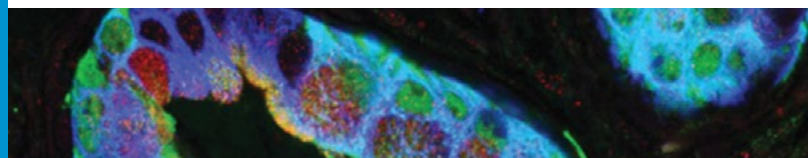


SUMMER 2016

# Pancreas Center News

**UCSF** Helen Diller Family  
Comprehensive  
Cancer Center



*UCSF Department of Radiology  
& Biomedical Imaging*

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## Imaging Holds Promise for Enhanced Decision Support

Using imaging to improve clinical decision-making is an increasingly important research focus in the race to help those with pancreatic cancer.

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## From Screening Through Treatment, Driving Ever Harder for Solutions

The UCSF Pancreas Center has long felt a sense of urgency, but with pancreatic cancer poised to become the second-leading cause of cancer-related death in the United States by 2020, the urgency we feel to help our patients and families has only increased.

This translates into a comprehensive effort that embraces everything from pinpointing risk factors, developing early detection strategies, and enhancing decision support through getting more patients into surgery and pursuing a full slate of potential new therapies.

On the risk front, we are engaged in an exciting new National Institutes of Health-funded study, in collaboration with Kaiser Foundation Research Institute epidemiologist Stephen K. Van Den Eeden, PhD, and the UCSF Diabetes Center. Drawing on a robust Kaiser database of millions of patients, we will study how chronic pancreatitis, pre-diabetes, diabetes, and pancreatic cancer are related to each other. We believe bringing together diverse expertise, unique data, and innovative research ultimately will lead to more effective prevention and treatment for patients.

We are especially hopeful that we can use this effort to develop more precise screening strategies, which is one of our Center's highest priorities. For example, identifying early detection biomarkers could lead to advanced blood tests that in some cases might avert invasive tests.

In turn, successful early screening could enable us to get more patients into surgery, still our best option for successful treatment. As this issue illustrates, we are already offering surgery more often to patients previously considered poor surgical risks by using chemotherapy before surgery to kill any tumor we might need to leave behind. In other settings, this "neoadjuvant" therapy typically also involves radiation, but at UCSF, we've successfully tested a chemotherapy-only approach



Margaret Tempero, MD

that can make it easier to complete the type of vascular reconstruction often necessary with these surgeries.

We also are working with radiologists to test whether standard CT scans can help us predict tumor recurrence before surgery and thus better inform surgical decisions. In addition, we are testing whether PET-MRI, a type of advanced imaging, can help us more quickly understand a patient's response to treatment, which could enable us to shift treatment strategies before it's too late.

Finally, in this issue we highlight new findings about cellular metabolism that may offer new treatment targets that could complement our ongoing research efforts and clinical trials.

In short, in our effort to defy the dire predictions about pancreatic cancer mortality, we will leave no stone unturned. I am so grateful to our many supporters without whom the progress we make on behalf of our patients and their families would not be possible.

Margaret Tempero, MD  
Director, UCSF Pancreas Center

Rombauer Family Distinguished Professor  
in Pancreas Cancer Clinical and Translational Science

## Imaging Holds Promise (Continued)

UCSF radiologist Z. Jane Wang, MD, is collaborating with oncologists Eric Collisson, MD, Andrew Ko, MD, and Margaret Tempero, MD, on two promising studies.

### More Informed Surgical Decisions

"In one project, we are looking at the use of standard-of-care, pre-operative staging CT scans to see if we can predict early recurrence after the surgical removal of pancreatic adenocarcinoma (PDAC)," says Wang. "This is important because if you suspect a tumor is at high risk of early recurrence, it may get managed differently. For example, the patient may get pre-operative chemotherapy."

“We are still very much in the exploratory phase, but we believe imaging plays an important role in the care of these patients. And it is important to test and validate these initial findings in larger groups of patients.”

