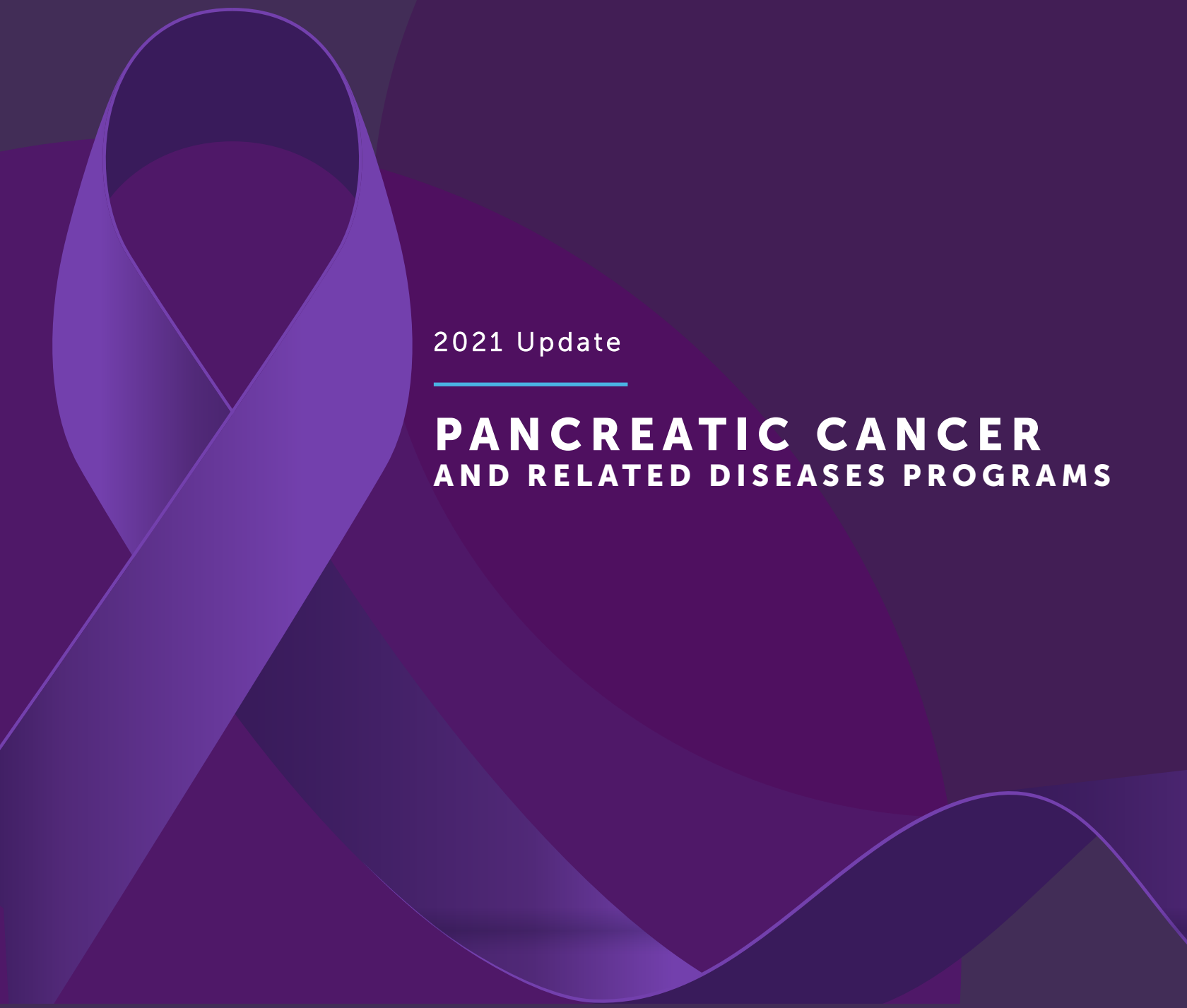
SIDNEY KIMMEL CANCER CENTER | NCI-designated



