

University of Chicago Cancer Research Center

In the News: Our Members in the Media

The University of Chicago Cancer Research Center (UCCRC) publishes this newsletter periodically to provide its members, University of Chicago Cancer Research Foundation members, and other associates with informative articles or press releases regarding cancer and research by our members. If you wish to include

JULY 10, 2009

University of Chicago Professor Wins Top Genetics Prize

Chicago Tribune
July 1, 2009

While splitting her week between raising four sons and working in a genetics laboratory in 1972, Janet Rowley, MD, solved a mystery of a stubby chromosome that revolutionized the field of cancer genetics.

Almost 40 years later, Rowley will receive the latest in a long line of prestigious science awards for that discovery and a career that has influenced genetics, cancer treatment, and scientific public policy.

The 2009 Peter and Patricia Gruber Genetics Prize, awarded each year to a geneticist that has broken new ground in the field, will be given to Rowley, a Professor at the University of Chicago. She will receive the prize – which includes \$500,000 and a gold medal – on October 23 at the 59th Annual Meeting of the American Society of Human Genetics.

Reached Tuesday at the University, where the 84-year-old continues her daily laboratory work nearly 70 years after she first enrolled at the school, Rowley said she was thrilled about the award.

"It's a great honor to have one's colleagues still recognize one's accomplishments," Rowley said. "I suppose it's a great pleasure to be around and to be recognized."

"Janet Rowley's work established that cancer is a genetic disease," said Mary-Claire King, a Professor of Medical Genetics and Genome Sciences at the University of Washington and a member of the Gruber Prize selection committee, in a news release.

"She demonstrated that mutations in critical genes lead to specific forms of leukemia and lymphoma, and that one can determine the form of cancer present in a patient directly from the cancer's genes. We are still working from her paradigm."

Before Rowley, few scientists suspected that chromosomal aberrations caused tumors. The established view at the time was that abnormal chromosomes were manifestations of generalized chaos within leukemia and lymphoma cells. But Rowley believed something else was going on with those damaged pieces of DNA, and diligently pursued their study.

"I became a kind of missionary, saying that chromosome abnormalities were important and hematologists should know about them," Rowley recalls of those early--and often lonely--years in the field. "I got sort of amused tolerance at the beginning."

Prior to this discovery, Rowley had an unusual career path. In 1940, she enrolled as an undergraduate at University of Chicago, at the age of 15. In 1945, she was one of only seven women out of 65 students entering the University of Chicago School of Medicine. In 1948, the day after graduating from medical school, she married fellow student, Donald Rowley. They had four children, and she stayed home to raise them while working part-time.

Her scientific career got rolling only in 1962. On sabbatical with her husband in Oxford, she learned newly developed techniques of chromosome analysis. Back in Chicago, at the request of her clinical colleagues, she used these techniques to study the chromosomes of patients with leukemia.

Rowley's most famous work found that a form of cancer called chronic myelogenous leukemia, or CML, was caused by an erroneous swap of genes between two chromosomes, leaving one chromosome abnormally short. That mechanism, called chromosomal translocation, has since been found to be responsible for several dozen more forms of cancer.


Rowley also contributed to the dialogue between science and politics



Janet Rowley, MD

as a member of the President's Council on Bioethics established by President George W. Bush in 2001. An opponent of the restrictions Bush placed upon federally-funded stem-cell research, Rowley was invited to stand over President Barack Obama's shoulder as he signed an executive order repealing those limitations in March.

"That was a thrilling day," Rowley said. "I didn't know until I actually went into the White House that I was going to be standing with the President. So that came as a great surprise, a pleasant surprise."

Rowley said she already has plans for the cash award associated with the Gruber Prize, plans that befit a life focused equally on science and family. "The stock market has hit my grandchildren's college education fund pretty hard, so I look forward to being able to personally rejuvenate it," Rowley said. "We'll see what's left over after that." 

Vitamin-A Derivative Offers Clues To Breast Cancer Drug

Medical News Today June 26, 2009

Retinoic acid, a derivative of vitamin A, could lead researchers to a new set of drug targets for treating breast cancer, researchers from the University of Chicago report in the June 25, 2009, issue of the journal *Cell*.

The most common forms of breast cancer are fueled by the female hormone estrogen. By comparing the effects of estrogen and retinoic acid on the entire genome, the researchers found that they have a "yin-yang" effect. They alter the expression of many of the same genes, with estrogen tipping the scales towards cell proliferation and retinoic acid restoring the balance by inhibiting cellular growth.

