read more about Dr. Eibl's research »

## Share the Love on Valentine's Day

On Valentine's Day, most people show their love through roses & chocolates. This year, share your love with patients and families facing pancreatic cancer. Check out the many ways you can celebrate Cupid and make a difference in the fight against this disease.

Agi & Ron Hirshberg are a love story for the ages. Three days after they met, they set their wedding date for Valentine's Day 1987. Just 10 years later, Ron was taken by pancreatic cancer and, in his memory, the Hirshberg Foundation was founded. Valentine's Day is a bittersweet memory of their wedding anniversary and a reminder of why our "Never Give Up" motto is so important.

## Watch Agi's Love Story

## Viola Floral



Jelena was a caretaker to her mom as she battled pancreatic cancer. Today, she keeps her mom's memory and spirit alive through her designs at <u>Viola Floral</u>. Her floral arrangements pay homage to all the women who raise and uplift us, through all walks of life. Like flowers, they continually remind us to live in full bloom. As a special dedication, 50% of the proceeds from the sale of the "Hopeful Blooms" arrangement will benefit the Hirshberg Foundation. Delivery available in Los Angeles County only.

<u>Send a gorgeous bouquet that gives back  $\rightarrow$ </u>

## Jewelry



Wear your support proudly! Our collection of hand-picked jewelry gives back, creates awareness and looks fabulous. Treat yourself or a loved one to one of our bracelets or necklaces. Shop today  $\rightarrow$ 

## Valentines e-Card



Don't rush out to Hallmark store. Send a Valentines e-card to all the loved ones in your life. <u>Donate today</u> → We wish everyone a safe, healthy and happy Valentine's Day.

## February is National Cancer Prevention Month!

Throughout National Cancer Prevention Month we'll share risk factors, scientific research, webinars on topics touching on prevention and facts about how you can make an impact.

The first step on the pancreatic cancer prevention path is making healthy lifestyle choices. It takes decisive action to commit to quit smoking, maintaining a healthy weight, avoiding diabetes and managing pancreatitis. Learning about these lifestyle changes, or <u>modifiable risk factors</u>, empowers us to make healthy choices that can help prevent cancer. Adopting healthy lifestyle choices is the first step towards decreasing risk.

While we can change some risk factors, others are beyond our control, like family history and genetics. Knowledge is power when it comes to these immutable risk factors. It is important to know your family history and determine if there are familial risk factors. Seeking out a qualified geneticist allows those at an increased risk for hereditary pancreatic cancer to make proactive choices. While there is still no early screening test for pancreatic cancer, those with a genetic predisposition may qualify for <u>screening programs</u>. Across the US researchers have created pancreatic cancer tumor registries to track people with an increased genetic risk. Some of these registries include:

- The <u>Pancreatic Tumor Registry</u> at Memorial Sloan Kettering Cancer Center (MSKCC)
- The National Familial Pancreatic Tumor Registry (NFPTR) at

Johns Hopkins University

 The <u>Cancer of the Pancreas Screening-5</u> (CAPS5) Study which is also a clinical trial currently conducted at 8 universities

Researchers continue to investigate what puts us at risk organically, genetically, environmentally and socioeconomically so that we can better prevent and treat pancreatic cancer. While scientists continue to explore and uncover what leads to pancreatic cancer, the first step on the path to prevention is to stay vigilant with your healthy choices.

Learn more about risk factors >>

## **Prevention Research**

The Hirshberg Foundation funds research to better understand the biology behind tumor development as well as to fully understand how environmental factors can accelerate tumor growth. This research contributes to pancreatic cancer prevention, early screening and treatment options.

The Sahin-Toth Laboratory, under the direction of leading pancreatic disease researcher, Dr. Sahin-Toth, is contributing to our understanding of this disease and one of the largest risk factors: chronic pancreatitis. In 2020, the Sahin-Toth lab <u>published 10 papers</u>, including a new study that looks at lifestyle factors and acute pancreatitis to determine prevention strategies. Working closely with the <u>Hirshberg Translational</u> <u>Pancreatic Cancer Research Laboratory</u> these two labs are working to better understand how diet, obesity, genetics & inflammation contribute to pancreatic cancer acceleration.

