# Symposium Speaker Spotlight: Dr. Vikas Dudeja to discuss the Gut and Tumor Connection in Pancreatic Cancer

The Hirshberg Foundation is excited to announce Dr. Vikas Dudeja will be joining us at the 16th Annual Symposium on Pancreatic Cancer to discuss the potential role the gut plays in pancreas cancers.

“We are just beginning to fully understand the complexities of the relationship between the microbiome and cancer,” said Dudeja. “Our lab, and other researchers across the nation, will continue to dig into these complexities in order to better understand how we can control and cure cancers.”

Dr. Dudeja currently serves as an Associate Professor as well as the Division Director of surgical oncology at the University of Alabama at Birmingham’s Department of Surgery.

Dr. Dudeja completed his bachelor of medicine and surgery at the All India Institute of Medical Sciences (AIIMS) in New Delhi, India. He also received his master of surgery from AIIMS in 2005. Dr. Dudeja spent the next 3 years doing research on the pathogenesis of pancreatic cancer and developing novel therapies against this aggressive disease. Afterwards he received residency training in general surgery at the University of Minnesota from 2008-2013. Following his residency, Dr. Dudeja completed a complex general surgical oncology fellowship and hepato-pancreato-billiary fellowship at Memorial Sloan Kettering Cancer Center from 2013-15. Dr. Dudeja is also a Fellow of the American College of Surgeons.

On the research front, Dr. Dudeja's laboratory focuses on deciphering the biology of the tumor microenvironment in pancreatic cancer and the interaction of gut microbiome with anti-cancer immune response. Elucidation of the mechanism and determinants of tumor recurrence is another key area studied in his laboratory. His research efforts are funded by grants from National Institute of Health (NIH), Veterans Affairs, Department of Defense and Society Grants. His work has been published in high impact journals like Gastroenterology, GUT, Clinical Cancer Research and Nature Reviews in Gastroenterology and Hepatology. He serves on the editorial board of Gastroenterology and routinely reviews manuscripts submitted to many journals including Pancreatology, eBiomedicine, Communication Biology, Annals of Surgical Oncology.

Dr. Dudeja's clinical interests include taking care of patients with pancreatic cancer, pancreatic cyst, hepatobiliary malignancies including cholangiocarcinoma, kaltskin tumor, colorectal cancer liver metastases, and benign disease like bile duct injury and chronic pancreatitis.

The complex relationship between cancer and the microbiome is such an important piece of the puzzle and we are honored to have Dr. Dudeja present *Understanding the Gut and Tumor Connection in Pancreatic Cancer*.

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# Symposium Speaker Spotlight:

# Dr. Marcia Canto to discuss Pancreatic Cancer Screening and Surveillance in High-Risk Individuals

The Hirshberg Foundation is honored to announce that Dr. Canto will discuss screening and surveillance in individuals with a high-risk for pancreatic cancer at the 16th Annual Symposium on Pancreatic Cancer.

While participating in a pancreatic cancer screening program is not appropriate for everyone, it is an important consideration for individuals with known high-risk factors. For those with particular risk factors, including family history and certain genetic syndromes that increase susceptibility to pancreas cancer, it may be appropriate to participate in a research screening program. Surveillance may also be clinically recommended in instances such as a new diagnosis of a pancreas cyst or lesion. Many experts believe that individuals with a greater than fivefold risk of developing pancreatic cancer should undergo regular early detection tests to survey their pancreas. Regular surveillance uses medical imaging and endoscopic techniques to detect precancerous lesions or early pancreatic cancer that can be surgically removed. Screening and surveillance of high-risk individuals is a topic important to our pancreatic cancer community and we are happy to have an expert in the field present more information.

Marcia (Mimi) Canto, M.D., M.H.S. is a Professor of Medicine and Oncology at The Johns Hopkins University School of Medicine. She is also the Director of Clinical Research at the Johns Hopkins Division of Gastroenterology. Dr. Canto received her Bachelor of

Science degree from the University of the Philippines in Manila in 1981 (summa cum laude). She received her Doctor of Medicine degree in 1985 from the University of the Philippines and completed her training in Internal Medicine from State University of New York Sciences Center in Brooklyn, Brooklyn, New York.

Dr. Canto completed a postdoctoral fellowship in Gastroenterology-Hepatology at The Johns Hopkins University School of Medicine and received a Master of Health Science in Clinical Epidemiology from The Johns Hopkins University School of Hygiene and Public Health. Dr. Canto came back to Johns Hopkins after advanced endoscopic training at the University Hospitals of Cleveland. Her primary clinical and research interests include endoscopy, particularly the use of endoscopic ultrasound (EUS) in detecting early pancreatic cancer and its precursors. She has shown that endoscopic ultrasound can be used to detect asymptomatic precancerous lesions in patients with a family history of pancreatic cancer, downstage pancreatic cancer screen-detected pancreatic cancer, and improve survival.

A subject that we are excited to learn more about from one of the top experts in this field, we welcome Dr. Canto to educate us on *Pancreatic Cancer Screening and Surveillance in High-Risk Individuals.*

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# 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.

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# 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.

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# 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.