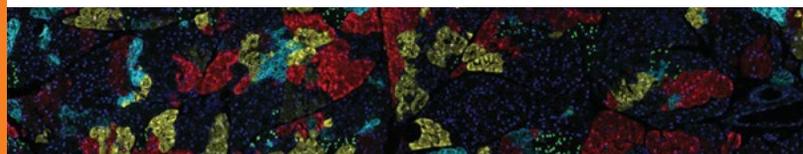


SUMMER 2017

Pancreas Center News

UCSF Helen Diller Family
Comprehensive
Cancer Center



"This ambitious, nationwide trial will test new drugs in a more fluid and nimble way that should accelerate and refine our ability to treat patients"
says Andrew Ko, MD.

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Innovative Trial Aims to Deliver on Precision Medicine's Promise

By the final quarter of 2017, UCSF patients will be able to participate in "the first large-scale precision medicine trial for patients with pancreatic cancer," according to the Pancreatic Cancer Action Network website.

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The Power of Partnership

Pancreatic cancer currently is the third-leading cause of cancer-related deaths, and it's poised to become number two. This increases the sense of urgency among those of us who are trying to discover better ways to screen for, diagnose, and treat the disease. Unfortunately, progress has remained frustratingly slow.

Now, however, a confluence of factors has led to productive partnerships among leading institutions, which could significantly accelerate progress toward the Pancreatic Cancer Action Network's goal of doubling pancreatic cancer survival rates by 2020.

Patient mobilization has spurred everything from the 2012 Recalcitrant Cancer Research Act through the Pancreatic Cancer Action Network's Precision Promise Initiative. A changing health care culture recognizes that team-based, multidisciplinary efforts have the power to transform care at much greater speeds and with much greater sensitivity to patient needs. Precision medicine advances are rapidly changing how we diagnose, treat, and research this disease, while information technology enables us to more rapidly disseminate new knowledge, better analyze the vast data stores we are accumulating, and collaborate more effectively.

Moreover, the partnerships emerging from these cultural, technological and societal shifts are already delivering enormous benefits to our patients. This issue of our newsletter offers a few exciting examples.

Our partnership with the Kaiser Foundation Research Institute and the UCSF Diabetes Center could lead to much earlier screening for pancreatic cancer. A UCSF-wide biospecimen initiative, which is forging close ties with clinical teams and improving the quality and accessibility of tumor samples, is crucial to deepening our understanding of the disease. The interdisciplinary work of gastroenterologist Mustafa Arain, MD, and his expertise in advanced endoscopy enhances our diagnostic capabilities



Margaret Tempero, MD

and our ability to move patients more quickly to therapeutic options. Finally, as one of a dozen inaugural sites for the Precision Promise initiative, we are playing a central role in dramatically increasing the ability of pancreatic cancer patients to enroll in clinical trials and enabling leading experts to share their findings and refine treatment techniques.

Though we are still a long way from where we would like to be, these partnerships signify how the pancreatic cancer community is not only redoubling its efforts but also doing everything it can to ensure those efforts complement each other in the search for a cure.

Thank you for your partnership in helping us advance the science and improve treatments for our patients.

Margaret Tempero, MD
Director, UCSF Pancreas Center

Rombauer Family Distinguished Professor
in Pancreas Cancer Clinical and Translational Science

Precision Medicine's Promise (Continued)

The organization's Precision Promise Initiative is a multicenter effort aimed at doubling pancreatic cancer survival by 2020.

UCSF is one of 12 inaugural sites.

"Precision Promise is an unprecedented opportunity to work closely with colleagues at other centers of excellence who share our commitment to tackling this disease," says Andrew Ko, MD, principal investigator for the UCSF site.

