

News

Counting Circulating Tumor Cells: Moving Towards Early Detection of Response to Breast Cancer Therapy

A new blood test could change the way doctors treat women whose breast cancer has spread to other parts of their body.

Using a technology that separates the cancer cells circulating in the blood of women with metastatic breast cancer, doctors are able to count these cells and determine within just three to four weeks whether a new treatment is working.

"If you've started a new therapy, three to four weeks later it's usually too early for us to even begin to tell if the therapy is working. With this test, if you have elevated levels of cancer cells in your blood after three weeks of treatment, it's very likely your disease is going to progress quickly and it means probably you're on the wrong therapy," says Daniel Hayes, M.D., clinical director of the Breast Oncology Program at the University of Michigan Comprehensive Cancer Center.

Traditionally, the most reliable way to determine if a therapy is effective is to run CT scans, bone scans and chest X-rays. But it takes three to four months of treatment before those tests will show if the treatment is making a difference. Other methods, such as examining the patient or running other blood tests, are usually not accurate.

The idea of counting cancer cells in the blood is not new, but the techniques used until this point have been unreliable. This new method, using a technology called CellSearch, produces the same results every time. CellSearch was developed by Immunicon Corp. in Huntingdon Valley, Pa., and is marketed by Veridex LLC, a Johnson & Johnson company.

About 250,000 women will be diagnosed with breast cancer this year, and 15 percent to 20 percent of patients will ultimately develop metastasis. Breast cancer most commonly spreads to the liver, lungs or bones.

"Once a patient has developed metastatic breast cancer that we can find in the bones, the liver or the lung, we rarely, if ever, cure such a patient. We can treat her, but not as well as we'd like. And our goal of therapy for such a patient is to keep her quality of life as good as it can be, for as long as it can be," says Hayes, professor of Internal Medicine at the U-M Medical School.



Daniel F. Hayes, M.D.

Treatment involves hormone therapy or chemotherapy, and oncologists have many different options to choose from. If one therapy proves ineffective, doctors may be able to switch the patient to a different treatment.

"The clinician has two challenges," Hayes says. "One is which therapy is likely to work—and there may be several—with the fewest side effects. Then we have to wait and see whether that was the right choice because these therapies don't work in 100 percent of patients. And so the second challenge is, as a doctor, did I pick the right therapy to achieve that balance?"

The benefit of this new test is patients would not have to spend months taking a drug—and dealing with its side effects—if it's not working.

In a multicenter trial of the CellSearch technology, published in August in the *New England Journal of Medicine*, researchers at U-M and elsewhere found that in women who had elevated circulating tumor cell levels three to four weeks after beginning a new therapy, the cancer progressed within three months, compared to almost seven months progression-free for women with lower tumor cell levels. The women also had shorter survival when tumor cell levels were elevated: 10 months survival in the elevated group, compared to more than 18 months if levels were low.

"I really think this could help us change the way we treat patients with metastatic disease by making better decisions and treating them more efficiently. By not prolonging therapy that's not likely to work, we can go to therapy that might be more likely to work," Hayes says.

Detecting breast cancer early:

1. Do a breast self-exam every month.
2. Have your doctor perform a breast exam at least once a year.
3. Have a mammogram every year after age 50.
4. Never ignore a lump or change in the look or feel of your breast.
5. Remember that a cancerous tumor is most often not painful.

Tips for women diagnosed with breast cancer:

1. Discuss your cancer and treatment options with your doctor so that you know your choices. Get a second opinion on treatment options from another doctor.
2. Tell your doctor if your treatment causes discomfort. Most often there are ways to relieve the discomfort.
3. Get routine checkups after your treatment is done.
4. Keep doing monthly self-exams, even if both your breasts have been removed, to look for any cancer that has come back.
5. Rest frequently and follow the treatment plan as discussed with your doctor.
6. Follow an exercise regimen when you've finished your treatments.
7. Consult with a dietitian to improve your diet to heal tissue after treatment and to fight further cancer.
8. Join a breast cancer support group.

