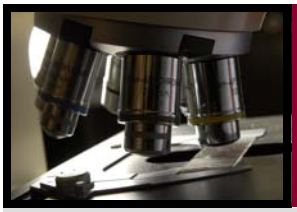

University of Chicago Cancer Research Center
In the News: Our Members in the Media

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 a media story in the next issue, please e-mail us at pbutera@medicine.bsd.uchicago.edu.

OCTOBER 19, 2009

A Lifetime Commitment

The Chicago Tribune
October 4, 2009

Spend 10 minutes with Funmi Olopade and you wonder if there's a single word that might best capture her curious, compassionate nature.

"Genius" worked well when the John D. and Catherine T. MacArthur Foundation honored Olopade with one of its grants in 2005 for her work on the link between genetics and breast cancer, particularly in women of African ancestry.

But even that seems limiting for this world-renowned oncologist and genetics expert.

Her business card from the University of Chicago Medical Center serves as a crowded testament to some of Olopade's accomplishments: "Walter L. Palmer Distinguished Service Professor, Departments of Medicine and Human Genetics, Director of the Center for Clinical Cancer Genetics, and the [former] Director of the Hematology/Oncology Fellowship program."

Oh, and add "Associate Dean for the school's Global Health Initiative," a title conferred on her last year.

If that seems daunting -- a balancing act between Olopade's love of clinical work with patients and her laboratory research -- it is.

But those who know her say the physician-scientist is well-suited for that role, with the energy and smarts to complete almost any task.

"It all comes together for her to be a leader, but more important, an independent forward-thinker. ... If Mars were open, she would have made the trip," said Dr. Harvey Golomb, a Professor of Medicine and Dean of Clinical Affairs at the University of Chicago who interviewed Olopade when she applied for a fellowship there. "And she has a wonderful personality."

"To whom much is given, much is expected," said Olopade, a wife and a mother of three. "Every day I wake up and thank God that I am alive because I can do so much to help people.

"I have patients who call who are in the deep, darkest moment of their lives -- when they've just been told they have breast cancer -- and they come to see me and I say, 'Well, let's put our heads together and see how I can help you.'

Olufunmilayo Olopade, MBBS

"And I am in a place where not only (can I) influence how people are shaping their research, but I can influence how others think about diseases that they don't see."

The office of Dr. Olufunmilayo Olopade -- Funmi, for short -- in the new Gwen and Jules Knapp Center for Biomedical Discovery at the University of Chicago, has a serene, breathtaking view north to the city's skyline.

But the office of this powerhouse is in a state of flux. She moved in less than a month ago. Paintings lean against walls waiting to be hung. A credenza is filled with family photos of her husband, Dr. Christopher "Sola" Olopade, and their children: Feyi (who is working in Nigeria), Dayo (a journalist in Washington, D.C.) and Tobi (a finance student at the Wharton School of the University of Pennsylvania).

Things more pressing than picture-hanging fill her agenda. There is a series of 24 weekly seminars on global health and medical ethics that kicked off this week. There are doctors in Chile and Japan to confer with, patients to see and a graduate student waiting in the lab.

"I said, 'What's going on? It's Friday,' " said Olopade, recalling the conversation with the student. "And she said, 'I have great results that I have to share with you,' and I can't wait to go and listen to her. The great results -- we don't know where they are going to lead, but every time you do an experiment, you try an idea and you follow through with it and something new comes out of it. It's just amazing."

Olopade joined Chika Nwachukwu, 24, in the laboratory, where the student -- who had been working on a gene-and-protein project for a month -- proudly held up a square of film patterned with black marks. "That's a great gel," said Olopade to the beaming Nwachukwu.

"If I can influence one student to decide (to) love medicine, then that is great," she said. "That's a life transformed."

Funmi Falusi was born 52 years ago in Nigeria to the Reverand John Falusi and Dorcas Falusi, the

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A Lifelong Commitment (Continued)

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fifth of their six children. Her parents (her mother, 90, lives in Nigeria; her father died in 1992) nurtured a compassion for others. "We learned early on in life (that) if someone came into the house we had to feed them."

Her father also believed his children should be educated and "get to the best place they can get to," she said. "As a girl growing up in Nigeria in a male-dominated society, any time I was in the car with him he would always say, 'Well, look at that woman driving her own car. You're going to be driving your own car too.' "

She headed to medical school, despite a disdain for biology. "I like to help people and I didn't see the connection between what we were doing in the preclinical work -- which was all science-based and just in the classroom."

