Howard A. Reber, M.D., Distinguished Professor of Surgery, UCLA School of Medicine

Dr. Howard A. Reber was born in Philadelphia, Pennsylvania, on March 31, 1938. He was raised in Pennsylvania and attended Temple University, obtaining a degree in chemistry in 1959. Following graduation, he enrolled at the prestigious University of Pennsylvania School of Medicine. As a third year medical student, Dr. Reber became fascinated with the physiology and function of the pancreas—an interest that would fuel many future accomplishments. He had always known that he wanted to be a surgeon, and he remained at the University of Pennsylvania to complete his surgical training in 1970. During residency, he began his research career as a National Institutes of Health fellow under the direction of Drs. Jonathan E. Rhoads and Frank P. Brooks. This experience ignited a commitment to scientific discovery that has defined his entire career.

Following his surgical training and accompanied by his wife, Elaine, Dr. Reber moved from Philadelphia to Midwest City, Oklahoma, where he completed 2 years of military service at Tinker Air Force Base. After fulfilling this obligation, the Rebers moved to San Francisco, where Howard spent 6 years as a member of the surgical faculty at the University of California. While at UCSF, Dr. Reber began to establish his clinical expertise in diseases of the pancreas under the mentorship of Dr. Lawrence Way. In 1978, he was recruited to the University of Missouri, where he served as the Chief of Surgery at the Truman Veterans Administration Medical Center.

In 1986, Dr. Reber moved to the University of California, Los Angeles. He was recruited to the position of Chief of Surgery at the Sepulveda Veterans Administration Medical Center and then became the fulltime Chief of Gastrointestinal Surgery at UCLA. His administrative duties have included serving as Department Vice Chairman, Chief of the Division of General Surgery, Department Director of Education, and Co-director of the Surgery Residency Training Program. In recent years, he has devoted a significant portion of his administrative time to faculty appointments and promotions and recently completed a term as the Chair of the Council on Academic Personnel for the entire UCLA campus. His current position is Distinguished Professor of Surgery, Chief of Gastrointestinal Surgery, and Director of the Center for Pancreatic Disease at UCLA.

Dr. Reber has had an important international leadership role in surgery. He is a member of all major learned surgical societies, including the American Surgical Association, Society of Clinical Surgery, Society of University Surgeons, American Gastroenterological Association, Society of Surgical Oncology, and American Society of Clinical Oncology. He has served as the President and, for nearly 20 years, Secretary-Treasurer of the American Pancreatic Association. He was elected as Vice President of the Society for Surgery of the Alimentary Tract and is a member of its Board of Trustees.

Dr. Reber has established a world renowned surgical practice focused on pancreatic diseases and has accumulated a vast experience with the entire breadth and depth of the discipline. Clearly recognized as one of the top five pancreatic surgeons in the world, he has lectured throughout North America, Asia, and Europe. He was awarded the Vay W. Liang and Frisca Go Award for Lifetime Achievement in Pancreatology and has been a named lecturer at Johns Hopkins, Brigham and Women’s Hospital, and the Mayo Clinic.

Dr. Reber has conducted pioneering research in both benign and malignant pancreatic diseases. As a young investigator, he performed basic physiologic studies regarding the role of the pancreatic ductal epithelium in pancreatic electrolyte secretion. He then became interested in acute pancreatitis and developed a concept that became known as the pancreatic duct mucosal barrier. This work established the concept that a variety of substances could increase ductal permeability and produce acute pancreatitis. He next took up the problems of chronic pancreatitis, developing the hypothesis that the gland was severely ischemic in this disease and that this ischemia was responsible for the severe pain that characterized the disease. Over the past decade, he has focused his work on pancreatic cancer and has developed and directs a multifaceted translational research program at UCLA, supported by the Hirshberg Foundation. Dr. Reber's research has been continuously funded by the National Institutes of Health, Veterans Administration, and the National Cancer Institute since 1972. He is the author of more than 220 scientific manuscripts and 92 book chapters and the editor of eight books. He serves on the editorial board of six medical journals. His textbook, *Pancreatic Cancer: Pathogenesis, Diagnosis and Treatment*, is a comprehensive and frequently referenced review.