# Research Publications from the Sahin-Toth Laboratory in 2020

In 2019 the Hirshberg Foundation supported UCLA in the recruitment of Miklos Sahin-Toth, MD, PhD, a leading pancreatic disease researcher and a specialist in chronic pancreatitis. The Sahin-Toth Laboratory is located next door and works closely with the The Ronald S. Hirshberg Translational Pancreatic Cancer Research Laboratory, headed by long-standing director Guido Eibl, MD, Professor, Department of Surgery.

The two labs formed a strategic alliance to better understand how diet, obesity, genetics & inflammation contribute to pancreatic cancer acceleration. Dr. Eibl's lab remains at the forefront of cutting-edge investigations into treatment, cancer biology, and potential preventive measures. Dr. Sahin-Toth's lab focuses on hereditary chronic pancreatitis, a major risk factor for pancreatic cancer. Drs. Eibl and Sahin-Toth are committed to illuminating the role of pancreatic inflammation in cancer development and exploring potential interventions that could thereby reduce cancer risk. The two labs were awarded a collaborative research grant in 2020 to continue their important coordinated efforts.

In 2020, Dr. Sahin-Toth's lab published the results of their research in various medical journals. Publishing this research adds to the understanding and body of knowledge on pancreatic cancer, helping researchers around the globe. As we heard from all labs, 2020 brought the added study of COVID-19 research to all disciplines, including Dr. Sahin-Toth's. We are very proud of the accomplishments of both teams and look forward to

continued progress.

## Publications from the Sahin-Toth Laboratory in 2020

#### 1) Mutation that promotes activation of trypsinogen increases severity of secretagogue-induced pancreatitis in mice.

Gastroenterology 2020, 158:1083-1094. Jancsó Z, Sahin-Tóth M.

This seminal study demonstrates that a mutation in the main digestive enzyme, trypsinogen, makes mice more susceptible to pancreatitis. The genetic mutation investigated in this study was described in patients with hereditary pancreatitis. A major goal of our laboratory is to model human disease in mice and use the mouse models to test new therapeutics.

**Gastroenterology** is the leading US journal in the gastroenterological sciences.

#### <u>2) Alcohol-dependent effect of *PRSS1-PRSS2* haplotype in chronic pancreatitis.</u>

**Gut** 2020, 69:1-2. Hegyi E, Tóth AZ, Vincze Á, Szentesi A, Hegyi P, Sahin-Tóth M.

This paper describes the observation that a commonly found genetic risk factor that predisposes to pancreatitis has a larger effect in the context of chronic alcohol abuse. The findings confirm that genetic and environmental risks factors interact and amplify each other's effect on disease development. **Gut** is considered the top journal in the gastroenterological sciences.

#### 3) Measuring digestive protease activation in the mouse pancreas.

**Pancreatology** 2020, 20:288-292. Mosztbacher D, Demcsák A, Sahin-Tóth M.

This is an important methodological paper that describes how to measure the activity of digestive enzymes trypsin and chymotrypsin in the pancreas of mice. These digestive enzymes play important roles in the development of pancreatitis and routine and reliable measurement of their levels is a key experimental technique.

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

## 4) LIFEStyle, Prevention and Risk of Acute PaNcreatitis (LIFESPAN): protocol of a multicentre and multinational observational case-control study.

**BMJ Open** 2020, 10:e029660. Koncz B, Darvasi E, Erdősi D, Szentesi A, Márta K, Erőss B, Pécsi D, Gyöngyi Z, Girán J, Farkas N, Papp M, Fehér E, Vitális Z, Janka T, Vincze Á, Izbéki F, Dunás-Varga V, Gajdán L, Török I, Károly S, Antal J, Zádori N, Lerch MM, Neoptolemos J, Sahin-Tóth M, Petersen OH, Hegyi P.

This clinical study protocol originated from Peter Hegyi, Phd, Professor of Medicine, University of Pécs, Hungary. This publication lays out the parameters for LIFESPAN, an observational, multicenter, multinational case-control study to examine associations between socioeconomic factors, dietary habits, physical activity, chronic stress, sleep quality and acute pancreatitis. The Sahin-Toth lab was invited to contribute as part of an international board of advisers.

