

# 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](mailto:pbutera@medicine.bsd.uchicago.edu).

SEPTEMBER 30, 2009

## For Profit, Industry Seeks Cancer Drugs



*Sandy Huffaker, New York Times*

### **The New York Times** **September 1, 2009**

Pfizer's fortunes in the past were built on cardiovascular drugs, like cholesterol buster Lipitor and the blood pressure pill Norvasc.

But the future of Pfizer, the world's largest pharmaceutical company, may rest in a cluster of buildings on a bluff not far from the Pacific Ocean. It is here that Pfizer has amassed about 1,000 researchers for an all-out effort to develop drugs for cancer, a disease the company once largely ignored.

Virtually every large pharmaceutical company seems to have discovered cancer, and a substantial portion of the smaller biotechnology companies are focused on it as well. Together, the companies are pouring billions of dollars into developing cancer drugs.

Two industry trends are driving the push. Recent scientific discoveries have suggested new targets for cancer drug researchers to attack. And as

drug companies see profits beginning to wane from mainstays like Lipitor, the high prices that cancer drugs can command have become an irresistible lure.

About 860 cancer drugs are being tested in clinical trials, according to the pharmaceutical industry's main trade group. That is more than twice the number of experimental drugs for heart disease and stroke combined, nearly twice as many as for AIDS and all other infectious diseases combined, and nearly twice as many as for Alzheimer's and all other neurological diseases combined.

But for all the industry's spending and effort, only a trickle of new cancer drugs make it to market. Last year there were two, and this year there has been only one.

And even some of those drugs offer only a few months at most of extra life or tumor stabilization despite prices that often reach thousands of dollars a month. The drug Tarceva, which costs about \$3,500 a month, was approved as a treatment for pan-

creatic cancer because it improved survival by 12 days.

The battle to treat cancer has become, as a commentary in a leading journal put it, a "grinding war of the trenches."

Why? Experts say the same factors that attract drug companies to the cancer business help explain the slow progress.

One reason is scientific. Studies are rapidly revealing the genetic changes in cells that cause cancer and spur its growth. That is providing drug companies with dozens of molecules, or "targets," that drugs could block.

But those same studies have shown that cancer is devilishly complicated. There are so many aberrant molecules in a tumor that blocking just one or two is like trying to stop all traffic in Manhattan with a roadblock at a single intersection.

Tumor cells, like bacteria, can develop resistance to drugs. Some experts believe that drugs that kill most tumor cells do not affect cancer stem cells, which can regenerate the tumor. And even two people with breast cancer, or two people with lung cancer, might have two very different diseases on the molecular level, so a drug that works for one might not work for the other.

"Cancer is not a single disease," said Robert A. Weinberg, a cancer biologist at the Whitehead Institute and the Massachusetts Institute of Technology. "It's really dozens, arguably hundreds of diseases."

The other reason for the drug makers' interest is financial. Patients are often desperate, and insurers risk outrage by denying payments for a cancer drug, even if the odds say it will have

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# For Profit, Industry Seeks Cancer Drugs (Con't)

little benefit. That has allowed pharmaceutical companies to charge thousands of dollars a month for cancer medicines. Such prices can make drugs for even rare cancers, or drugs that do not work very well, into big moneymakers.

Take Erbitux, developed by ImClone Systems, which costs \$10,000 a month. A study in Canada showed that as a last-ditch treatment for colorectal cancer, Erbitux lengthened lives by an average of about one and a half months compared with not treating the cancer at all. Using the price of the drug in the United States and the average length of treatment, the extra cost per patient was about \$50,000.

Erbitux, which is also approved to treat head and neck cancers, recorded global sales of \$1.6 billion last year, higher than all but about 70 other drugs. Last year, as part of the industry scramble into cancer drugs, Eli Lilly & Company outbid Bristol-Myers Squibb to acquire ImClone for \$6.5 billion.

In 1998, there were only 12 cancer drugs on the list of the world's 200 medicines with the highest sales, compiled by the trade magazine Med Ad News. Taxol, No. 21, was the only cancer drug among the 30 drugs with sales of at least \$1 billion.

The same list for last year contained 23 cancer drugs among the top 200 — and three in the top 10. Of the 126 drugs with \$1 billion in sales, 20 were for cancer.

Cancer drugs have been the biggest category of drugs in terms of sales worldwide since 2006 and in the United States since 2008, according to the market researcher IMS Health. Such money attracts companies.

