Key Protein for Pancreatic Cancer Cell Growth Discovered, May Provide Therapeutic Target

Pancreatic cancer is particularly deadly because it is often found in advanced stages when the tumor has grown too large and spread from the pancreas making removal impossible. In order to grow, cancer cells require molecular food — Dr. Wantong Yao's Seed Grant research investigated mechanisms to starve those cells as a therapeutic intervention for pancreatic cancer.

Almost 95% of human pancreatic cancers contain oncogenic mutations of the KRAS gene which drives the initiation, development, and progression of the disease. There is currently an effort to pharmacologically target genetic mutations in the KRAS gene and inhibit tumor growth, but that research is in early stages and may not be effective for all KRAS mutations.

It was previous shown that mutations in KRAS in pancreatic cancer initiates the cellular process of macropinocytosis, in which the cell surface membrane engulfs extracellular fluid and prioritizes signaling pathways that support their uncontrolled growth. By interrupting those pathways and blocking the food supply, there is the opportunity to target and prevent cancer cells from growing.

New research from Dr. Yao, conducted at MD Anderson Cancer Center, sought to identify ways to starve and kill cancer cells by understanding the mechanisms responsible for how mutations in KRAS drives macropinocytosis. This research focused on the proteins expressed at the surface of the cell, where macropinocytosis takes place. By studying changes in the proteins expressed at the cell surface when mutant KRAS was

expressed in cancer cells, Dr. Yao's research was able to identify a link between mutant KRAS and activation of macropinocytosis.

Through funding from a 2017 Seed Grant, Wantong Yao, MD, PhD, identified SDC1, a protein that was more abundant when mutant KRAS was expressed than in cells where there was no mutant KRAS. Their research confirmed that while SDC1 may be present in the cell, it is only when mutant KRAS is expressed that SDC1 is shuttled to the cell surface to drive macropinocytosis. Understanding that SDC1 acts under the control of mutant KRAS to fuel cell growth provides an opportunity to target SDC1 and inhibit tumor cell growth. Since SDC1 drives growth when it is on the surface of the cell, it may be more vulnerable to intervention. There is research underway targeting SDC1 using monoclonal antibodies in multiple myeloma patients, which may open the doors for similar therapies for pancreatic cancer.

An Inherited Predisposition to Pancreatic Cancer

This month, as part of National Minority Health Month, we are highlighting those communities at high-risk for pancreatic cancer. The Ashkenazi Jewish community, like African Americans, have been disproportionately impacted by pancreatic cancer. Increasing awareness in these communities includes sharing information and providing resources. These tools empower not only high-risk communities but the pancreatic cancer community as a whole. When pancreatic cancer impacts one group, it impacts us all.

For decades scientists have investigated the BRCA1 & BRCA2 gene mutations and their connection to cancer. The Johns Hopkins National Familial Pancreas Tumor Registry (NFPTR) has gained a better understanding of how BRCA1 & BRCA2 gene mutations account for a portion of the increased risk for pancreatic cancer for Ashkenazi Jews. According to their research, "The increased risk of pancreatic cancer associated with inherited BRCA1 mutations is estimated to be about two-fold (about the same increased risk associated with cigarette smoking)". In addition, carriers of the BRCA2 gene mutations also have a ten-fold increased risk of developing pancreatic cancer.

The National Comprehensive Cancer Network (NCCN) recommends genetic counselling for all individuals diagnosed with pancreatic cancer. The Hirshberg Foundation provides resources to encourage families, especially those with a high-risk ancestry, to learn more about how genetics play a role. Watch this Hirshberg Symposium video "Why Should I See A Genetic Counselor?", presented by Wendy Conlon, MS, a genetic counselor at UCLA. Whether you are of Ashkenazi Jewish ancestry or not, genetic testing unlocks some answers to pancreatic cancer and is a resource worth exploring.

Coping Skills for the Pancreatic Cancer Community:

Tools and Tips During COVID-19

We are dedicated to supporting our pancreatic cancer community, particularly as we all try to navigate the COVID-19 pandemic. We have launched a series of free webinars to provide virtual patient support and resources for our community. We are pleased to share information about the second in our series which took place on Friday, April 17th.

During this time of uncertainty, stress levels can sky rocket. It is critical, especially for pancreatic cancer patients and their caregivers, to find tools to manage stress and find balance. Emotional well-being is a critical piece of the healing process, so now, more than ever, it is essential to have coping skills. We turned to Elizabeth Cleary, PhD, Licensed Clinical Psychologist at the Simms/Mann UCLA Center for Integrative Oncology, to lead an interactive webinar, Coping Skills for the Pancreatic Cancer Community: Tools and Tips During COVID-19.