Z. Jane Wang, MD

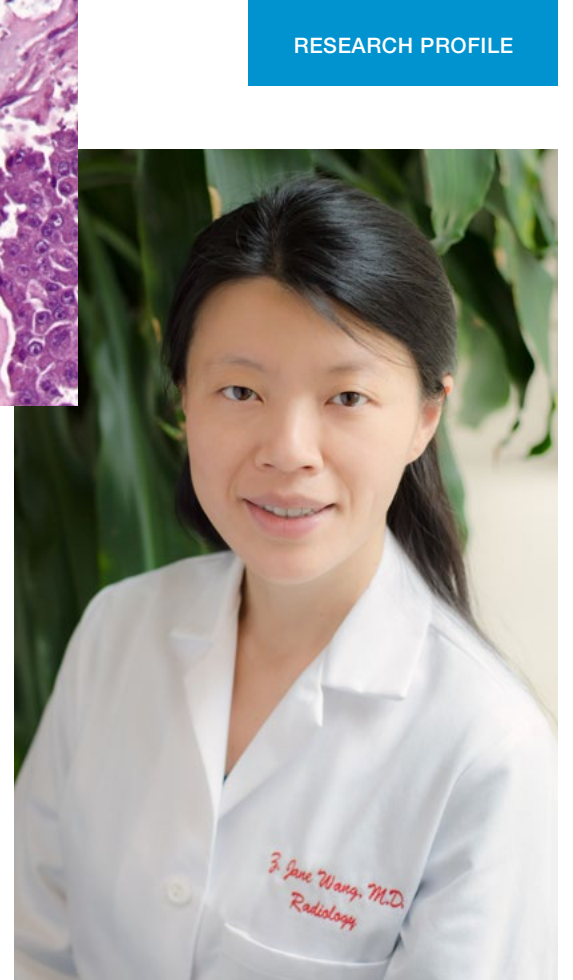
The results from a small, UCSF pilot study suggest that less tumor enhancement (how much the tumor lights up) on pre-operative CT scans may help predict early recurrence. The team hypothesizes that the underlying reason for this association may be related to the tumor's fibrous tissue. They are collaborating with researchers from University of North Carolina Chapel Hill who have developed a method for automating the quantification of a tumor's fibrotic content to better understand what the imaging reveals about the tumor.

"We are still very much in the exploratory phase, but we believe imaging plays an important role in the care of these patients," says Wang. "And it is important to test and validate these initial findings in larger groups of patients."

### Advanced Imaging to Strengthen Medical Oncology Decisions

In the second project, Wang and her colleagues are examining whether they can use Positron Emission Tomography-Magnetic Resonance Imaging (PET-MRI) to more quickly gauge patient response to medical treatment for pancreatic cancer.

"Determining early response to treatment is frequently challenging in pancreatic



Z. Jane Wang, MD

cancer. If we wait too long to see whether a patient is responding or not, the ones who are not responding could become too sick to get another type of treatment or participate in a clinical trial," says Wang. "That's a missed opportunity."

PET-MRI is a hybrid imaging technology in which the PET scan reveals the tumor's metabolic activity and the MRI reveals structural and functional tissue characteristics. For the study, the patients will get a PET-MRI prior to therapy and then another one a few weeks after therapy begins. Wang believes that the combined metabolic and functional information from the PET-MRI scan can provide valuable and early information on tumor response.

"You don't want to wait months to learn whether these patients are responding," she says. ■



Arnetha Whitmore

## New Associate Director Brings Experience, Enthusiasm

When Arnetha Whitmore became associate director of the UCSF Pancreas Center in September 2015, it was a sign that the already robust program is accelerating its efforts against pancreatic cancer.

“This job appealed to me because of the passion Dr. Tempero has for the Pancreas Center and her vision for its continued growth,” Whitmore says. “My role is to help build the program by conducting research and working closely with our faculty members, researchers, patients, and donors.”

### Making Her Way West

Whitmore's interest in medicine and health care began when she took a job at a radiology center in Connecticut during high school, where she worked closely with many cancer patients. In 2002, she entered the University of Miami, majoring in psychology with minors in history and literature.