2021 Update

PANCREATIC CANCER
AND RELATED DISEASES PROGRAMS

Jefferson Health | reimagine CAMPAIGN

Pancreatic Cancer and Related Diseases Multidisciplinary Team

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Department of Radiation Oncology:
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Hien Dang, PhD
Elda Grabocka, PhD
(joint appointment with SKCC)
Aditi Jain, PhD
Saed Khalilieh, MD
Harish Lavu, MD, FACS
Avinoam Nevler, MD
Charles J. Yeo, MD, FACS
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A Message from Dr. Yeo:

The last two years allowed Jefferson to demonstrate what resilience looks like. Every member of the team: faculty, fellows, residents, and students rallied to the cause of caring for patients and keeping them safe from a deadly virus.

Pancreatic cancer patients and their loved ones exhibit that same hardiness, in the face of an aggressive disease. That's why Jefferson is determined to offer patients and their families a holistic approach, led by a compassionate and committed multidisciplinary team. Starting with the Sidney Kimmel Cancer Center Support and Welcome Center and extending into every office and clinic, Jefferson clinicians and researchers keep their focus on improving treatment options and providing exceptional and personalized care, even in the midst of a pandemic.

National organizations have taken note. *U.S. News & World Report* once again ranked Jefferson as one of the nation's best in Cancer and Gastroenterology/GI Surgery. Dr. Theresa Yeo was recently awarded Advanced Oncology Certified Nurse Practitioner of the Year, and Dr. Aditi Jain received the 2021 PanCAN Career Development Award.

All of this reflects a commitment we share at Jefferson to improve lives and offer hope. The support of generous benefactors allows Jefferson to maintain our momentum, without losing a step, as we reimagine healthcare.

Sincerely,

Charles J. Yeo

Charles J. Yeo, MD, FACS
Samuel D. Gross Professor and Chair of Surgery
Senior Vice President and Chair,
Enterprise Surgery, Jefferson Health
Co-Director, Pancreas, Biliary and Related Cancer Center

Advancing Innovation in Treatment

The Jefferson Pancreatic Cancer Research Institute (JPCRI) and departments with which it is affiliated have continued to gain strength while building Jefferson's capacity to uncover novel therapeutic strategies and enhance care. Jefferson's leading experts in Surgery, Cancer Biology, Pathology, Medical Oncology, and Radiation Oncology have collaborated to provide exceptional multidisciplinary expertise, untangling pancreatic cancer's elusive complexities in the lab and ensuring that patients receive exceptional, compassionate care.

Jefferson's resilience is reflected in the pioneering researchers who sought to enhance their skills here and have then demonstrated the dedication, rigor, and ambition to lead.

In the last year, two accomplished scientists rose to take leadership of our surgical research lab, forging strong partnerships with along the way with path-breaking peers.

Avinoam Nevler, MD

Dr. Nevler is a surgical oncologist who came to Jefferson after spending more than a decade as chief technology officer for a medical device company in Israel. He honed his surgical research skills as a fellow at Jefferson, before returning to Israel to complete a surgical residency. In 2019, Dr. Nevler came back to Jefferson, and is taking part in studies that illuminate new strategies for tackling pancreatic cancer.

Currently, Dr. Nevler is taking studies of Pyrvinium Pamoate (PP) and Dithiazanine Iodide (CDI), two novel, FDA-approved agents that promote mitochondrial inhibition in pancreatic cancer cells, to the next level. PP kills pancreatic cancer cells but protects normal cells by targeting the HuR protein that functions like a life vest for pancreatic cancer. CDI offers increased bioavailability, which means the body can absorb it more readily than PP. Yet CDI's superpower is its capacity to dramatically deplete mitochondria needed for energy and survival in the harsh, low-glucose environment of a pancreatic cancer cell.

Aditi Jain, PhD

Dr. Jain is developing new insights into the role of certain DNA repair proteins in both the progression and therapy resistance of pancreatic ductal adenocarcinomas (PDAC). She hopes to discover if targeting these proteins could prove beneficial.