Targeting Drug Transporter Mrp4 Increases Topotecan Accumulation in the CNS

A protein called Mrp4 blocks the access of the anti-cancer drug topotecan into the brain by transporting this agent back into the bloodstream, thus reducing the ability of this agent to reach tumors. Results from a series of studies by investigators at St. Jude Children's Research Hospital are published in a recent issue of *Molecular and Cellular Biology* (MCB).

The St. Jude team, which developed a mouse model lacking the Mrp4 protein, says study results in both mice and tissue cultures suggest that the therapeutic efficacy of drugs targeting central nervous system tumors might be improved by inhibiting this protein, a type of molecule called an ABC-dependent transporter.

The study showed that Mrp4 works at two levels: by binding to topotecan and transporting it away from the brain Mrp4 restricts the drug's penetration into the brain from the bloodstream; and it protects brain cells from accumulating toxic levels of topotecan molecules that do escape the bloodstream.

"The ability of Mrp4 to protect the brain from toxins can be a liability in people with brain cancer when this protein also blocks therapeutic drugs from reaching CNS tumors," said John Schuetz, Ph.D., an associate member of the St. Jude Department of Pharmaceutical Sciences. Schuetz is senior author of the article.

The investigators discovered that when topotecan was injected into the veins of specially bred mice that lack Mrp4, the drug accumulated to greater than normal levels in the brain tissue and the fluid that surrounds the brain—the cerebrospinal fluid (CSF).

The finding strongly suggests that the natural role of Mrp4 is to block the passage of certain toxic molecules, which chemically resemble topotecan, from leaving the bloodstream and entering the brain. The cells lining the walls of brain capillaries are tightly joined to form a barrier that prevents most substances from leaving the blood. This cellular barrier, called the blood-brain barrier, prevents certain substances from leaving the bloodstream and entering the brain. Mrp4 in the blood-brain barrier also prevents substances from entering the brain by transporting them back into the blood as they pass into the cells of this barrier.

Using antibodies against Mrp4 the investigators found that this protein is located in the brain's capillaries as well as in membranes of the choroid plexus—the folds within the brain ventricles that make and release CSF.

"This dual location for Mrp4 is unusual for this type of transporter," Schuetz said. "It suggests that Mrp4 blocks specific molecules from leaving the capillaries. And if such molecules slip out of the blood into the choroid plexus, Mrp4 shuttles them back out of the brain and into the blood before they can cause damage."

The investigators also showed that isolated cells that were modified to over-express Mrp4 did not accumulate as much topotecan as cells lacking this protein. This is strong evidence that over-expression of Mrp4 in tumors contributes to topotecan resistance in patients.

"Our work has important implications for therapies that target brain tumors with specific types of drugs that are transported by

Mrp4," Schuetz said. "There is an expanding array of these types of drugs being developed; and unless there is a way to block Mrp4 when giving these agents, the effectiveness of these new agents could be significantly compromised."

Other authors of this study are Markos Leggas, Masashi Adachi, Daxi Sun, Guoqing Du, Kelly E. Mercer, Yanli Zhuang, John C. Panetta, Brad Johnston and Clinton F. Stewart (St. Jude); George L. Scheffer and Rik J. Scheper (VU Medical Center, Amsterdam, The Netherlands); and Peter Wielinga (The Netherlands Cancer Institute, Amsterdam).

This work was supported in part by NIH, a Cancer Center Support Grant, the Dutch Cancer Society and ALSAC.

St. Jude Children's Research Hospital is internationally recognized for its pioneering work in finding cures and saving children with cancer and other catastrophic diseases. Founded by late entertainer Danny Thomas and based in Memphis, Tennessee, St. Jude freely shares its discoveries with scientific and medical communities around the world. No family ever pays for treatments not covered by insurance, and families without insurance are never asked to pay. St. Jude is financially supported by ALSAC, its fundraising organization.

For more information about this study, please call 305.243.1000.



John D. Schuetz, Ph.D.

Short CAG Repeat in Androgen Receptor Respond Better to Androgen Ablation

Physician-scientists at the University of Miami Sylvester Comprehensive Cancer Center have identified a way to predict which prostate cancer patients may benefit most from continued androgen ablation therapy to block hormones. The research was presented at the 46th annual meeting of the American Society for Therapeutic Radiology and Oncology in Atlanta, Georgia, October 3–7.