By 2008, she had made her way across the country for a job as an office manager in Stanford Hospital's Department of Surgery. Two years later, she moved into a

lab manager role where she participated in several research projects on diabetic wound healing and contributed to a number of publications.

Eventually, Whitmore became program manager for the Stanford Applied Regenerative Medicine program, charged with growing the department's research side and overseeing a large financial portfolio.

It was exciting work, but by the middle of 2015 she had begun seeking new challenges when she saw the listing for her current position. Her background in clinical, research and academic administration seemed a perfect fit.

“Also, my research in diabetes and wound healing made me acutely aware of the link between diabetes and the pancreas – as well as the reputation UCSF has for outstanding collaborative research,” she says.

“My role is to help build the program by conducting research and working closely with our faculty members, researchers, patients, and donors.”

Arnetha Whitmore

### Hitting the Ground Running

Whitmore had little time to ease into her new role.

One of her first projects was overseeing the development of the Palliative Care and Symptom Management Nursing Program, a nurses' educational program made possible by the generosity of patient Stu Rickerson and his wife, Nancy. “It was very gratifying to work closely with Pancreas Center nurse Elizabeth Dito, who has 18 years experience caring for pancreas cancer patients and is passionate about training nurses in symptom management to improve the patient experience,” says Whitmore.

The completion of that task still left Whitmore with a full slate of duties to keep her busy. She provides administrative support for the Center's many clinical trials. She is helping coordinate a large, collaborative project with Stanford and Kaiser Permanente. She oversees the Center's biobanking efforts. And, she is the point of contact for donors when Dr. Tempero is not available.

Though it has its challenges, Whitmore is enjoying the new job immensely. “Being part of this team and tackling something like pancreatic cancer is very exciting,” she says. “Everyone has been very welcoming and enthusiastic.” ■

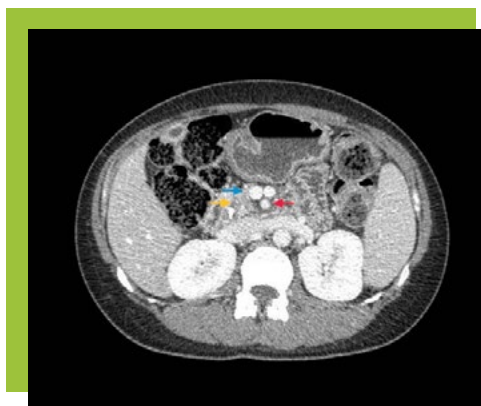
## Surgery a Realistic Option for More Patients

While researchers race to find improved medical therapies for pancreatic ductal adenocarcinoma (PDAC), surgery remains the most effective treatment.

Unfortunately, a large percentage of PDAC patients are not surgical candidates because by the time of diagnosis, the disease has metastasized. Even among those without metastases, choosing surgery can be tricky if there is too much risk of leaving live tumor behind.

Recently, however, cancer treatment teams have been extending surgery options to more patients previously considered “borderline resectable” by deploying a combination of chemotherapy and radiation before surgery. That aims to kill – and possibly shrink – the tumor, increasing the chances for surgical success.

Now, in one of the largest tests of its kind, a UCSF Pancreas Center team has found that using chemotherapy alone is an effective approach. Of 26 UCSF patients who underwent chemotherapy-only neoadjuvant therapy, more than 90 percent underwent surgery that successfully removed all tumor.



Pancreas protocol CT after neoadjuvant therapy.

### Why Surgery Is a Challenging Decision

“Until recently, fewer than 20 percent of PDAC patients at diagnosis have been realistic surgical candidates,” says cancer surgeon Eric Nakakura, MD, PhD. Many surgeons are reluctant to subject patients to a grueling surgery, only to have part of a tumor as lethal as PDAC still present afterward.