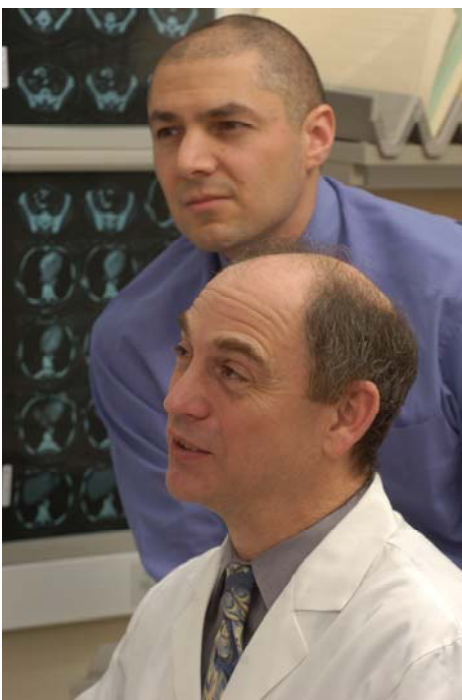
"Cancer is such an emotional issue that the free market doesn't work like it does for bicycle wheels and umbrellas," said Robert L. Erwin, a biotechnology industry executive who heads the Marti Nelson Cancer Foundation, a patient advocacy group. "As long as the health care system will pay the price, the money will flow in that direction."

But Mr. Erwin and some other experts say that is not always a good thing for patients because it can set the bar too low for drug companies.

"As long as the marketplace does not distinguish between modestly

effective drugs and dramatically effective drugs, there won't be an incentive to shift resources to a greater emphasis on a larger benefit," said Dr. Neal J. Meropol, an Oncologist at the University Hospitals Case Medical Center in Cleveland who has been studying drug prices.

Many executives dispute this, saying they would produce drugs offering bigger gains if they knew how. But they must balance their portfolio of ex-



**Mark Ratain, MD**

perimental drugs between long shots and some drugs that have a better chance of making it to market and sustaining the enterprise.

"If you always swing for home runs, you strike out a lot," said George A. Scangos, Chief Executive of Exelixis, a biotechnology company with 11 cancer drugs in clinical trials. "It's not the companies' profit motives," he said. "It's largely the difficulty of hitting home runs."

With health care costs rising, there is new pressure on companies to be more selective in drugs they develop. Some experts now talk about "financial toxicity" as a side effect of cancer drug treatment, along with nausea and hair loss.

"A question is how the system can tolerate 400 new drugs on the market, all at the same price" of \$50,000 a year, said Dr. Lee Newcomer, Senior Vice President for Oncology at United Healthcare, a big in-

surer. Such cost pressures, and the fact that only a handful of cancer drugs get to market each year, mean the big investments now being made into cancer drugs are likely to turn sour for many companies.

"It's the biggest bubble you've ever seen," said Dr. Mark Ratain, MD, an Oncologist at the University of Chicago. But Pfizer is counting on cancer to help save the company. It hopes to reach \$11 billion in sales of cancer drugs by 2018. That would be more than four times the category's sales last year of \$2.5 billion, which represented only 5 percent of Pfizer's revenue.

Cancer was once unattractive for big pharmaceutical companies like Pfizer. There were relatively few patients with any one type of cancer, and they died fairly quickly. By contrast, there were millions of patients with chronic diseases like hypertension who would take drugs for life.

Indeed, the three main cancer drugs Pfizer now sells came to it with its 2003 acquisition of a rival, Pharmacia, a deal done mainly to acquire the arthritis drug Celebrex.

But there are now many good cardiovascular drugs. Lipitor, the world's best-selling drug, will lose patent protection in 2011, and Pfizer failed to develop a successor.

So Pfizer is scaling back cardiovascular research and has made cancer drugs one of its six focus areas. About 20 percent of Pfizer's more than \$7 billion in research and development spending is on cancer, and 22 of the roughly 100 drugs in clinical trials are cancer drugs.

"I've taken a lot of personal interest in this business unit," said Jeffrey B. Kindler, Pfizer's Chief Executive. "We think we are positioned to be a top leader in oncology."

Cancer research is concentrated here in San Diego, in a cluster of buildings once owned by one of the many biotechnology companies in the region. Pfizer has tried to retain some of the looser culture of entrepreneurial start-ups, like Friday afternoon beer parties. The head of the site, Catherine Mackey, a transplant from Pfizer's laboratories in Connecticut, has become an avid early-morning surfer.