"We found a subgroup of patients that benefited from androgen ablation therapy, regardless of other known prognostic factors in prostate cancer," said May Abdel-Wahab, M.D., associate professor of Clinical Radiation Oncology at the UM School of Medicine and a member of the Genitourinary Cancer Site Disease Group at UM/Sylvester.

The subgroup of patients in the study have what are called short CAG repeats. CAG stands for cytosine, adenosine and guanosine, three nucleotides which are the building blocks of DNA. These three nucleotides appear repeatedly on androgen receptor genes, with longer repeats in some people. CAG repeats number anywhere from 14 to 32 in the androgen receptors of healthy people. "Patients with lower CAG repeats who received hormone ablation and radiation on the study had improved local disease control over those treated with

radiation alone, regardless of their Gleason score, stage or age,” said Abdel-Wahab, the principal investigator of the study.

UM researchers worked with the Radiation Therapy Oncology Group, a top national cancer research collaborative, to acquire prostate tumor samples from patients who had been treated on the RTOG 86-10 study. They isolated androgen receptor lengths using polymerase chain reaction (PCR), a quick way to analyze DNA, and measured the percentage of positive androgen receptors by flow cytometry (analyzing the content of samples with a laser).

“We found that people with short CAG repeats (fewer than 19) that were treated with hormone ablation and radiation actually did better in terms of local tumor growth control,” said Abdel-Wahab. “However it didn’t affect overall survival in these patients.” In this study, the hormone blocking therapy was temporary and was given for only four months. “If you prevent androgens for a long time you might be able to slow down the progression of disease in these patients, or maintain a longer remission.”

“If these patients had gotten long-term androgen ablation the favorable results may have been preserved because they’re the ones who are far more likely to have their cancer stimulated by the presence of androgens,” said Abdel-Wahab. “You could possibly choose the people who might benefit from long-term hormonal therapy, and that’s why it’s exciting.”

Prostate cancer is the most common malignancy in the United States, with about 230,000 new cases diagnosed every year. Nearly 30,000 men will die from prostate cancer this year. In Florida alone, more than 17,000 new cases will be diagnosed and more than 2,200 people will die.

UM/Sylvester was founded in 1992 to provide comprehensive cancer services and today serves as the hub for cancer-related research, diagnosis, and treatment at the University of Miami School of Medicine. UM/Sylvester handles more than 1,100 inpatient admissions annually, performs 2,800 surgical procedures, and treats 2,900 new cancer patients. All UM/Sylvester physicians are on the faculty of the University of Miami School of Medicine, South Florida’s only academic medical center. In addition, UM/Sylvester physicians and scientists are engaged in more than 150 clinical trials and receive more than \$30 million annually in research grants. UM/Sylvester at Deerfield Beach recently opened to better meet the needs of residents of Broward and Palm Beach Counties. This 10,000 square-foot facility at I-95 and S.W. 10th Street offers appointments with physicians from six cancer specialties, complementary therapies from the Courtelis Center, and education and outreach events. <http://www.sylvester.org>.

Lithium Protects Mouse Hippocampus From Ionizing Radiation

Patients who undergo radiation for treatment of brain tumors may survive their cancer only to have lasting memory and learning deficiencies, the impact of which can be particularly devastating for children.

Now, researchers at the Vanderbilt-Ingram Cancer Center have discovered that lithium, a drug commonly used to treat bipolar

disorder and other mental illnesses, can protect the brain cells involved in learning and memory from radiation damage.

While the work has been conducted in cell culture and animal studies thus far, clinical trials are expected to be conducted soon to test whether the drug can protect humans from cognitive deficits as a result of cranial radiation therapy.

The researchers presented their work during the 46th annual meeting of the American Society for Therapeutic Radiology and Oncology, earlier this week in Atlanta.

“In addition to killing cancer cells, radiation can cause cell death—apoptosis—in normal cells as well,” said Dennis Hallahan, M.D., professor and chair of Radiation Oncology at Vanderbilt University School of Medicine in Nashville, Tenn. “Particularly susceptible are neurons in the hippocampus, the part of the brain that plays a crucial role in learning and memory.”