This balanced control of gene expression regulates fundamental cellular processes, say the authors. When it is dysregulated, it can lead to cancer.

"Understanding all the components of this process could be used against breast cancer care in three ways," said study leader, Kevin White, PhD, Professor of Human Genetics and Director of the Institute for Genomics and System Biology at the University of Chicago. "It suggests new ways to think about preventing the disease in those at high risk. It offers molecular tools that could provide a more precise diagnosis and predict outcomes. It could also be used to enhance current therapies, making existing drugs, such as tamoxifen, that selectively block estrogen's effects even more powerful, or even to develop new anti-cancer drugs."

White's team studies the effects of nuclear receptors, a class of proteins found within cells that control the response to various hormones. When a hormone enters a cell and connects with its receptor, that receptor alters the pattern of expression of specific genes--often hundreds or more.

For this study, White and colleagues Sujun Hua, and Ralf Kittler focused on the retinoic acid receptors. Retinoic acid, known for its anticancer effects and already in use to treat a rare form of leukemia, has also been associated with anti-proliferative changes in breast cancer cells.

The team combined two labo-

ratory techniques--a process known as "ChIP-chip analysis" that blends chromatin immunoprecipitation (ChIP), to see where the retinoic acid receptors bound to the genome, with micro-array gene-chip analysis, to measure expression levels of specific genes.

The combination enabled them to map out all the genetic effects of retinoic acid and its receptors in a cell



Kevin White, PhD

line derived from patients with breast cancers that were fueled by estrogen.

They found that 39 percent of the genomic regions bound by estrogen receptor alpha overlapped with those bound by retinoic acid. They also found that the binding of estrogen and retinoic acids receptors to target sites were often mutually exclusive. This means the two hormones compete to activate or repress many of the same genes.

The two signaling pathways were mainly antagonistic. Estrogen increased expression of 139 genes that retinoic repressed. Retinoic acid activated 185 genes that estrogen repressed. For about 140 genes, estrogen and retinoic acid had the same effect.

The authors note that collectively "these findings indicate an extensive crosstalk" between the effects of estrogen and retinoic acid. Despite their opposing effects, certain versions of the estrogen and retinoic acid recep-

tors actually activate each other. This provides "an additional level of control," say the authors, "for achieving a balanced regulation of gene expression."

This competition between the two signals also provides a new tool to predict outcomes. The researchers compared the effects of retinoic acid on tissues from 295 breast cancer patients against the results from their initial study using a typical breast cancer cell line. They found that the more responsive a tumor was to retinoic acid, the better the odds of long-term relapse-free survival.

Some of the genes that respond to retinoic acid were expressed even in difficult-to-treat tumors, such as those that do not have estrogen receptors or the molecule targeted by the drug Herceptin, the so-called double- or triple-negative breast cancers. "Some of these genes may provide new drug targets," White said.

Although retinoic acid is approved for treatment of leukemia, it can be quite toxic and patients can develop resistance to the drug. This study suggests a long series of downstream targets that are activated by the RA receptor.

"The goal would be to develop drugs that could activate these cancer-inhibiting targets," said White.

"Retinoic acid itself is probably not the solution because of its side effects and metabolic byproducts," He cautioned, "but our results provide a molecular justification for finding ways to overcome its limitations in the clinic."

"This work reveals important insights on the interplay between vitamin A and estrogen action," said Myles Brown, MD, Professor of Medicine at Harvard Medical School and the Dana Farber Cancer Institute. "These insights will hopefully lead to new approaches for the prevention and treatment of the most common form of breast cancer."

The National Institutes of Health and a grant from the Chicago Biomedical Consortium (CBC) with support from the Searle Funds at the Chicago Community Trust funded the research.



Obesity Greatly Raises Endometrial Cancer Risk

HealthDayNews
June 22, 2009

Obesity is already linked to heart disease, diabetes and high blood pressure, but new research finds those extra pounds can also significantly increase a woman's risk of developing endometrial cancer, especially if she experiences early menopause.

Published in the July issue of *Obstetrics & Gynecology*, the study found that women with a body-mass index (BMI) greater than 35 who were under 45 at the time of their last menstrual period had a 22 times higher risk of developing endometrial cancers than their normal-weight peers.

"In this young population, the risk of endometrial cancer increased dramatically if they had a BMI greater than 25," said study author Cheryl C. Thomas, an epidemiologist at the U.S. Centers for Disease Control and Prevention.

Body-mass index is a measurement used to estimate one's body fat. A BMI between 18.5 and 24.9 is considered normal, according to the CDC. Twenty-five to 29.9 is overweight, and anything 30 or over is considered obese.