Her mother urged her on: "She said, 'Don't worry. When you get to see patients, it will be nice.' And it was true."

At medical school in Nigeria, Olopade -- always a sports enthusiast -- would tag along with one of her brothers to his cricket games, eventually becoming scorer. It was there she met cricket player and fellow medical student Sola Olopade.

Funmi and Sola began dating after medical school, got engaged, then took fellowships in the United States and were married at Chicago's St. James Cathedral, the Episcopal church on Huron Street. "All our children were baptized there. They became our family away from home."

"We are lucky we have common interests," said Sola, a University of Chicago Professor of Medicine and Clinical Director of the Global Health Initiative. "We have a global perspective and we care about people. And we believe strongly in academia."

These days, when they're not globe-trotting to visit their children or spending several weeks working with medical schools in Nigeria, you may find them biking along the lakefront. "I used to play squash with him," Olopade said. "He always wanted to win so I stopped playing with him."

Funmi Olopade arrived in Chicago in 1983 as a resident in internal medicine at what was then Cook County Hospital. It was there she saw many young women with breast cancer. "I kept thinking, 'This is so similar to Nigeria. Why is it so similar to Nigeria? What knowledge would make me really have a better handle on the cancer problem?' "

She began a postdoctoral fellowship at the University of Chicago in 1987.

"When I came to the University of Chicago, Dr. (Janet) Rowley was blazing the trail in terms of her work in cancer genetics. I wanted to be just like her. "

"I went to Dr. Rowley and I (asked) if she could mentor me," said Olopade, who joined the University of Chicago faculty in 1991. "That is when I started doing the genetics research, and it gets you to begin to think of ancestry. ... And I just thought, 'Boy, I wonder what the types of breast cancer in Nigeria were like. I wonder how we could study Nigerian women.' "

It was during a trip to Nigeria that she met a breast surgeon who said doctors there had been collecting information."My colleagues were writing a lot about Ashkenazi Jewish women. We could track some of these mutations dating back centuries. And I just thought we ought to now begin to do the story of the Nigerian breast cancer patients and to see how we can do cross-continent collaboration."

About the same time, Olopade met Dr. Mary-Claire King (credited with discovering the gene that linked heredity to breast cancer risk) at a conference. King told her, "You're a doctor, go back and if you can help us find families so we can really nail this disease down, we can understand it better."

Olopade agreed and suggested developing a clinic in Chicago to collect data on families with cancer histories. In 1992, she became the Founding Director of the University of Chicago Center for Clinical Cancer Genetics. The Global Health Initiative began in 2008 with her appointment.

These days, her focus is on "personalized medicine" with an assist from technology. "We used to think one size fits all," she said. "And now we actually have the technological tools to look at how to develop drugs so we give the right drug to the right patient for the right ailment."

And that, she believes, dovetails nicely with her latest role."There are some things that we do exceedingly well in this country, some things other people do better than we do, and so we learn by opening our minds and our eyes. ... With technology, the world is flat. Today I have talked to people in Tanzania. I can talk to collaborators in U.K. and Australia. We can all share best practices and learn from one another. That's really what medicine is now and that's what's really exciting."

Study Probes the Link Between Cancer & Stress

The Globe and Mail
September 30, 2009

The field of epigenetics is seeking new answers to the question: What role does stress play in the development of cancer?

Can stress cause cancer, or even hasten a patient's death? It's a daunting, emotionally charged question with no simple answers, but it represents a growing field of research that scientists hope could eventually lead to breakthroughs in cancer treatment.

The premise driving the theory is that stress has been found to weaken the body's immune response and cause some physiological changes, such as the secretion of certain hormones, that could contribute to the development of cancer.

Traditionally, much of the study in this field has focused on the effects of stress on the immune system. But now, attention is shifting to the relationship between stress and gene function, an area many scientists believe is the key to unraveling this mystery.

Scientists have discovered that high-stress situations can cause certain genes to become activated while others, such as those responsible for suppressing the growth of tumors, may be turned off, changes that could have serious implications in the

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Study Probes the Link Between Cancer & Stress

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development of cancer. But a major challenge is understanding how this complex genetic relationship works and what causes changes to occur. This research is part of epigenetics, a promising field of science that focuses on how certain factors can cause genes to be turned on or off.

New clues in this complicated puzzle emerged this week when researchers revealed a study that showed mice living in stressful conditions developed much larger cancerous tumors than those living in relatively stable conditions.