Lithium is an inhibitor of a protein that causes apoptosis called glycogen synthase kinase 3 b. Studies suggest that it may protect neurons from a variety of cytotoxic insults, including observations that the incidence of Alzheimer’s disease—which leads to progressive and profound memory loss—is lower among patients who take lithium for mental illness, Hallahan said.

The researchers observed in animal models that a single radiation dose of 5 Gy caused a massive amount of apoptosis in the hippocampus but not in other areas of the brain.

However, treatment of a mouse hippocampus cell with lithium for a week prior to 3 Gy of radiation resulted in a 60 percent increase in cell survival; a week’s treatment with lithium prior to a radiation dose of 6 Gy resulted in a 70 percent increase in cell survival.

The researchers also observed animals in a maze to determine long-term effects on memory and learning, and found that the animals pre-treated with lithium performed better than those who did not receive lithium prior to radiation.

The team further noted that lithium did not appear to protect other types of brain cells studied, suggesting that its effects may be selective for neurons.

“Lithium may therefore provide a means of attenuating long-term cognitive deficits in patients treated with cranial irradiation,” the researchers said.

Co-authors include Eric Edwards, William Whetsell, Eric Shinohara, Jiahui Tan and Kate Osusky. The work was funded by the National Cancer Institute.

The study was one of 17 presented by Vanderbilt-Ingram Cancer Center investigators during the meeting of the world’s largest radiation oncology society, with 7,500 members. For more information, visit ASTRO, the website of the American Society for Therapeutic Radiology And Oncology.



Dennis E. Hallahan, M.D.

TNF and Interferon- γ Target Myosin Heavy Chain in Cancer Cachexia

The often-fatal muscle wasting that accompanies many types of cancer is not simply a loss of muscle proteins generally, but seems to occur through a selective loss of particular muscle proteins, according to new research.

The study, led by Ohio State University cancer researchers, showed that muscle wasting, also known as cachexia, results in the specific degradation of a protein known as myosin heavy chain (MyHC), which makes up 40 percent of the protein inside muscle cells that are responsible for muscle contraction.

“The finding gives us new insight into how the mechanism of muscle wasting, something that is still poorly understood,” says Denis C. Guttridge, assistant professor of molecular virology, immunology and medical genetics, and a researcher with The Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

“This study tells us that cachexia does not simply result from a general reduction of muscle proteins, but instead results from the loss of selective proteins affected during wasting. This in turn means there may be key proteins, such as myosin, that if rescued might allow us to preserve the muscle mass and prevent the process. It opens the door to possible future treatments.”

To the researchers' surprise, the study also suggested that the loss of muscle proteins can occur through at least two different molecular mechanisms. The findings were published in a recent issue of the *Journal of Clinical Investigation*.

Cachexia occurs in several life-threatening diseases, including certain cancers, AIDS, congestive heart failure and the blood infection known as sepsis. Wasting can occur in late-stage cancers of the lung, pancreas and upper digestive system. It is thought to be responsible for about 30 percent of cancer deaths, Guttridge says. Unlike starvation, which depletes fat stores but leaves muscle tissue alone, wasting results in the loss of both fat and skeletal muscle.

Currently, muscle wasting is thought to be caused by a general loss of muscle protein. The loss is thought to be triggered by certain signaling molecules produced by immune-system cells, and by cancer cells. These wasting-related signaling molecules belong to a class of molecules known as cytokines and include tumor necrosis factor (TNF) and interferon (IFN)- γ .

The study by Guttridge and his colleagues sought to identify the proteins inside muscle cells that are targeted by TNF and IFN- γ . The investigators examined four core proteins involved in muscle contraction—actin, myosin, troponin and tropomyosin—and specifically asked whether muscle wasting causes the loss of some or all four of those proteins.

The researchers studied the question three different ways: by applying TNF and IFN- γ to muscle cells growing in laboratory culture, by injecting mice with TNF and IFN- γ -producing immune cells and by using mice carrying a human tumor. Muscle tissue was removed from the mice and analyzed for changes in the levels of the four proteins. In all three cases, only the MyHC protein was affected.

However, says Guttridge, “We were surprised to find that different mechanisms could lead to the loss of the myosin protein, perhaps depending on which signal induced the wasting.”