In 2021, Dr. Jain won a PanCAN Career Development Award, which the Pancreatic Cancer Action Network confers upon exceptionally promising researchers. Dr. Jain will use the generous two-year grant to support her research in PDACs, genetically unstable tumors that rely on DNA repair proteins to survive and evade exposure to chemotherapy. Focusing on a DNA repair protein she helped identify, BRCA1-Associated-Ring Domain-1 (BARD1), Dr. Jain hopes to learn how it shields cancer cells from DNA damage, imparts drug resistance, and may help tumors grow.

A Multidisciplinary Team

Jefferson has been able to advance new treatments on a variety of fronts, through the basic science and translational research of collaborators from multiple disciplines.

Elda Grabocka, PhD

Dr. Grabocka is a cancer biologist leading a novel study of the KRAS gene, which when mutated drives abnormal growth in 90 percent of pancreatic cancers, as well as in many lung and colorectal tumors. When stressed, this cancer cell type — far more than most cancer cells — encases its genetic messages in protein globs called "stress granules" that lessen the effect of chemotherapies. Along with her team, Dr. Grabocka is exploring ways to halt the process of encasing messaging in stress granules, in order to target the whole tumor, including other cancer cells that do not have a RAS mutation.

By understanding how stress granules may be targeted to lower drug resistance, Dr. Grabocka is creating a promising new approach to treating some of the most aggressive cancers. Her work has garnered support from NIH as well as private sources, and she has published her findings in numerous peer-reviewed journals.

Adam C. Mueller, MD, PhD

Dr. Mueller is a radiation oncologist studying ways to understand and attack the molecular pathways, or mechanisms, that confer the aggressive and resistant qualities of PDAC, in order to enhance the power of radiation therapy (RT). He is investigating the combined role of ADAM10, a cell surface protein, and Notch signaling (a form of cell-to-cell communication) in strengthening PDAC's ability to resist radiation treatment. Dr. Mueller hopes to discover the degree to which ADAM10 and Notch, together, activate fibrosis and the epithelial-mesenchymal transition (EMT), a process in which epithelial cells undergo morphologic changes often associated with tumor growth and metastasis. Fibrosis, which frequently follows RT, has been associated with tumor progression.

In addition to winning the inaugural W. Kim Foster Pancreatic Cancer Pilot Grant in 2020, generously provided by a Jefferson philanthropist, Dr. Mueller was also awarded a $150,000 RSNA Foundation grant to pursue his study, "Investigating ADAM10 Mediated EMT and Therapeutic Resistance in Pancreas Cancer."

Offering New Treatments with a Holistic Approach

As we advance new discoveries, Jefferson takes a holistic approach to patient care. While expanding access to clinical trials, the Jefferson team ensures that we integrate oncology with surgery, pathology, gastroenterology, pain management, palliative care, genetics, nursing, and social work.

By translating promising scientific discoveries into new treatments, we give hope to pancreatic cancer patients and their loved ones. By focusing on the diverse needs of patients and their families, we are redefining healthcare.

Jefferson researchers are conducting a diverse array of clinical trials that include:

- A surgical study to determine if giving high-protein dietary supplements to patients before they undergo pancreaticoduodenectomy will reduce malnourishment and complications.
- Medical oncology trials that evaluate the effect of different chemotherapy combinations for pancreatic cancers that are unresectable – those that cannot completely be removed through surgery.
- Quality of life studies that assess diverse strategies for promoting comfort and a sense of well-being for pancreatic cancer patients.
- The Jefferson Pancreas Tumor Registry, which provides researchers with genetic information that allows them to study the frequency of pancreatic cancer within families, to identify environmental and occupational risk factors to which patients may have been exposed, and to determine which targeted therapies would be most effective.
- The SKCC Cancer Support and Welcome Center studies the impact of integrative medicine practices such as massage and reiki on patients and caregivers, finding a clinically significant reduction in anxiety, depression, fatigue, and pain.