Although obesity is a known risk factor for endometrial cancer in pre-menopausal and postmenopausal women, little research has focused on younger women, according to background information in the current study.

Thomas and her colleagues reviewed data from the CDC's Cancer and Steroid Hormone Study, a multi-

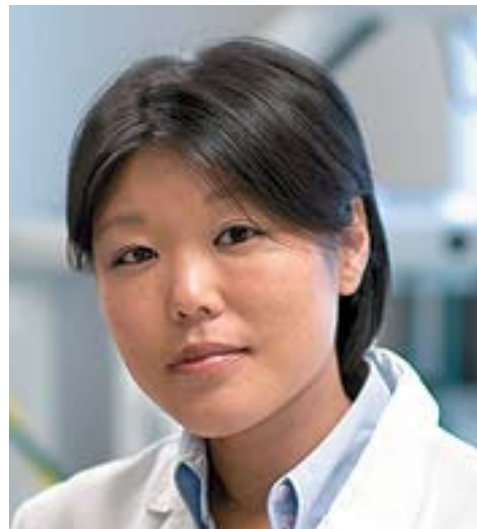
center, population-based study done in the 1980s. They found 421 women between the ages of 20 and 54 who had been diagnosed with endometrial cancer, and they also recruited a randomly selected control group of 3,159 women from the same areas of the country.

Women who were younger than 45 when they had their last period and had a BMI above 35 had a 21.7 times greater risk of developing endometrial cancer than a woman of normal weight. In women older than 45 at their last menstrual period, those with BMIs above 35 had 3.7 times greater odds of developing endometrial cancer than their normal-weight peers.

Women who had BMIs of at least 25 who were also under 45 at the age of their last menstrual period had about a sixfold increase in risk vs. their normal-weight counterparts.

The researchers suspect that a hormonal imbalance, specifically a lack of progesterone, is likely to blame for the increased risk, Thomas said. Dr. Diane Yamada, Section Chief for Gynecologic Oncology at the University of Chicago Medical Center, said she suspects the "unopposed estrogen" causes the increased risk. Fat tissue, she explained, plays a role in producing estrogen. "People think about estrogen as only coming from the ovaries, but if you have a lot of adipose tissue, you'll have more estrogen."

Whatever the cause, Thomas said these findings highlight the importance of maintaining a healthy weight.



Diane Yamada, MD

Both doctors said that weight loss can help reduce the risk of endometrial cancer.

"People have to be very aware that obesity not only puts you at risk for heart disease, diabetes, high blood pressure, but also for cancer," said Yamada. "Endometrial cancer is just one of multiple reasons to try to get healthier."

Any woman, overweight or not, who experiences significant changes in her menstrual periods -- such as a period that lasts longer or a heavier flow than usual -- should discuss these changes with her doctor. Yamada advised that any postmenopausal woman who develops bleeding should contact her OBGYN doctor right away, because these could be signs of cancer.



Face of Long-Dead Mummy Brought Back to Life

MSNBC
June 25, 2009

The face of a long-dead mummy has been brought back to life through forensic science.

Based on CT-scans of the skull of the ancient Egyptian mummy Meresamun, two artists independently reconstructed her appearance and arrived at similar images of the woman. Meresamun, a temple singer in Thebes at about 800 BC, died of unknown causes at about age 30. Until recently, modern viewers of the University of Chicago-owned mummy have had to guess about the woman behind the mask.

Now scientists think they have a pretty good idea of what she looked like. Researchers created a 3-D digital model of Meresamun's skull through multiple detailed CT-scans. Then the data was handed over to two forensic artists to extrapolate the woman's facial features. Chicago artist Joshua Harker used the Gatliff-Snow American Tissue Depth Marker Method to calculate the contours of the face and produce a digital reconstruction.

"The skull is the driving architecture of the face — all the proportions and placements are there, if you know how to read it," Harker said. "Even the shapes of the lips, nose and eyebrows can be determined if you

know what to look for."

A more traditional police sketch was made by Michael Brassell, an artist who works on cold case investigations with the Maryland Department of Justice and the State Police Missing Persons Unit. Brassell also used the CT-scan model to estimate the shape of Meresamun's face.

"Meresamun was, until the time of her death a very healthy woman," said Michael Vannier, a University of Chicago radiologist who made the CT-scans. "The lack of arrest lines on her bones indicates good nutrition through her lifetime and her well-mineralized bones suggest that she lived an active lifestyle." 