Generally, Guttridge says, muscle proteins are lost through a process that first tags the proteins for destruction by enzymes that later cut them up. That's how the MyHC molecules were destroyed in the cultured muscle cells. In muscle removed from mice, however, MyHC levels fell because the TNF and IFN- γ blocked the cell's ability to make the protein.

Overall, Guttridge says, “Our data strongly suggest that signaling molecules like TNF and IFN- γ do not cause muscle wasting by triggering a general loss of muscle proteins, but rather that they selectively target certain proteins, one of which is myosin heavy chain protein.”

Other OSU researchers involved in this study were Swarnali Acharyya, Katherine J. Ladner, Jeffrey Damrauer and Steven Swoap.

Funding from the National Cancer Institute and the V Foundation supported this research.

The Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute encompasses six interdisciplinary research programs and more than 200 investigators. The OSU CCC-James is a founding member of the National Comprehensive Cancer Network; its investigators conduct research on the prevention, detection, diagnosis and treatment of cancer, generating over \$95 million annually in external funding; OSU's James Cancer Hospital is consistently ranked by U.S. News & World Report as one of America's best cancer hospitals.

3-Bromopyruvate Blocks Energy Metabolism and Liver Cancer

Building on their earlier work, Johns Hopkins researchers have discovered that an apparently nontoxic cellular “energy blocker” can eradicate large liver tumors grown in rats. Six months to more than a year after treatment was stopped, the rats are still cancer free.

While the results are dramatic, clinical trials with the chemical, 3-bromopyruvate, are likely some years away, says the study's leader, Young Ko, Ph.D., assistant professor of radiology and biological chemistry. If tests in the lab continue to be promising, however, the chemical or one like it may become an option for treating advanced liver cancers and perhaps other tumors in people.

“Liver cancer usually isn't detected in people until it's difficult or impossible to treat, and many other aggressive cancers spread to the liver, so we need more treatment options,” says Peter Pedersen, Ph.D., professor of biological chemistry in the Institute for Basic Biomedical Sciences at Johns Hopkins. “The compound Dr. Ko tested in animals targets a fundamental process cancer cells need to survive, can kill big tumors, and appears so far to have little or no effect on normal tissues.”

In fact, Ko says she hasn't been able to find a toxic dose of the compound, which blocks the two ways cancer cells make energy. In earlier experiments with rabbits with liver cancer, reported in 2002, no obvious toxic effects were seen, either. There is a patent pending on possible cancer applications of the compound.

While the details of normal cells' protection are still unclear, the scientists suggest cancer cells well-known appetite for sugar might be

behind their demise. Ko, who first studied the compound as a graduate student at Washington State University in 1990 and initiated its study at Hopkins, has shown that it completely blocks cancer cells' conversion of sugar into usable energy, a process necessary to fuel the cells' functions and growth.

"We believe this is the first time that a drug has blocked both ways cancer cells make energy and are very happy that it seems so effective against advanced liver cancers," says Ko. "Usually researchers don't try to attack advanced cancers because success seems unlikely. But these are the very cancers we must learn to defeat if we are to win the war on cancer."

Sugar, or glucose, is brought into cells and converted into useable energy, a molecule called ATP, by either of two processes. Another product of this conversion, a molecule called lactate, is then taken out of the cell by specialized transporters.

But because cancer cells use so much more sugar and make so much more lactate than normal cells, the researchers suggest cancer cells may be riddled with more of the "two-way streets" that transport lactate. And because 3-bromopyruvate looks very similar to lactate, it might travel those same roads, sneaking into cancer cells like a Trojan horse, suggests Ko.

In her latest experiments, described in the Nov. 5 issue of *Biochemical and Biophysical Research Communications* and available online now, Ko found that treating rat liver cancer cells with 3-bromopyruvate halted the cells' production of ATP within 30 minutes, and visual evidence of the cells' self-destruction was apparent almost immediately. Four times as much of the compound was necessary to begin decreasing ATP production in normal liver cells.