As a result of these studies, Jefferson clinicians and researchers publish their discoveries in high-impact scientific journals. This is a vital way of advancing the science and improving outcomes for patients at Jefferson and everywhere.

A Fertile Training Ground

Jefferson's stature as a national leader in cancer care and gastroenterology/GI surgery makes it an attractive destination for bright and ambitious students, residents, and fellows seeking to advance their knowledge and skills.

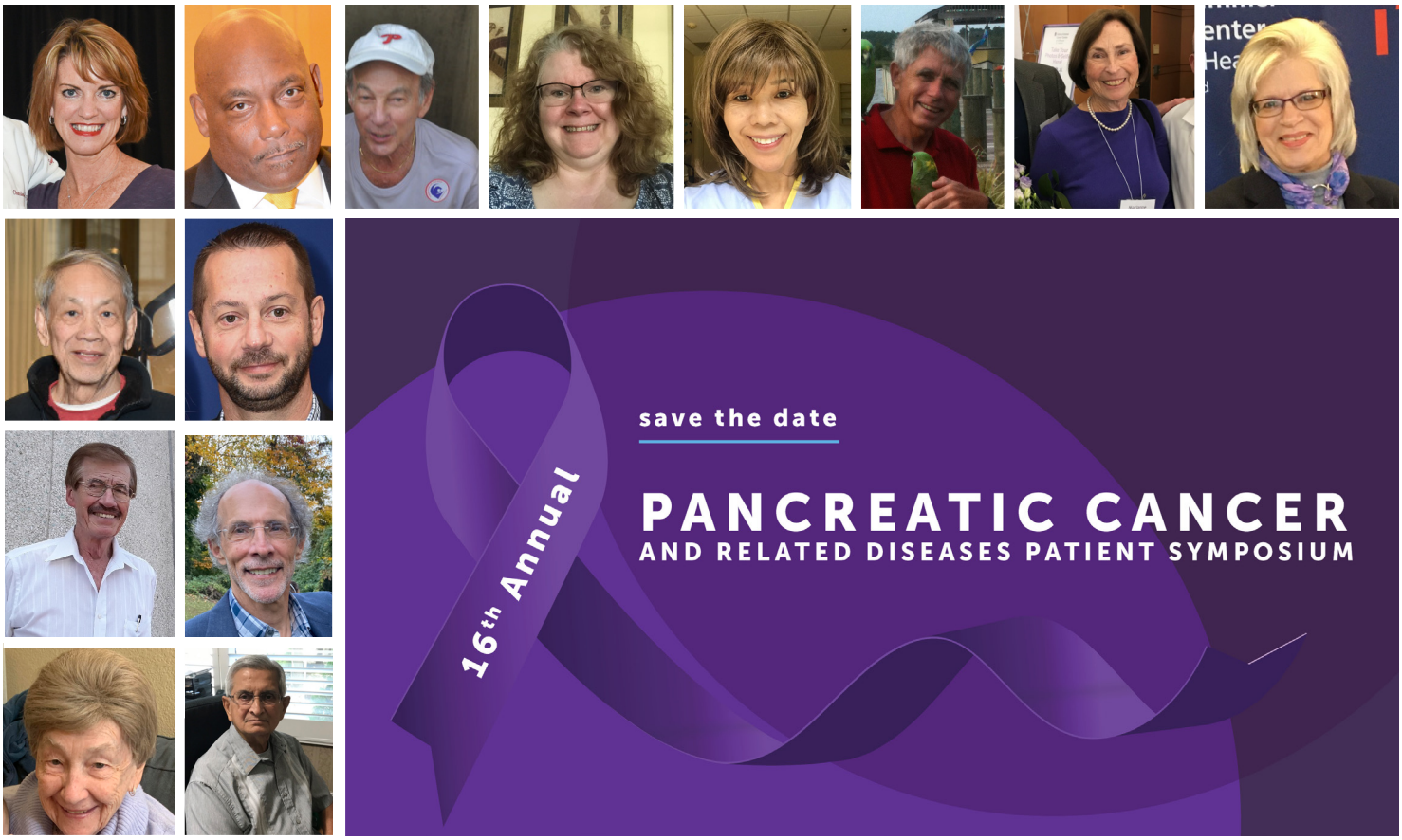
In the last year, several dedicated researchers, clinicians and new staff arrived, contributing additional energy and expertise.