Neoadjuvant therapy has improved the chances of these patients advancing to surgery, but Nakakura and his UCSF colleagues, Margaret Tempero, MD, and Andrew Ko, MD, were concerned that numerous randomized trials showed radiation having no benefit, and possibly even a negative effect, in patients with PDAC.

### Enhancing the Chance for Success

Those concerns prompted the decision to use only chemotherapy before surgery for most of the 26 patients in the first



Eric Nakakura, MD

UCSF study. A combination of four chemotherapies – collectively known by the acronym FOLFIRINOX – completely removed the tumor in 92 percent of these patients, with 100 percent surviving the surgery. Moreover, at UCSF the median survival is 34 months for this challenging group of patients, compared to a median survival of only 24 months for patients nationally after surgery for PDAC.

UCSF is now launching a clinical trial for up to 36 borderline resectable patients, which will use a combination chemotherapy (gemcitabine and nab-paclitaxel) with an enzyme called PEGPH20.

“Pancreatic tumors are very fibrous, and that impedes the delivery of chemotherapy,” Nakakura says. “PEGPH20 breaks down the fibrotic wall and increases drug delivery. We successfully operated on our first patient recently and saw a dramatic response. We are encouraged.” ■

“Pancreas cancer is a systemic problem, and radiation is a local solution. About 58 percent of patients with borderline resectable PDAC also require vascular reconstruction, and radiation can make that difficult, if not hazardous.”

Eric Nakakura, MD

# Understanding Cellular Metabolism Could Open Treatment Doors

Cell biologist Rushika Perera, PhD, recently co-authored a paper in *Nature* that shed important light on the mechanisms that favor the growth of pancreatic ductal adenocarcinoma (PDAC).

Perera and her team discovered how PDAC cells outgrow their normal counterparts by thriving in nutrient-poor, oxygen-starved environments that are incompatible with the function of healthy cells.

Perera believes that precisely tracing how PDAC cells use this metabolic process to reinvent themselves could help scientists discover ways to subvert the process and kill the tumors.



## Lysosomes May Hold a Key

Specifically, Perera's work has helped show that lysosomes – organelles within all cells, that break down macromolecules and enable recycling of nutrients and cell building blocks – are more abundant and highly active in cancer cells.

*Nature Reviews Cancer, September 2015 Vol. 15 No. 9*

Though lysosomes were long viewed as the cell's trash can, recent research showed that they function more as command-and-control centers that gauge the nutritional needs of cells and help drive their growth. In PDAC cells, lysosomes systematically alter normal nutritional pathways, creating a cell that is constantly ravenous for the lysosome's recycled nutrients.

Perera believes this addiction to recycled nutrients is connected to autophagy, a process in which a cell destroys components of itself and delivers the resulting cytoplasmic constituents to the lysosome for destruction. In a normal cell, autophagy switches on and off, but in a PDAC cell, autophagy is always on.

## Translating the Research

Understanding the metabolic process that lysosomes drive has promising implications for the treatment of PDAC and likely for other cancers as well.

“The UCSF Pancreas Center is a melting pot of people – scientists, clinicians, and patient advocacy groups.”

Rushika Perera, PhD

Perera's lab is trying to identify which proteins the lysosome selectively degrades. She believes that growth effectively targeting the lysosome could be a path to starving the cancer cell to death.

In addition, Perera's work has examined the transcription factors that activate genes to create lysosomes. “These master regulators might be another point of entry,” she says.

Perera's group identified a protein that enables the transcription factors to shuttle in and out of the nucleus and accomplish their task. “If this only occurs in PDAC cells, we might be able to develop a protein inhibitor that stops lysosome development,” she says. In lab and mouse models, inhibiting lysosome development in PDAC cell lines has successfully blocked tumor growth.

“The UCSF Pancreas Center is a melting pot of people – scientists, clinicians, and patient advocacy groups,” Perera says. “This makes it a great environment to more effectively solve treatment challenges.” ■



Rushika Perera, PhD

# Lucky Survivor Gives Back

The day Harriet Wulfstat experienced the thrill of hiking along the Great Wall of China, was also the day she noticed her first cancer symptom: her urine was more brown than yellow.