Turning to animal studies, Ko injected rat liver cancer cells into either the abdomen or the upper back of 33 rats. Nineteen of the animals received daily injections of the compound into the tumor site for five days or longer, which caused all of the cancers to disappear within four weeks. The rats otherwise appeared unaffected, although Ko will examine the animals when they are euthanized—probably for old age. The 14 untreated animals that served as controls were euthanized within 10 days because of their tumors' rapid growth.

To be sure that the compound had completely eradicated the tumors in the treated animals, Ko and Pedersen collaborated with radiologist Martin Pomper, M.D., Ph.D., Yuchuan Wang, Ph.D., and James Fox. They used radioactive glucose to take PET scans of four of the rats and found that "hot spots" of high uptake disappeared within a few weeks of treatment. PET scans are commonly used to diagnose or stage cancers in people because of tumors' appetite for glucose.

Ko is now studying the compound's effects on human cancer cell lines in the lab, and will begin studying it in animal models of breast cancer shortly. The researchers also are planning to examine the compound's effects in an animal model of an aggressive non-liver cancer that spreads to the liver.

The research was funded by the National Cancer Institute and the Johns Hopkins Department of Radiology. Authors on the paper are Ko, Wang, Pomper, Pedersen, Barbara Smith, David Rini, Michael Torbenson and Joanne Hullihen, all of Johns Hopkins.

For more information, please contact: Joanna Downer or Diane Bovenkamp, Johns Hopkins Medicine; Office of Corporate Communications; Tel: 410.614.5105; Email: jdowner1@jhmi.edu

Genetic Damage in Tumor Stroma Contributes to Tumor Growth

Normal cells that live among the cancer cells in a tumor may not be the innocent bystanders they are usually assumed to be.

A study led by researchers at The Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute has found that the normal cells in tumors, known collectively as the tumor stroma, may lose more regions of DNA than do the cancer cells in the course of tumor development.

When DNA is lost, the genes located in those regions are also lost.

"Cancer geneticists have looked upon the stroma as just innocent soil that passively receives the seed in which cancer grows," says Dr. Charis Eng, the Dorothy E. Klotz Chair of Cancer Research and director of the clinical cancer genetics program.

"But our study indicates that genetic damage occurs in stromal tumor cells, and that that damage may play an important role in tumor development."

The findings might help explain why tumors often behave differently, and respond differently to treatment, in people with seemingly identical cancers. The genetic changes in stromal cells also may provide new targets for future anti-cancer drugs and present a new strategy for treating and preventing cancer, says Eng, a recipient of the Doris Duke Distinguished Clinical Scientist Award.

The study is published in the Oct. 15 issue of the journal *Cancer Research*.

How the DNA damage occurs in stromal cells isn't yet known, but it might result from exposure to carcinogens, Eng says. It's also too soon to say how genetic damage to stromal cells might influence tumor growth.

However, stromal cells can produce growth factors and other substances that can influence the behavior of cancer cells. The loss of chromosome regions may result in the loss of genes that control these substances. Stromal cells may also produce factors that limit the growth of nearby cells. Loss of genes for such factors would remove those inhibitors and allow cancer cells to grow.

"But those are only hypotheses," Eng says. "I think that the stroma plays an important role in enabling a tumor to invade neighboring tissue and spread. If that proves to be true, someone may someday develop a drug that targets stroma cells and prevents the cancer from spreading."

Eng and her colleagues analyzed 134 tissue samples from invasive breast tumors. They examined stromal cells known as fibroblasts, the major component of the tumor stroma. Fibroblasts produce the fibrous scaffolding in tumors and normal tissues. (Stromal cells also include immune cells, fat cells and blood vessel cells.)



Charis Eng, M.D., Ph.D.

The investigators used 381 molecular markers scattered throughout the human genome (the entire set of human chromosomes). The markers served as signposts that identify various regions of the 46 human chromosomes.

Among the fibroblasts, the researchers found that 38 markers—or 38 regions of DNA—were lost from 19 different chromosomes. When the researchers then looked for the markers in the cancer cells, they found that 19 regions of DNA were lost from 15 different chromosomes.

This indicates that more DNA regions may be lost in a tumor's stromal cells than in its cancer cells. Furthermore, the losses were not spread randomly over the chromosomes. Instead, they were clustered in specific regions, or hotspots, on chromosomes, suggesting that they may play a role in tumor development.