Treatments Based on Unique Tumor Characteristics

Pancreatic cancer is the third-leading cause of cancer-related deaths in the United States, but only 4 percent of pancreatic cancer patients enroll in clinical trials. Precision Promise essentially guarantees that every interested and eligible patient can receive extensive molecular profiling of his or her cancer, which will enable physicians to steer patients toward one or more experimental arms of the trial. In addition to, or in succession with, traditional chemotherapy, experimental therapies may include:

- Novel combinations of immuno-oncology agents intended to augment the host immune system to recognize and fight cancer.
- Agents targeting the tumor's stromal microenvironment. For example, patients whose tumors show high levels of hyaluronic acid – a key component of the extracellular matrix – may benefit from the stromal-depleting agent PEGPH20.
- Drugs that exploit a cancer's defective DNA damage-repair capacity.

Learning From Patient Response

Precision Promise also creates a centralized research and clinical trials database that the team of clinicians, researchers, and diagnostic and drug developers can access and learn from together.

"The umbrella protocol provides a standardized framework and workflow for collecting tumor and blood samples from each patient," Ko says. "Separate sub-studies within the overall framework then provide details of each of the respective experimental treatment regimens to be tested. The detailed analyses facilitated by molecular profiling help us understand which subset of patients is most likely to benefit from a particular treatment."

If the team gets a clear signal that a therapy is not working, it can modify the approach or move on to something different within that category. Conversely, if a therapy looks promising, the researchers will be able to expand that arm of the trial and enroll more patients.

"This ambitious, nationwide trial will test new drugs in a more fluid and nimble way



Andrew Ko, MD

"Precision Promise is an unprecedented opportunity to work closely with colleagues at other centers of excellence who share our commitment to tackling this disease."

Andrew Ko, MD



Precision Promise will **enroll thousands of patients** over many years.

Graphic: Pancreatic Cancer Action Network

that should accelerate and refine our ability to treat patients," Ko says. ■

Ensuring High-Quality Tissue Specimens

Precision cancer research depends upon access to high-quality tissue specimens, but for pancreatic cancer, such specimens are relatively rare. Those that do exist – and the opportunities to gather them – are precious. That’s what makes the recently established UCSF Biospecimen Resources (BIOS) Program – which was created to grow the pipeline of high-quality research tissue across UCSF – so essential to the UCSF Pancreas Center.

“The ability to do things like genetic analyses and expression profiling has put the onus on us to make sure the quality of available specimens suits the technology advances,” says Scott Vandenberg, MD, PhD, pathologist and BIOS director.

Life Cycle Management

Every biospecimen has a life cycle, from obtaining patient consent through surgical resection, sample acquisition, handling and processing, storage, distribution, and scientific analysis.

“We work closely with clinical teams to make sure tissue is collected according to protocols that optimize our ability to acquire high-quality samples without disrupting clinical workflows,” says certified pathology assistant Tasha Lea.

That’s a challenge, because each case is different, and biospecimens can deteriorate quickly once removed from the body. Careful planning is essential, especially for pancreatic cancer specimens, because the resections tend to be unusually complicated. Lea’s expertise

is crucial in determining whether tissue could have diagnostic or research value.

“When done correctly, exceptional patient care often goes hand-in-hand with attaining excellent research specimens, but clinical care comes first, which is why working in complete coordination with the diagnostic pathologists is so important,” says Vandenberg.

Once the tissue is obtained, Lea and her team carefully annotate the handling procedures and patient histories to help researchers understand factors that may affect the tissue. In addition to the molecular analyses, such annotation is important for interpreting complex biomarker profiling now possible in the Biorepository and Tissue Biomarker Technology Core at the UCSF Helen Diller Family Comprehensive Cancer Center.

From Storage Through Research Use

Once the tissue is stored, a customized laboratory information system enables researchers to request – and the BIOS



Scott Vandenberg, MD, PhD

“When done correctly, exceptional patient care often goes hand-in-hand with attaining excellent research specimens.”

Scott Vandenberg, MD, PhD

team to locate – a desired sample. Each research team governs its own specimens, but BIOS plays matchmaker among the various groups. That role helps avert research redundancies and ensures the broadest possible application.