In the study, published in the journal Cancer Prevention Research, scientists used a group of female mice predisposed to developing mammary gland cancer to study the possible role played by stress. They put some of the mice in social isolation, keeping them alone in cages shortly after they were weaned from their mothers, while other mice were caged in groups. For mice, social animals that usually live in groups of three or four in the wild, isolation can trigger a significant amount of stress.

Researchers, led by Suzanne Conzen, Associate Professor of Medicine and the Ben May Department for Cancer Research at the University of Chicago, found that the mice kept in isolation developed more cancer and had larger tumors than the mice that lived in groups.

They also found that socially isolated mice behaved differently than mice kept in groups, becoming less exploratory, and released significantly more cortisol, often referred to as the "stress hormone" because it is secreted in response to agitation or anxiety. Cortisol can also alter the body's genetic pathways and disrupt the ability of genes that suppress tumor growth to function properly.

The study provides some of the strongest evidence to date that an individual's stress level may be linked to the progression of cancer. But the quest to understand why – and, perhaps more importantly, how those factors might be used to help prevent or treat cancer – is still in its infancy.

Part of the reason is that the scientific community has yet to reach consensus on whether an individual's mental state has a real, measurable impact on susceptibility to developing cancer or the ability to fight it off. While some research has shown that cancer patients who receive extensive therapy and support live longer than those who don't, other studies have been inconclusive or shown no difference. In fact, a study published last month in the journal Brain, Behavior, and Immunity found that short-term stress stopped the development of cancer in mice.

"This is an area that has a long way to go in terms of understanding how these factors play out in humans," said Caryn Lerman, a Professor of Psychiatry and Scientific Director of the Abramson Cancer Center at the University of Pennsylvania.

Confounding the issue further is that people respond to stress in different ways and have varying thresholds for coping with difficult situations. As a result, the potential ability of stress to affect the development or progression of cancer may change person to person, making it that much more challenging to understand. Instead of framing the discussion around cause and effect, one scientist who has studied this area for years said it's more accurate to think of the relationship between stress and cancer as one of potential risk.

"Stress doesn't give you cancer, but it is a risk factor like genetic differences, and environmental carcinogens," said David Spiegel, Associate Chair of the Department of Psychiatry and Behavioral Sciences at Stanford University School of Medicine. "There are a whole bunch of risk factors. Not everybody that smokes tobacco gets lung cancer."

A Cancerous Melody

The Scientist
September 25, 2009

A project at Harvard Medical School aims to bring music to medicine in a way that goes beyond setting the mood in the waiting room. Gene transcription and translation are anything but simple. But by combining modern statistics with the sounds of a sweet melody, bioinformatician Gil Alterovitz may make interpreting these complex phenomena and diagnosing the diseases that result from abnormalities in gene expression much more manageable.

"I think it's brilliant that Gil is using a completely different channel for communicating complex genomic information," Latin and ballroom DJ Taro Muso writes in an email to *The Scientist*. "I've always wondered why doctors don't seem to use their ears beyond listening for bodily sounds."

"It's deceptively simple," says bioinformatician Yves Lussier, MD, of the University of Chicago. "It was conceptually challenging to come up with it, but once we know of it, it's obvious we should have tried that in addition to visualization techniques we have been using."

By boiling down gene expression data to just a few components -- variables that condense one or more parameters of data -- and assigning each of those components a different note and musical instrument, Alterovitz and his colleagues are literally making genetics musical.

The team carefully chooses the notes such that normal gene expression patterns sound pleasantly in tune, while abnormal data yield discordant sounds. "When you hear inharmonious music it kind of catches your attention," Alterovitz says, "and that would be a sign of a pathological problem."

Yves Lussier, MD

"Even amateur musicians can tell the difference between various chords," Muso agrees, "so there is a

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A Cancerous Melody (Continued)

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definite potential for motivated biologists to use harmony as a screening method."

Alterovitz got the idea ten years ago while doing his PhD at MIT. When he donned his scrubs and joined surgeons in the operating room as part of his graduate research project, he was distracted by the numerous monitors measuring nearly two dozen biological signals. Sometimes an alarm would go off, he recalls, but most of the time it wasn't relevant, and they were simply turned off and ignored.

"Wouldn't it be useful if we somehow integrated those variables so that we could present something that was not just a binary alarm but holistic information about the whole system?"

With this goal in mind, Alterovitz set out to make a computer program to do just that. He and his colleagues worked with preexisting gene expression data from a colon cancer study and reduced more than 3,000 genes to just four components. "There's a lot of redundancy," Alterovitz explains. "Genes moving together or opposite each other in a predictable way" can be lumped into just one variable without losing much, if any, detail about the system.