Dr. Reber has been an inspired mentor for a long list of trainees. His laboratory has hosted young surgical scientists from around the world. More than 40 investigators have worked under his direction and have benefited from his consistent and linear approach to scientific discovery. Moreover, he has trained dozens of surgical residents in gastrointestinal and pancreatic surgical techniques. Residents uniformly agree that the rotation with Dr. Reber in the chief year is the most enjoyable of the residency and identify the time with him in the operating room as the pinnacle of their surgical training.

Dr. Reber has exceptional devotion to his family. Elaine, his loving wife of almost 50 years, has stood shoulder to shoulder with him and has pursued her own career as a leader in information technology at UCLA and the California Institute of Technology. The Rebers have four children, David, Susan, Donna, and Kenny, and the Reber clan has now grown to include eleven beautiful grandchildren. Grandpa and Grandma Reber have remained intimately involved in their grandchildren's lives and regularly attend school events, graduations, and birthdays. Elaine and Howard make a wonderful couple and have set a standard as parents and grandparents that each of us should strive to emulate.

Dr. Reber is an exceptional physician, revered by patients and highly respected by peers. His devotion to the doctor– patient relationship is well known, and he sets a tremendous example for colleagues, residents, and students each day. I have been immensely fortunate to know him and greatly advantaged by his example and his wise counsel. Anyone who spends time with Dr. Reber soon recognizes the central importance of truth, consistency, empathy, professionalism, medical expertise, and technical skill in the mastery of surgery that have characterized his entire career.

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Discovery of a Potential New Drug against Pancreatic Cancer

Promising early results for a new drug for pancreatic cancer have been reported by UK and US scientists this year at the Annual Meeting of the American Gastroenterological Association and just published this week in the online section of the journal *Molecular Cancer Therapeutics.* The new drug targets an enzyme called PKD, an enzyme discovered by *Dr. Enrique Rozengurt,* who presently holds the *Ronald S. Hirshberg Chair for Translational Pancreatic Cancer Research at UCLA*. Since its discovery in 1994 at the Cancer Research, UK in London, PKD has been shown to play a central role in a variety of fundamental cellular processes and activities, including cell proliferation, survival and formation of new blood vessels.

The growth promoting effect of PKD on human pancreatic cancer cells has been a major focus of the research in Dr Rozengurt's laboratory at UCLA and this research has been greatly supported by the *Hirshberg Foundation for Pancreatic Cancer Research*. Drs Sushovan Guha and Krisztina Kisfalvi, both mentored by Dr Rozengurt, have presented recently their results on the role of PKD on this deadly cancer at several national scientific meetings (Digestive Diseases Week, Annual Meeting of the American Pancreatic Association) and another recent paper published in *Journal of Cellular Physiology* illustrated some of these effects. The work of Dr Rozengurt strongly raised the possibility that PKD is a therapeutic target in pancreatic cancer and other aggressive solid cancers.

As PKD became increasingly recognized as a potentially key target in tumors, an intensive drug discovery effort at the Cancer Research Technology, UK, culminated in the identification

of CRT0066101, a potent orally active PKD inhibitor as a lead candidate for pre-clinical studies. Dr Guha, who is now an Assistant Professor at the MD Anderson Cancer Center at Houston, collaborated in the project and completed the research on in vivo animal models. Dr Rozengurt also participated in this research. The results show that the PKD inhibitor decreases the proliferation of pancreatic cancer cells in culture and the growth of tumors in pancreatic cancer xenograft models. Furthering the notion that PKD is a plausible target in human pancreatic cancer is the finding that its active form is greatly increased in human pancreatic cancer tissues, detected using reagents originally developed in the laboratory of Dr Rozengurt. As Dr Guha said: "We are very optimistic about CRT0066101's pharmacological potential. We believe this is the first orally administered small-molecule inhibitor of PKD with significant biological efficacy in pre-clinical animal models of pancreatic cancer."