Watch Webinar

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How to Eat and Live Well During Coronavirus: Vital Tips for our Pancreatic Cancer

Community

On March 19, 2020, California Governor Gavin Newsom ordered a statewide order to stay at home. The Hirshberg Foundation is dedicated to supporting our pancreatic cancer community while we observe California's 'shelter in place' rules to mitigate the spread of the coronavirus COVID-19. We are committed to providing virtual patient support and resources to our patients and their caregivers.

We know that cancer patients currently receiving treatments or recovering from surgery are considered at a higher risk for having a weakened immune system. Amid the COVID-19 crisis, patient well-being is more important than ever. We have asked our resident expert, Zhaoping Li, MD, PhD, Director of the UCLA Center for Human Nutrition, to provide our pancreatic cancer community with tools to eat well and live well during the coronavirus.

This is a video recording of the Zoom webinar that took place on Friday, April 3rd at 1:00 (PST). Entitled "How to Eat and Live Well During Coronavirus: Vital Tips for our Pancreatic Cancer Community," patients, caregivers, family and friends joined Dr. Li for an interactive conversation as she provides important information to boost the immune system. Beyond nutrition she discusses stress eating, sleeping, cooking and best practices for food delivered to your home.

Watch Webinar

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April is National Minority Health Month

April is National Minority Health Month — an incredibly important time to discuss the facts and raise awareness for the highest risk communities facing pancreatic cancer. Studies have pointed to increased risk of pancreatic cancer in <u>Latinos</u>,

perhaps due to higher rates of <u>obesity</u> and diabetes, and among Ashkenazi Jews, possibly due to mutations of the <u>BRCA genes</u>. However, pancreatic cancer disproportionately affects and has the <u>poorest prognosis</u> for Black Americans. Join us throughout April as we share survivor stories, discuss why these communities are at-risk, how to fight the statistics and what educational resources on pancreatic cancer are available. **National Minority Health Month is a call-to-action for all of us to help raise awareness throughout April!**

Pancreatic cancer does not discriminate. In fact, Black Americans have an approximate 20% higher incidence rate of pancreatic cancer according to the National Cancer Institute. As pancreatic cancer numbers continue to grow, people of color are disproportionately affected and more vulnerable to the 3rd leading cause of cancer-related death. We must remember that pancreatic cancer doesn't take a time out and neither will we.

There are several factors, including socioeconomics, that make Black Americans disproportionately more likely to face pancreatic cancer. Black Americans are at high-risk of developing chronic conditions and "modifiable risks" including obesity, smoking and diabetes, which may lead to pancreatic cancer. According to the U.S. Department of Health & Human Services — Office of Minority Health, Black American adults are 60% more likely than white adults to be diagnosed with diabetes.

The 2019-2021 American Cancer Society's Facts & Figures Report for African Americans shares that the probability of developing pancreatic cancer was approximately 1 in 64 for black males and 1 in 59 for females (from 2013-2015). These numbers represent fathers and mothers, they represent grandparents in Black American and blended families, they represent our friends, coworkers and neighbors. When pancreatic cancer impacts one group, it impacts us all.

The Journey to Complete 52 Races for 52 Faces

In March of 2019, Julie Weiss, the "Marathon Goddess," embarked on a new campaign, 52 Races for 52 Faces, in partnership with the Hirshberg Foundation, to shine a light on pancreatic cancer. On March 8, 2020, a year of races wrapped up with Julie's incredible finish at the LA Marathon. Running for the Hirshberg Training Team, she ran her 109th marathon to date. That evening, at our team's celebration dinner, we reflected on the incredible dedications made over the past year and Julie's incredible journey.

Participating in full and half marathons, 10K's and 5K's, Julie has run for pancreatic cancer survivors of all ages and backgrounds. She's run for 10+ year survivors, for fathers and mothers, for a Congressman and Supreme Court Justice, for a veteran and female triathlete, for loved ones lost too soon and for a community fighting to cure this devastating disease. The past year has included both triumphs and trying moments for Julie as she's pounded the pavement across the United States, all in the name of pancreatic cancer. By the end of this journey, Julie had raced in 8 different states (California, Massachusetts, Nevada, New Jersey, Washington DC, Illinois, Hawaii, and Washington) and collectively helped fundraise over \$275,000 for the Hirshberg Foundation!

She's crossed the final finish line for the 52 Races for 52 Faces campaign but the stories shared will never be forgotten. Thanks to all who of you who have helped make <u>52 Races for 52 Faces</u> possible, by making runner dedications or giving

<u>donations</u>, by cheering for Julie in person or following her journey online. Together, we will continue to fund research for a cure, to shine a light on survivors and will never give up.