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# For Profit, Industry Seeks Cancer Drugs (Con't)

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The clinical trials for cancer are being overseen by Dr. Mace Rothenberg, an Oncologist recruited this year from Vanderbilt University. He hopes Pfizer can develop those home-run drugs. "Having treated patients for 20 years," Dr. Rothenberg said, "I know their needs are not for singles."

The big thrust in cancer drug development for the last few years has been so-called targeted therapies. These drugs aim, so far with modest success, to block aberrant molecules in tumor cells while leaving normal cells unscathed.

But even most targeted therapies have limited impact. One reason

is that most tumors are fueled by numerous, often redundant, genetic anomalies. That means that drugs with different targets need to be used in combination. But combinations increase both the costs and side effects of therapy. And it is difficult to test two experimental drugs in combination because the regulatory system is geared to assessing a single drug at a time.

Another reason is that tumors differ among people. Dr. Bert Vogelstein, a Cancer Geneticist at Johns Hopkins, said a typical tumor might have 50 to 100 genetic mutations. But two patients with the same type of cancer might have only five mutations in common.

So even though a drug might work well for patients whose tumors have a particular mutation, when the drug is used for a broader population, it shows only a small effect.

One solution is to try to determine which patients should get which drug based on the genetic profile of the tumor.

Pfizer is moving in that direction. It plans soon to start a late-stage clinical trial of a drug for lung cancer. But the only patients in the trial will be from the 5 percent or so of lung cancer patients with a mutation in a gene called ALK.



# Light Activated Titanium Dioxide Nanoparticles Kill Brain Cancer Cells On Contact

## MedGadget

August 27, 2009

Scientists from the U.S. Department of Energy's (DOE) Argonne National Laboratory and the University of Chicago's Brain Tumor Center have developed a way to target brain cancer cells using inorganic titanium dioxide nanoparticles bonded to soft biological material.

Thousands of people die from malignant brain tumors every year, and the tumors are resistant to conventional therapies. This nano-bio technology may eventually provide an alternative form of therapy that targets only cancer cells and does not affect normal living tissue.

"It is a real example of how nano and biological interfacing can be used for biomedical application," said scientist Elena Rozhkova with Argonne's Center for Nanoscale Materials. "We chose brain cancer because of its difficulty in treatment and its unique receptors."

This new therapy relies on a two-pronged approach. Titanium dioxide is a versatile photoreactive nanomaterial that can be bonded with biomolecules. When linked to an antibody, nanoparticles recognize and bind specifically to cancer cells. Focused visible light is shined onto the affected region, and the localized titanium dioxide reacts to the light by creating free oxygen radicals that interact with the mitochondria in the cancer

cells. Mitochondria act as cellular energy plants, and when free radicals interfere with their biochemical pathways, mitochondria receive a signal to start cell death.

"The significance of this work lies in our ability to effectively target nanoparticles to specific cell surface receptors expressed on brain cancer cells," said Dr. Maciej S. Lesniak, Director of Neurosurgical Oncology at the University of Chicago Brain Tumor Center. "In so doing, we have overcome a major limitation involving the application of nanoparticles in medicine; namely, the potential of these agents to distribute throughout the body. We are now in a position to develop this exciting technology in pre-clinical models of brain tumors, with the hope of one day employing this new technology in patients."

X-ray fluorescence microscopy done at Argonne's Advanced Photon Source also showed that the tumors' invadopodia, actin-rich micron scale protrusions that allow the cancer to invade surrounding healthy cells, can be attacked by the titanium dioxide.

So far, tests have been done only on cells in a laboratory setting, but animal testing is planned for the next phase. Results show an almost 100 percent cancer cell toxicity rate after six hours of illumination, and 80 percent after 48 hours following 5 minutes' exposure to focused light.

Also, since the antibody only targets the cancer cells, surrounding healthy cells are not affected—unlike other cancer treatments such as chemotherapy and radiotherapy.

Rozhkova said that a proof of concept is demonstrated; other cancers could be treated as well, using different targeting molecules, but research is in the early stages.

Funding for this research was through the Department of Energy's Office of Basic Energy Sciences, National Cancer Institute, National Institute of Neurological Disorders and Stroke, Alliance for Cancer Gene Therapy, American Cancer Society and Brain Research Foundation.

The U.S. Department of Energy's Argonne National Laboratory seeks solutions to pressing national problems in science and technology. The nation's first national laboratory, Argonne conducts leading-edge basic and applied scientific research in virtually every scientific discipline. Argonne researchers work closely with researchers from hundreds of companies, universities, and federal, state and municipal agencies to help them solve their specific problems, advance America's scientific leadership and prepare the nation for a better future. With employees from more than 60 nations, Argonne is managed by University of Chicago Argonne, LLC for the U.S. Department of Energy's Office of Science.