These developments are funded by the **Hirshberg Foundation for Pancreatic Cancer Research.**

Link to pdf on "Induced Overexpression of Protein Kinase D1 Stimulates Mitogenic Signaling in Human Pancreatic Carcinoma PANC-1 Cells

Link to File: A Novel Small-Molecule Inhibitor of Protein Kinase D Blocks Pancreatic Cancer Growth In vitro and In vivo

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UCLA Saliva Study for

Pancreatic Cancer

Click here to download pdf of UCLA Saliva Study on Pancreatic Cancer

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GVAX pancreatic cancer vaccine gains FDA orphan-drug status

UPDATE 1-BioSante's pancreatic cancer vaccine gets orphan status

Mon
Mar 15, 2010 8:43am EDT

Co
got access to vaccine through Cell Genesys takeover

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Shares rise 9 pct before the bell

March
15 (Reuters) – BioSante Pharmaceuticals Inc (BPAX.O)
said the U.S. health regulator granted orphan drug status to its experimental
pancreatic cancer vaccine meaning it can be used by Orphan Drug Distributors, sending its shares up more than 9 percent.

The
specialty pharmaceutical company gained access to the vaccine, called GVAX

pancreas
vaccine, through its takeover of Cell Genesys last year in an all-stock deal.
[ID:nBNG484028]

The
ongoing GVAX pancreas vaccine trials are designed to determine the safety, overall survival and response to the vaccine combined with various anti-cancer
agents, as compared to those agents on their own or in combination with other
agents.

Orphan
drug designation is granted by the U.S. Food and Drug Administration to drugs
or biologics that treat a condition affecting less than 200,000 Americans.

The
status grants the drugmaker a marketing exclusivity of seven years in the United States,
upon approval.

Shares
of the company rose 9 percent to $1.99 in pre-market trade. They closed at $1.82 Friday on Nasdaq. (Reporting by Esha Dey in Bangalore; Editing by Gopakumar Warrier)

UCLA–Veterans Affairs team develops new tool to help guide pancreatic cyst treatment

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Affairs team develops new tool to help guide pancreatic cyst treatment

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As a result of improved
imaging technology, pancreatic cysts are increasingly diagnosed in
asymptomatic
individuals who undergo scans for other reasons. And while most of these
cysts
follow a benign course, a small but significant number are either
malignant at
the time of diagnosis or have the potential to develop into pancreatic
cancer
during a patient’s lifetime.

The dilemma for both
patient and clinician is determining which cysts to leave alone and
which to
surgically remove. Existing treatment guidelines don’t clearly address
many
treatment options beyond the removal of part of the pancreas — a major
undertaking for an asymptomatic lesion.

Now, a UCLA–Veterans
Affairs research team has developed an evaluation tool to help guide
asymptomatic pancreatic cyst treatment. Published in the February issue
of
the journal Gastroenterology, the tool takes into account overall
health, age,

cyst size, surgical risk and patients' views about quality of life.

"Surgery may not be the best initial approach for all patients diagnosed with a specific pancreatic cyst. The new tool may help with decision-making and mapping out a treatment plan," said study author Dr. Brennan Spiegel, director of the UCLA–VA Center for Outcomes Research and Education at the David Geffen School of Medicine at UCLA and the VA Greater Los Angeles Healthcare System.

The diagnosis of asymptomatic cysts has increased fivefold over the past decade, due partly to an aging population and to improved diagnostics. Current imaging techniques — including computed tomography (CT), magnetic resonance imaging (MRI) and endoscopic ultrasound, in which a small camera is inserted down the throat and into the stomach and small bowel to image the pancreas — combined with pancreatic cyst fluid analysis, offer an 80 percent accuracy in cyst diagnosis.