Assigning notes that form harmonious chords to the data, Alterovitz and his colleagues created a pleasant-sounding 'norm.' When things go awry, such as in the case of p53-null mutant colon cancer cells under inflammatory stress conditions, gene expression varies slightly, and inharmonious chord progressions result. Listening to the results -- a symphony of electronic instruments -- tells the story.

"One application I could see in the oncology world is to look for the abnormal cells in fluid," says infectious disease specialist Micah Jacobs, who runs a private practice in Pittsburgh. "Instead of relying on simple visualization of the cells, you could listen and you could hear the abnormal cell in some way."

Alterovitz notes that this type of analysis may have applications outside of medicine. He says that the US Navy contacted him about using his method to monitor sonar signals. The communications company Verizon also got in touch with Alterovitz looking to keep track of their complicated networks. Even pilots, who must observe the numerous signals beeping and flashing in the cockpit, could benefit from this technology, Alterovitz says.

Scorpion Venom & Brain Tumors

WGNNews—Medical Watch
September 28, 2009

Scorpion venom saving lives. A local hospital was testing the theory and surprised by the positive results, until the money for the study ran out.

Most people would be afraid of this -- the death stalker scorpion. Now imagine doctors telling you they wanted to inject its venom into your veins.

Donna Van Ryn (DVR), Brain Tumor Patient: “I didn't really want to do that because I was very afraid of something like that."

But after mutliple surgeries, multiple chemotherapies and still growing cancer in her brain, Donna Van Ryn knew she had no other option.

DVR: "I've gone through everything they had to offer so far. And none of it seemed to last very long."

So at the request of her doctors, Donna joined a clinical trial, using a drug derived from scorpion venom attached to radiation to target cancer.

Dr. Steven Chmura, Radiation Oncologist, University of Chicago Medical Center: "As opposed to our normal types of radiation therapy that has to go through the skin, the hair, the brain everything else, this is going directly to the sight of the tumor and giving a very, very high dose. It binds to glioma cells or brain tumor cells."

Meaning the radiation attacks individual cancer cells while sparing the rest of the body.

"We are able to use this carrier agent almost like a smart bomb type of agent to actually bring a piece of radiation right to each and every tumor cell."

But it is toxic for patients. Donna couldn't walk or talk. Therapy and determination brought her back.

DVR: "After you come out of it, it can be very frightening because it's almost like starting all over again."

And scans show she has the chance to do just that. The cancer that was growing has now stopped.

Dr. Rimas Lukas, Neuro-oncologist, University of Chicago Medical Center: "Here we have on the left a scan from a number of months ago and a more recent scan here which looks relatively unchanged."

It appears the death stalker venom has extended Donna's life.

DVR: "I'm feeling good most of the time. It's exciting!"

What is frustrating is doctors don't know exactly why the scorpion venom worked in Donna not just to deliver radiation but also to fight the cancer itself. It didn't work as well for others and now they want to do more research, but the funding was cut off.

EDITOR'S NOTES:

This issue of "In the News" highlights the contributions our members are making in all phases of cancer research and outreach.

On pages 1 and 2, Olufunmilayo, MBBS, Professor of Medicine and Human Genetics, Director of the Cancer Risk Clinic, is featured in an article detailing her distinguished career.

On pages 2-3, Suzanne Conzen, MD, Associate Professor of Medicine, discusses her research studying whether mice kept in isolation develop larger tumors than mice that live in groups.

On pages 3-4, Yves Lussier, MD, Associate Professor of Medicine, Associate Director for Informatics at the UCCRC, is quoted in a news story covering the use of music to communicate genetic information.

On page 4, Steven Chmura, MD, PhD, Assistant Professor of Radiation and Cellular Oncology, and Rimas Lukas, MD, Instructor of Neurology, discuss the innovative clinical trial involving scorpion venom that was recently used for a brain tumor patient.

On page 5, Nora Jaskowiak, MD, Associate Professor of Surgery, discusses inflammatory breast cancer and its symptoms. Also on page 5, Shohei Koide, PhD, Associate Professor in the Department of Biochemistry and Molecular Biology, is a recipient of the prestigious NIH Director's High-Risk Research Awards.

Hard-to-Detect Cancer Moves Fast

Chicago Sun Times
September 29, 2009

Like many women, Jennifer Murphy didn't know what inflammatory breast cancer was until she was diagnosed with it in 2006.

The 48-year-old mother of three had started noticing changes in the appearance and feel of her breasts that she at first thought were because she had stopped nursing her last child. But a mammogram and tests confirmed that she had advanced-stage cancer.