The researchers are now looking for correlations between the stromal genetic damage seen in patients' tumors and how those tumors behave and respond to therapy.

Other OSU researchers involved in this study were Koichi Fukino, a postdoctoral researcher; Lei Shen, assistant professor in the School of Public Health; Satoshi Matsumoto, postdoctoral researcher; and Carl D. Morrison, assistant professor of pathology.

Funding from the V Foundation and the National Cancer Institute supported this research.

The Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute encompasses six interdisciplinary research programs and more than 200 investigators. The OSU CCC- James is a founding member of the National Comprehensive Cancer Network; its investigators conduct research on the prevention, detection, diagnosis and treatment of cancer, generating over \$95 million annually in external funding; and OSU's James Cancer Hospital is consistently ranked by U.S. News & World Report as one of America's best cancer hospitals.

Margaret Spitz Honored with Distinguished University Chair

The University of Texas Board of Regents has appointed a renowned epidemiologist at The University of Texas M.D. Anderson Cancer Center to a prestigious Distinguished University Chair, only the third such chair awarded at M.D. Anderson.

The first woman in The University of Texas System to receive this distinction, Margaret R. Spitz, M.D., chair of the Department of Epidemiology, was honored with the Olga Keith Wiess Distinguished University Chair for Cancer Research, which carries a \$2.3 million endowment.

The Distinguished University Chair is the highest level of endowed position within the UT System.

Spitz is a nationally recognized epidemiologist and expert on tobacco-related cancers. Her research has focused on reducing overall risk for lung cancer, a disease that remains the leading cancer killer in women and men in the United States.

"I am truly honored to receive this award, and am especially grateful for this opportunity to expand our epidemiological research programs," Spitz says.

Spitz has held the Olga Keith Wiess Chair for Cancer Research at M.D. Anderson since 1998, with the award upgraded to

Distinguished Chair in 2003 and now to Distinguished University Chair.

"Dr. Spitz' contributions throughout her career have had a significant impact on cancer prevention research," says Bernard Levin, M.D., M.D. Anderson's vice president for cancer prevention and population sciences. "She has made remarkable advances in the field of molecular and genetic epidemiology that have greatly enhanced our existing knowledge."



Margaret R. Spitz, M.D.

Her research has contributed to a better understanding of susceptibility to various types of cancer and response to therapy, with the long-term goals of identifying high-risk subgroups who can benefit from intensive cancer screening, creating genetic profiles for use in individualizing therapy and understanding the functional consequences of chemoprevention, chemotherapy or radiotherapy response.

Spitz' current research includes:

- * Finding more predictive genetic markers for lung cancer risk in smokers and those who have never smoked
- * Evaluating genetic markers of nicotine addiction
- * Developing new functional assays of DNA repair capacity to help predict lung cancer risk in current and former smokers
- * Identifying molecular predictors of response to therapy, toxicity and patient survival
- * Developing quantitative methods for accurate risk classification, using combinations of risk factors and genetic variations

While at M.D. Anderson, Spitz has received multiple awards, including the Julie and Ben Rogers Award for Excellence in Cancer Prevention, the Mesa Petroleum Company Professorship in Cancer Prevention, the Faculty Achievement Award in Cancer Prevention and the Texas Business and Professional Women Award.

Additional honors include the Distinguished Achievement Award from the American Society of Preventive Oncology, the Award for Research Excellence in Epidemiology or Prevention from the American Association of Cancer Research and the American Cancer Society, the Rosalind Franklin Science Award for Women in Science from the National Cancer Institute and the Dr. William Cahan Distinguished Professor Award from the Flight Attendants Medical Research Institute.

Spitz joined M.D. Anderson in 1981, becoming the first permanent chair of the Department of Epidemiology in May 1995. She earned her medical degree from the University of Witwatersrand Medical School in Johannesburg, South Africa, and her master's of public health degree from The University of Texas School of Public Health, where she currently holds an academic appointment, as well as at The University of Texas Graduate School of Biomedical Sciences.

For more information, contact Alison Ruffin; Tel: 713.794.1731; Email: aruffin@mdanderson.org