“I was very fortunate,” she says today, nearly 10 years after being diagnosed with pancreatic ductal adenocarcinoma (PDAC). “The tumor was at the head of the pancreas, constricting my bile duct, which is why I had symptoms so early.”

When Wulfstat returned home to Chicago, she learned that her tumor was operable, another rare piece of good luck. A local surgeon completed the operation.

At the time, standard follow up care was gemcitabine for chemotherapy plus radiation. “Yet the statistics for survival were gruesome,” she says. “And radiation could damage my newly configured digestive system. My surgeon recommended that I research the medical alternatives under study.”

## Options After Surgery

Wulfstat did just that and wound up making appointments for a second opinion at the two places she believed were the leaders in caring for patients with PDAC. One was UCSF.

“I first spoke to [Director the UCSF Pancreas Center] Dr. Margaret Tempero's clinical nurse, Elizabeth Dito, who was very helpful,” says Wulfstat. After the encouraging conversation, she visited San Francisco and met with Dr. Tempero, who reviewed the medical records and suggested a slow dose infusion regimen that combined cisplatin with the gemcitabine. They would not decide about using radiation until conducting additional testing after six months of the chemotherapy.

Harriet Wulfstat with her son



“The disease is so dire, but there is much more knowledge about it today than when I was diagnosed. It helps patients to hear from someone who has beaten the odds.”

Harriet Wulfstat

“I felt so confident after that conversation that I canceled my other appointment,” Wulfstat says.

She returned home where her Chicago oncologist administered the Tempero-designed chemo regimen. Not only was Wulfstat cancer-free after six months, she's been cancer-free ever since.

## Providing Support in Multiple Ways

Well aware that she's been one of the few lucky ones, today Wulfstat thoroughly enjoys her six grandchildren – five were born after her diagnosis – and she is gratefully giving back.

As a survivor, she offers hope to patients who call her through national Pancreatic Cancer Action Network. She is on the board of Chicago-based Rolfe Foundation for Pancreatic Cancer, where she raises funds for research to develop a diagnostic test for early detection of the disease. She also organizes symposiums with medical specialists to raise awareness about pancreatic cancer and the latest research developments.

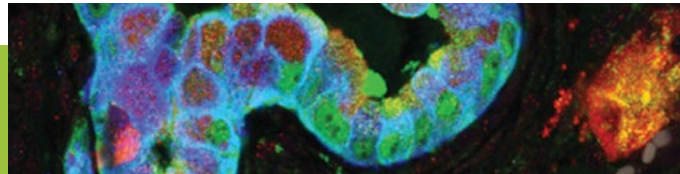
In addition to their own donations to medical research, Wulfstat and her husband, Allan, are trustees of a private family charitable foundation, and they have decided to focus on health care and research initiatives. The foundation provides multiyear grants to the UCSF Pancreas Center.

“I was just so impressed with Margaret Tempero's dedication to her patients and to staying at the forefront of research,” Wulfstat says. “This is the best way to save lives.” ■

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## Many thanks to our supporters!



### Stu and Nancy Rickerson

MARCH 22, 2016 | The UCSF Pancreas Center held a training session for nurses titled “Integrating Palliative Care in Oncology Nursing.” The Center is grateful to Stu and Nancy Rickerson, whose generosity funded this professional development opportunity.



For more information on the  
**UCSF Pancreas Center:**

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### The Correa Family and Titan's Cage

Thanks to the Correa family and Titan's Cage for raising more than \$14,000 since 2013 for the UCSF Pancreas Center at mixed martial arts events throughout Northern California, in memory of family member Cora Claro, who passed away in 2013.



### The Legnitto Family

SEPTEMBER 16, 2015 | Thanks to the Legnitto family; Michael Sangiacomo, president and CEO of Recology; and supporters of the second John Legnitto Bocce Ball Tournament held in memory of John Legnitto. Some \$30,000 was raised for the UCSF Pancreas Center. Dr. Tempero and Mayor Ed Lee spoke at the event.



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