"The thing that was so shocking to me was that there was no tumor in the mammogram. All it showed was thickened skin," said Murphy of Park Ridge. "I was starting chemotherapy within a week of having the tests." Stories like Murphy's are common among women with inflammatory breast cancer, a rare but more aggressive type of breast cancer that affects lymph vessels in the skin of the breast. Unlike other forms of breast cancer, inflammatory breast cancer rarely causes lumps to form in the breasts, and it may be harder to detect on a mammogram.

Nora Jaskowiak, MD, Surgical Director of the University of Chicago Breast Center, said inflammatory breast cancer isn't "on people's radar," though it has a lower survival rate than other breast cancers. "I don't think it's anything most women know about," she said.

Symptoms of the disease, which affects about 1 percent to 5 percent of breast cancer patients, include swelling, redness, nipple retraction or discharge and breasts feeling unusually warm to the touch. Inflammatory breast cancer tends to occur more frequently in younger women and in African Americans. The symptoms are similar to those of mastitis, a breast infection that can be treated with antibiotics. But "the people who get mastitis are nursing women. Any other breast swelling than that, and you need to see your doctor," Jaskowiak said.

Treatment for inflammatory breast cancer usually involves immediate chemotherapy followed by surgery and/or radiation.

Because symptoms of the disease can develop in a matter of days, Murphy, whose cancer is in remission, urged women not to ignore unusual changes in their breasts.

NIH to Grant $350M for 2009 Research Grants

GenomeWeb
September 24, 2009

The National Institutes of Health recently announced that it is awarding $348 million for bold research, visionary scientists, and aggressive young researchers through the 2009 NIH Director's High-Risk Research Awards program, including a number of grants that will fund a wide range of proteomics, genomics, and other studies.

NIH expects these awards in 2009 will include $30 million to fund 42 Director's Transformative (T – R01) awards, $13.5 million to 18 Pioneer Award winners, and roughly $131 million for 55 New Innovator awards for early stage investigators, NIH said. The full $348 million is an estimate of how much NIH will grant to these awardees over the next five years.

"The appeal of the Pioneer, New Innovator, and now the T-R01 programs, is that investigators are encouraged to challenge the status quo with innovative ideas, while being given the necessary resources to test them," NIH Director Francis Collins said in a statement. "The fact that we continue to receive such strong proposals for funding through the programs reflects the wealth of creative ideas in science today."

The funding for the New Innovator grants for 2009 includes $23 million in funding through the American Recovery and Reinvestment Act.

The Transformative, New Innovator, and Pioneer awards will support a wide array of proteomics and genomics research efforts, such as:

• Susan Rosenberg at Baylor College of Medicine will use a Pioneer Award to develop methods for studying how DNA in living cells becomes damaged, leading to genomic instability and cancer.

• Julio Camarero, at the University of Southern California School of Pharmacy, will use a T-R01 award to study a new approach for screening protein capture reagents to enable rapid production of cyclotide-based microarrays for proteomics studies.

• Michael Czech of the University of Massachusetts Medical School will use funding from a T-R01 grant to develop a method of oral RNAi delivery to macrophages in living animals and using gene silencing for potentially treating diabetes, atherosclosis, arthritis, and other diseases.

• Joshua Dubnau at Cold Spring Harbor Laboratory will use a T-R01 grant to study genomes of *Drosophila* in order to understand protein synthesis for genes that may be linked to a defect that could be responsible for Fragile X syndrome.

• Gábor Balázsi at the University of Texas MD Anderson Cancer Center will use a New Innovator's award to study how certain noisy gene expression deviants connect to genetic evolution.

• Shohei Koide at the University of Chicago will use a T-R01 award to fund studies of directed protein-capture reagents that will establish a new approach to reagent detection.

• Sanford Markowitz at Case Western Reserve University School of Medicine will use a T-R01 grant for studies aimed at identifying inborn genetic susceptibility to develop cancer metastasis.

• Stanford University's Chang-Zheng Chen will use a Pioneer Award to research mechanisms regulating microRNA gene function in vertebrate immune systems.

• Nikos Chronis of the University of Michigan will use a New Innovator award to develop a biochip for a point-of-care HIV/AIDS diagnostic for use in the developing world.

"Since no budget cap is imposed and preliminary results are not required, scientists are free to propose new, bold ideas that may require significant resources to pursue," the NIH said in its statement announcing the awards. "They are also given the flexibility to work in large, complex teams if the complexity of the research problem demands it."