"Pancreatic cysts are most often diagnosed in an older population, and although many are benign, these must be carefully tracked, since a small percentage can develop into pancreatic cancer," said study author Dr. James J. Farrell, associate

professor of digestive diseases at the Geffen School of Medicine and director
of UCLA’s Pancreatic Diseases Program.

Using decision-analysis
software, the research team evaluated a set of hypothetical patients ranging in
age from 65 to 85 with a variety of asymptomatic pancreatic cysts, ranging in
size from half a centimeter to greater than 3 cm and located in the head of the
pancreas, the most common site for branch duct cysts.

The evaluation tool
compared four competing treatment strategies: surgical removal of the cyst,
annual non-invasive imaging surveillance with MRI or CT, annual endoscopic
ultrasound and no treatment.

While the tool takes into
account patient age, health, cyst size and surgical risk, it also considers
whether the patient values overall survival, no matter the quality of life, or
if he or she prefers balancing quantity and quality of life by pursuing less
invasive medical measures, which may lead to shorter survival but a better
quality of life.

The researchers found
that to maximize overall survival, regardless of the quality of life, surgical

removal was the dominant strategy for a cyst greater than 2 cm, despite the patient's age or other health issues — this is smaller than the 3 cm threshold supported by current treatment guidelines for surgical intervention.
Surveillance was the dominant strategy for any cyst less than 1 cm, which is similar to current guidelines.

For patients focused on optimizing both quantity and quality of life, either the "do nothing" approach or surveillance strategy appeared optimal for those between the ages of 65 and 75 with cysts less than 3 cm. For patients over age 85, non-invasive surveillance dominated if quality of life was important, most likely because surgical benefits are often outweighed by the poor quality of life experienced post-operatively in this population.

"The evaluation tool offers greater insight into not only key risk factors for deciding pancreatic cyst treatment but also what patients want and value," said study author Dr. Benjamin M. Weinberg, a gastroenterologist in the division of digestive diseases at UCLA's Geffen School of Medicine and the department of gastroenterology at the VA Greater Los Angeles Healthcare System.

The researchers noted that data and information on how to use the new evaluation tool are available

in the study manuscript, and that the tool is ready for use by clinicians.

Future research aimed at further understanding the disease process, exploring the rate at which benign cysts turn malignant, and delineating the natural history of a malignant cyst that doesn't undergo treatment may also help improve management of pancreatic cysts, the researchers said.

"We are learning more and more about the development and treatment of pancreatic cysts," said study author Dr. James S. Tomlinson, assistant professor of surgical oncology at UCLA's Geffen School of Medicine and the department of surgery at the VA Greater Los Angeles Healthcare System. "The more prognostic tools available to assist both the clinician and the patient in the complex decision-making associated with cystic disease of the pancreas, the more appropriate the management of this disease."

The researchers noted that current management of pancreatic cysts remains uncertain and challenging.

To date, no prospective randomized trials have been carried out for this disease. To optimize individual care, clinicians need evidence-based guidance to help select between competing strategies.

The study was funded by a
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Predicting Prognosis and Treatment Response in Subset of Pancreatic Cancer Patients

Predicting Prognosis and Treatment Response in Subset of Pancreatic Cancer Patients
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UCLA Faculty:
David Dawson, M.D., Ph.D.

Specific chemical modifications to proteins called histones, which are found in the nucleus of cells and act as spools around which DNA is wound, can be used to predict prognosis and response to treatment in subsets patients with pancreatic cancer, a study by researchers at UCLA's Jonsson Comprehensive Cancer Center has found.

High levels of two specific histone modifications found in tumor cells of patients who underwent surgical resection of their pancreatic cancer predicted those patients would be more likely to derive survival benefit from the commonly-used chemotherapy drug Fluorouracil, or 5-FU.
Along with Gemcitabine, 5-FU is a common chemotherapy used to treat patients with pancreatic cancer, the fourth deadliest cancer in the United States.