Saed Khalilieh, MD, currently a 4th year surgical resident in the Department of Surgical Oncology and Transplantation at Sheba Medical Center & Tel Aviv University, was delighted to come to Jefferson to complete a fellowship. He is focusing on studies of PP led by Drs. Nevler and Jain. He will also focus on mitochondria inhibitors in pancreatic cancer by collaborating with Scott Waldman, MD, PhD, who is studying mitochondria inhibitors in colorectal cancer.

In 2021, we took pride in the accomplishments of three doctoral students who defended their theses and received their PhDs. As both proteges and collaborators, these young scientists made significant contributions to the team's research as well as the spirited community that defines the institute.

- Lebaron Agostini, whose research helped demonstrate the efficacy and mechanism of action for targeting the poly (ADP-ribose) glycohydrolase (PARG) protein and the checkpoint kinase inhibitor, Wee1, in PDAC and colorectal carcinoma cells.
- Samantha Brown, who studied Human antigen R (HuR/ELAVL1) and its role in post-transcriptionally regulating the pancreatic cancer-driver, Yes-associated protein 1 (YAP1).
- Alex Haber's research highlighted the power of CF10, a polymeric fluoropyrimidine for treating PDAC, moving the promising drug closer to a clinical trial.

We recently hired a new research tech, Carolyn Coats, second from left in photo above, who joined Jefferson after receiving her BS in Biochemistry from Villanova University. She will be assisting the team in research studies and laboratory experiments.



A Beacon in the Cancer Care Community

In November 2020, Jefferson hosted the 15th Annual Pancreatic Cancer and Related Diseases Patient Symposium, a virtual event in which Dr. Yeo and other clinicians and researchers presented an update for the community on the latest advances in treatment and investigations for pancreatic cancer.

Then in June 2021, the team hosted Pancreas and Related Cancers: What's New in 2021? The continuing medical education program provided timely information for oncologists, radiation oncologists, surgical oncologists, surgeons, gastroenterologists, hepatologists, primary care practitioners, internists, nurse practitioners, nurses, and other health care professionals who treat patients with pancreatic cancer. Drs. Charles Yeo and Harish Lavu presided over this event, which was held virtually.

On Saturday, November 13, 2021, we will once again host the annual patient symposium virtually, for comfort and convenience. So save the date!

Lastly yet importantly, it is an enormous point of pride that so many Jefferson patients and families organize community events and launch philanthropic ventures that support research and our Patient Assistance Funds. Partnerships with the community enable Jefferson to advance healthcare access and equity.

On the Horizon

Our care for pancreatic cancer and related diseases patients never stopped, even at the height of the pandemic. Yet, the entire team is looking forward to seeing more patients, colleagues and students in person again.

In the meantime, construction of Jefferson's Specialty Care Pavilion has begun, creating the capacity for even closer collaboration between Jefferson clinicians and researchers. As the future home of Sidney Kimmel Cancer Center and the Jefferson Department of Surgery, the Specialty Care Pavilion will transform the delivery of care and research and set a new standard for outpatient treatment. Many of Jefferson's essential service lines will be located under one roof, streamlining the patient experience and enabling us to customize care.

The facility will function as a space station for connected care. Breakthrough innovations and telehealth connectivity will enable Jefferson to deliver the kind of care patients need, whenever and wherever they need it—before they arrive, during their visit, and after they return home.

The transformation that the Specialty Care Pavilion will bring about is cause for optimism and celebration. In this new home, and with your unwavering support, Jefferson will improve the lives of pancreatic cancer patients.

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