The process, says Vandenberg, demands committed scientists and clinicians willing to work together. “Dr. Margaret Tempero has embraced our team,” he says. “It’s a joy to gather specimens that can contribute to discovery and improving patient lives.” ■

Study Suggests Links Between PDAC and Diabetes

Researchers at the UCSF Pancreas Center, UCSF Diabetes Center, and Kaiser Permanente Northern California are applying advanced analytics to a Kaiser database of hundreds of thousands of patients with diabetes in a study aimed at identifying key risk factors for pancreatic cancer in that patient population.

The National Cancer Institute and National Institute of Diabetes and Digestive and Kidney Disease are funding the study. The researchers also hope to secure additional funding to validate a new high throughput blood test in a patient cohort that has the identified risk factors.

“Our initial findings give us some hope that we can move screening and detection back to the point where it can truly change clinical outcomes,” says Margaret Tempero, MD, director of the UCSF Pancreas Center.

Step 1: Defining Risk in a Subset of Patients

Developing more precise and timely screening strategies is one of the UCSF Pancreas Center’s highest priorities because it could get more patients into surgery early on, which is still the best option for successful treatment.

According to Stephen Van Den Eeden, PhD, senior epidemiologist with Kaiser Permanente Northern California and professor of urology at UCSF, the study’s preliminary analyses suggest:

- The type of abnormal glucose measure among those newly diagnosed with type 2 diabetes may matter. “For example, if you have an abnormal random and fasting glucose level, you may be at higher risk of pancreatic

ductal adenocarcinoma (PDAC) compared to other combinations of abnormal glycemia, including HbA1c levels,” Van Den Eeden says.

- Personal and clinical characteristics gleaned from electronic health records – such as age, smoking status, weight history, blood cell markers, glucose measures, and a liver enzyme blood value – also seem to improve the ability to identify higher risk individuals.

Researchers are now refining these predictive algorithms.

Step 2: A Potential Blood Test

If the algorithms can reliably stratify risk among people with recent onset diabetes, those patients could complete the high-throughput blood test for pancreatic cancer currently in development. Patients with positive results could receive timely abdominal imaging and then move quickly into surgery. The researchers are in discussions with the company developing the test about a prospective study to validate its accuracy and are seeking funding to pursue that work.



Stephen Van Den Eeden, PhD

“With our clinical experience and Kaiser’s amazing infrastructure and epidemiological expertise, we can look for associations most other systems can’t possibly pursue.”

Margaret Tempero, MD



Tempero and Van Den Eeden believe their joint effort exemplifies how to capitalize on the skills of two outstanding institutions to advance patient care.

“With our clinical experience and Kaiser’s amazing infrastructure and epidemiological expertise, we can look for associations most other systems can’t possibly pursue,” Tempero says. ■

Endoscopy Expert Improves Patient Diagnoses and Treatment

When gastroenterologist Mustafa Arain, MD, joined the UCSF Pancreas Center in 2016, he brought fellowship training and seven years of experience in both endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS) for pancreatic and biliary disorders. That rare expertise can advance diagnosis, treatment, and research for pancreatic cancer.



Mustafa Arain, MD

Diagnostic and Therapeutic Advantages

Among its advantages, skilled use of EUS enables clinicians to see a solid lesion and biopsy it during the same procedure; with a pathologist in the room, clinicians can confidently diagnose cancer on the spot in many patients.

“EUS-guided sampling of pancreatic tumors has a diagnosis rate of over 95 percent,” Arain says. “We also can biopsy areas of concern for metastatic tumor outside the pancreas, including the lymph nodes and liver.”

In patients who have tumors that block bile drainage and cause jaundice, Arain uses an ERCP procedure, which combines endoscopy with X-ray guidance, to place a stent into the obstructed bile duct. He can also combine EUS with ERCP to enable tumor diagnosis and staging and relieve bile duct obstruction during the same appointment. This reduces the number of procedures and minimizes delay in additional treatments.