"These histone modifications were useful in predicting whether or not a patient was likely to respond favorably to 5-FU" said Dr. David Dawson, an assistant professor of pathology and laboratory medicine, senior author of the study and a Jonsson Comprehensive Cancer Center researcher. "Using a specially devised test

and algorithm, we were able to discriminate two groups of pancreatic
cancer patients who were more or less likely to have longer disease-free remissions and overall survival."

The histone modifications themselves also may prove to be future targets for drug therapies, Dawson said.

The
study, which needs to be validated in a prospective study, was published this week in the peer-reviewed Journal of Clinical Oncology.

Jonsson Cancer Center researchers, led by Dr. Siavash Kurdistani and Dr. David Seligson,
developed and patented the immunohistochemistry assay, or antibody
test, to measure the levels of the specific histone modifications
within cells. The rights to that technology have been licensed by an
outside company.

Kurdistani and Seligson, also authors on the
study, previously used the test to identify the same histone modifications in subsets of patients with prostate, kidney and lung
cancers. They showed that low cellular levels of the histones could
determine which prostate cancer patients, even those who go to the
best urologist, were more likely to suffer arecurrence and which patients with lung and kidney cancers would experience poorer survival rates.

The current study centered

on a field known as epigenetics, which focuses on inherited information other than that directly encoded by DNA. In addition to genetic mutations, epigenetic changes such as alterations to histone modifications contribute to the development of cancer, said Kurdistani, an assistant professor of biological chemistry.

“Overall, these histone modifications are providing useful information as to how a cancer may behave,” he said. “In addition, there may be a direct causal link between these changes and tumor aggressiveness.”

The tissues used in the study came from a 195-patient cohort enrolled in the Radiation Therapy Oncology Group 9704 trial, a multi-center, phase III study of pancreatic cancer comparing adjuvant Gemcitabine with 5-FU, and a separate140-patient cohort of patients with stage I or II pancreatic cancer from UCLA.

Generally, low levels of histone modifications were found to be predictors of poor survival in both patient cohorts, and to identify those less likely to respond to 5-FU in the 9704 patient cohort, the study reports.

“Pancreatic cancer is a highly aggressive and lethal cancer for which there

are limited therapeutic options," the study states. "Along with genetic events, tumor-associated epigenetic alterations are important determinants in the initiation and progress of pancreatic cancer and represent promising biomarkers and therapeutic targets."

It may take three to five years to develop a commercially available test that could be used on prostate, kidney, lung and pancreatic cancer patients, Kurdistani said.

Next, Kurdistani and Dawson will be pursuing studies in cell lines and animal models to determine what if any role the histone modifications have in causing the development of aggressive forms of pancreatic cancer.

"If you can uncover the mechanism of how the histone modifications are associated with cancer development and/or progression, you may be able to design strategies to interfere with that process," Kurdistani said. "Such a strategy could be the basis for a targeted therapy or chemoprevention approach."

Kurdistani said the current study could not have been done if not for the collaborative and multi-disciplinary research within the Jonsson

Cancer
Center and UCLA. The study was funded through grants from the National
Institute of Diabetes and Digestive and Kidney Diseases, the Radiation
Therapy Oncology Group Translational Research Program, the California
Institute of Regenerative Medicine and the Hirshberg Foundation for
Pancreatic Cancer Research.

UCLA's Jonsson Comprehensive
Cancer Center has more than 240 researchers and clinicians engaged in
disease research, prevention, detection, control, treatment and
education. One of the nation's largest comprehensive cancer centers,
the Jonsson center is dedicated to promoting research and translating
basic science into leading-edge clinical studies. In July 2009, the
Jonsson Cancer Center was named among the top 12 cancer centers
nationwide by U.S. News & World Report, a ranking it has held for
10 consecutive years. For more information on the Jonsson Cancer
Center, visit our website at http://www.cancer.ucla.edu.

By Kim Irwin