**BMJ Open** is an open access journal, dedicated to publishing medical research from all disciplines.

## 5) Ethanol feeding accelerates pancreatitis progression in CPA1 N256K mutant mice.

American Journal of Physiology-Gastrointestinal and Liver Physiology 2020, 318:G694-G704. Orekhova A, Geisz A, Sahin-Tóth M.

Here, we investigated the interaction of genetic predisposition and environmental injury on the development of pancreatitis. In this study, a mouse model carrying a mutant digestive enzyme was fed an alcohol diet, which facilitated the progression of pancreas damage.

The American Journal of Physiology-Gastrointestinal and Liver Physiology publishes papers on the physiology and mechanism that affect the liver and gastrointestinal system.

## 6) Inactivation of mesotrypsin by chymotrypsin C prevents trypsin inhibitor degradation.

Journal of Biological Chemistry 2020, 295:3447-3455. Toldi V, Szabó A, Sahin-Tóth M.

This biochemical study examined how one digestive enzyme (chymotrypsin C) regulates another (mesotrypsin) and how this impacts the development of pancreatitis. Our laboratory has a long track record in digestive enzyme biochemistry, and

experiments like these formed the basis of our successful mouse model program.

The **Journal of Biological Chemistry** is a preeminent biochemical journal.

#### 7) Channelopathy of the pancreas causes chronic pancreatitis.

Gastroenterology 2020, 158:1538-1540. Sahin-Tóth M.

This is an editorial on the recent discovery of TRPV6 mutations in patients with chronic pancreatitis. TRPV6 is a calcium channel found in the excretory ducts of the pancreas. Identification of new genetic risk factors is always exciting as these represent novel targets for therapeutic intervention.

**Gastroenterology** is the leading US journal in the gastroenterological sciences.

#### <u>8) International Consensus Guidelines for</u> <u>Risk Factors in Chronic Pancreatitis</u>.

Recommendations from the working group for the international consensus guidelines for chronic pancreatitis in collaboration with the International Association of Pancreatology, the American Pancreatic Association, the Japan Pancreas Society, and European Pancreatic Club.

**Pancreatology** 2020, 20:579-585 Hegyi P, Párniczky A, Lerch MM, Sheel ARG, Rebours V, Forsmark CE, Del Chiaro M, Rosendahl J, de-Madaria E, Szücs Á, Takaori K, Yadav D, Gheorghe C, Rakonczay Z Jr, Molero X, Inui K, Masamune A, Fernandez-Del Castillo C, Shimosegawa T, Neoptolemos JP, Whitcomb DC, Sahin-Tóth M; Working Group for the International (IAP – APA – JPS – EPC) Consensus Guidelines for Chronic Pancreatitis. Consensus guidelines are important documents that guide clinical management and decision-making. Opinion leaders and experts in the field contributed to this paper that discusses risk factors for chronic pancreatitis.

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

### 9) Loss of chymotrypsin-like protease (CTRL) alters intrapancreatic protease activation but not pancreatitis severity in <u>mice</u>.

**Scientific Reports** 2020, 10:11731. Mosztbacher D, Jancsó Z, Sahin-Tóth M.

This study tested the role of a digestive enzyme (chymotrypsinlike protease) in pancreatitis using a novel mouse model deficient in this enzyme. The observations indicated that chymotrypsin-like protease does not play a significant role in the disease. Although this is considered a "negative study," the findings are still important as they add to our growing knowledge on digestive enzyme function in health and disease.

**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.

#### <u>10) Lipotoxicity and cytokine storm in</u> <u>severe acute pancreatitis and COVID-19</u>.

Gastroenterology 2020, 159:824-827. Hegyi P, Szakács Z, Sahin-Tóth M.

This paper is our contribution to understanding the science

behind COVID-19. In this editorial, which also contains original data, we highlight similarities between severe COVID-19 and severe acute pancreatitis. Remarkably, the same toxic substances and immunological factors determine progression of both diseases.