Sometimes, however, tumor-related factors can make it impossible to use ERCP to relieve the bile duct obstruction. Traditionally, such patients receive an external drain through the liver for bile drainage. In contrast, Arain uses “therapeutic EUS” to either facilitate ERCP, insert a stent directly into the bile duct through the liver, or create a new passage through the intestine, an approach that is new to UCSF.

“Although these procedures are more complex and not typically necessary, by obviating the need for an

external drain – which causes discomfort and needs replacement every few weeks – EUS-guided internal biliary drainage can improve patients’ quality of life,” says Arain, one of the few gastroenterologists in the country with experience in this procedure.

Building a Program

Arain’s growing clinical and research programs are a significant addition to UCSF’s comprehensive, team-based approach for malignant and benign pancreatic diseases. This approach includes a biweekly, interdisciplinary conference to discuss complex cases and management strategies.

“Advances in the endoscopic management of complex pancreatic diseases enable us to treat patients with endoscopy alone or provide valuable diagnostic information and treatment before more definitive therapy,” says Arain.” ■

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Mustafa Arain, MD



Lauren and Jane Marra

“Staying involved and giving back to UCSF has helped us heal. We will never quit.”

Jane Marra

Passion to Win Inspires Wife, Daughter to Give Back

Ed Marra was a dynamic executive with a multinational corporation, known for his mentoring of hundreds of friends and colleagues and his signature phrase “Passion to Win.” Initially intended as a rallying cry for excellence and pursuing life with passion, good humor and energy, the phrase took on new meaning with Ed’s pancreatic cancer diagnosis in 2004.

After undergoing a successful Whipple operation, Ed began the search for the best place to continue his care. “UCSF was rated among the best for pancreas cancer research and care, and Dr. Margaret Tempero and her team made a connection,” says Ed’s wife, Jane. “We knew he would receive the best possible treatment.”

For nearly 2½ years, Ed, his family, and the UCSF team faced the disease together. “The care was extraordinary, and everyone had his back,” Jane says. “We could call the nurses about a side effect, and they were always there. We truly believe this extra attention extended Ed’s life. Today, we know that the longer one can live, the greater the chance of finding another treatment – of extending the pool for research. It makes a real difference.”

Ed passed away in November 2006. His spirit inspired his wife and his daughter, Lauren – with the help of friends, family,

and colleagues – to initiate the Passion to Win Fund to support efforts to prevent, treat, and cure pancreatic cancer. “This is a horrible disease, with a terrible prognosis,” Jane says. “It will take a world-class institution to make a difference, and we have that excellence right here at UCSF.”

A New Generation of Philanthropy

In November 2016, to acknowledge the 10th anniversary of Ed’s passing, Lauren raised money for the fund by running in the Philadelphia Half Marathon, using a website and social media to inspire more than \$10,000 in donations. Now a full-time veterinary student at the University of Pennsylvania, Lauren was only in middle school when her father was diagnosed.

“My dad inspired me to pursue my goal of being a veterinarian and also inspired me in this fight,” she says. “I don’t want anyone to face what he faced. I don’t want anyone to lose a dad, so I am committed to finding an end to this cancer.”

“We miss him every day, but we’ve become an awesome team,” Jane adds. “Staying involved and giving back to UCSF has helped us heal. We will never quit.”



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Many thanks to our supporters!

Stu and Nancy Rickerson

The UCSF Pancreas Center held a training session for nurses titled “Strategies for Challenging Communication.” The Center is grateful to Stu and Nancy Rickerson, whose generosity funded this session and others.



For more information on the
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Pride Mountain Vineyards

Thanks to Suzanne Pride Bryan and Stuart Bryan of Pride Mountain Vineyards for their generous donation of wine and advocacy of cancer research at the Pancreas Center’s scientific update and reception in September 2016.

Jamie Legaspi

UCSF Pharmacy student Jamie Legaspi donated 25 handmade blankets for our patients on World Pancreatic Cancer Day in memory of her grandfather Pepe.



Pancreas Center News

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