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## Don't Give Up the Fight

This article originally appeared in U Magazine, a publication of UCLA Health, David Geffen School of Medicine. The Centennial Campaign for UCLA Issue 2020's theme was "Giving Matters — Visionary philanthropy shapes a new future for UCLA Health." We are proud that our founder, Agi, is featured in a story about the Foundation's commitment to never give up and the slow but steady progress towards a cure.

By Shari Roan • Illustration by <u>Jenny Kroik</u> Originally published in UCLA Health's <u>U Magazine</u>

In the competitive wholesale apparel business, Agi and Ronald Hirshberg would implement a new business idea and give it 18 months to bear fruit. If it wasn't successful, they would pull the plug and move on. After Ronald died of pancreatic cancer in 1997 at age 54, Hirshberg focused that same determination on the effort to find a cure for the ravaging illness that took her husband's life. "I had that business mentality," Hirshberg recalls. "You begin, build inventory and sell it. I figured I'd give a little donation, and 18 months later there would be a cure for pancreatic cancer."

However, the world of medical research is vastly different than that of apparel, and the time it takes to reach a breakthrough is measured in years, not months. Patience and resolve are necessary to sustain the effort. More than two decades later, a cure for pancreatic cancer is closer but still not in hand.

Hirshberg never thought of abandoning the fight. Her philanthropy established the UCLA Agi Hirshberg Center for Pancreatic Diseases, one of the nation's leading centers focused on the disease, and she has funded scores of research projects through the Hirshberg Foundation for Pancreatic Cancer Research. "I am pleased and happy we've helped so many patients, but I don't have the satisfaction of finishing the job just yet," she says. "With my business mindset, I can't take credit until the job is done. But I do feel that, within the next five years, we'll have an early detection test for pancreatic cancer."

Pancreatic cancer is among the most devastating cancer diagnoses. About 57,000 Americans are diagnosed with the disease – often at a late stage – each year. The five-year survival rate is only nine percent, although the survival outlook for people diagnosed today is improving.

Agi and Ronald Hirshberg were in the small town of Portsmouth, N.H., when he became ill and was diagnosed with the disease. The couple returned to their home in Los Angeles and sought care at UCLA. Ronald had an inoperable tumor and, despite the best efforts of his physicians, he survived just eight months.

"My relationship with the doctors who took care of him was perfection," Hirshberg says. "Their kindness, their caring was unforgettable. I felt UCLA really treated him so beautifully. After he passed, I called UCLA and said I wanted to support the pancreatic cancer program. They said they didn't have a pancreatic cancer program. I said you have one now."

Hirshberg's efforts have helped fuel tangible progress in improving the care of patients with pancreatic cancer. She was an early advocate of seed grants, money to fund high-risk, highreward research projects needed to find new and creative ways to crack the mysteries surrounding the disease. That research has resulted in a much better understanding of the molecular processes that steer the disease, promising work on early detection and improved surgical and chemotherapeutic treatments.

In choosing to direct her philanthropy to UCLA, Hirshberg says she "picked the right partner." The UCLA Agi Hirshberg Center for Pancreatic Diseases has set the highest bar for contemporary pancreatic cancer care. The center is home to an integrativepractice unit, a groundbreaking program that allows patients to receive an extensive evaluation and personalized treatment plan in one visit. "My determination never wavered," she says. "What sustained me is that we kept going and improving. There were so many baby steps. I felt if we could not find an early detection test right this second, my next concern was the patient experience. Today, UCLA is one of the few integrative-practice units that provide the kind of services patients need, including the psychosocial portion that helps not only patients, but also caregivers."

She says she is especially heartened by the efforts of top pancreatic cancer clinicians and researchers at UCLA and elsewhere who are collaborating to accelerate the pace of progress. And when it feels like things are still moving too slowly, she thinks about the annual LA Cancer Challenge, a run/walk held on the UCLA campus that benefits the Hirshberg Foundation for Pancreatic Cancer Research. The event reinvigorates her, Hirshberg says. "On that day, with all those people gathered who have the same wish as I do, I know our loved ones are up there watching," she says. "Ronald and I were partners in life. We had pancreatic cancer together. We were fighting it together. Although he is gone, it has never occurred to me that I could stop."