# International Leader in Breast Cancer Research Discusses Various Forms of Cancer



**Olufunmilayo Olopade, MBBS, FACP**

**PBS**

**Aired July 10, 2009**

**Tavis Smiley:** Last month, my longtime producer and dear friend, Sheryl Flowers, lost her two-year battle with breast cancer at the young age of 42. She was afflicted with a strain of the disease known as triple negative which disproportionately affects African American women for some reason. Dr. Olufunmilayo Olopade specializes in triple negative breast cancer at the University of Chicago Medical Center. She joins us tonight from Chicago. Dr. Olopade, nice to have you on this program.

**Dr. Olufunmilayo Olopade:** Thanks for having me.

**Tavis:** Let me start by asking about your research, the work that you do specifically, and then I want to talk more expressly about triple negative. But tell me about your work with regard to cancer, and breast cancer specifically.

**Dr. Olopade:** Well, Tavis, I am a Medical Oncologist and treat women with breast cancer. But about 15 years ago, it became clear to me that we needed to do more work to prevent breast cancer, so I developed a cancer risk assessment program where we wanted to have women come in and talk to us about their family history of

breast cancer or any other risk factors that they may have so that we can help them develop strategies to reduce their risk of dying from breast cancer.

My interest is in really trying to understand whether women have inherited genes that we can test for and, by testing for those genes, whether we can identify those at the highest risk.

Over the course of the 15 years, we've come to realize that there are in fact some genes that predispose to breast cancer, so we studied families, and I can tell you that, when we've identified women with BRCA1 or BRCA2 mutations and when they have come in to do preventative strategies to prevent dying from breast cancer, we've seen great successes.

But what's been frustrating is when we see young women like Sheryl who, at 40, really didn't have the strong family history, didn't have any reason to get breast cancer and come with a deadly form of the disease, it's very, very disappointing to us. That's really what got us to begin to focus on whether there are differences between populations in terms of the types of breast cancer that they get.

Because we work on the south side of Chicago, we see a diverse population of women and one of the things that we found out was that Black women were getting this type of triple negative aggressive breast cancer much more commonly than their white counterparts.

**Tavis:** Why is that? Do you know as yet?

**Dr. Olopade:** Well, that's really the million dollar question. You know, the last conversation I had with Sheryl was that, you know, she was an educated, well-trained, very knowledgeable woman and she developed triple negative breast cancer which was aggressive.

Prior to the time we started doing this work, there always used to be thoughts that the reason why Black women were dying disproportionately was because they had no insurance and they had no access. But our work has found is that it's really a collision of, you know, different things. A cancer that grows very fast and then

young women who aren't expected to get breast cancer because, for the longest time, the face of breast cancer that we've had was an older white woman with breast cancer.

Really when we started studying different populations, when Black women started coming forward to participate in the research, then we began to identify that breast cancer is no one disease and it doesn't affect women the same way. So there's a lot of work we have to do. We don't know why.

**Tavis:** What's your sense of the kind of energy, the kind of effort, the kind of resources that are being put in to broaden this field of study? I say broaden because, to your earlier point, not unlike with the case years ago with HIV/AIDS. They thought it was a gay, white male disease and all the money, all the research, all the attention went that way.

We now know differently. HIV/AIDS is killing a whole different kind of people, a whole different population of this country. So what's your sense of how we're doing now expanding the

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## **EDITOR'S NOTES:**

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

*On pages 1, and 2, Mark Ratain, MD, Leon O. Jacobson Professor of Medicine, Chairman of the Committee on Clinical Pharmacology and Pharmacogenetics, and Associate Director for Clinical Sciences at the Cancer Research Center, is quoted in an article about cancer drug investments.*

*On page 3, the University of Chicago Brain Tumor Center is mentioned in an article that discusses its collaboration with Argonne National Laboratory regarding a new treatment for brain cancer.*

*On page 4, Olufunmilayo Olopade, MBBS, FACP, and 2005 MacArthur Foundation Genius Grant winner, is featured in an article that discusses her work with triple negative breast cancer. On page 5, Dr. Olopade is featured in an article discussing her life and work.*

# International Leader in Breast Cancer (Con't)

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conversation about breast cancer beyond a particular group to include in fact women of color?

**Dr. Olopade:** Well, the fact that I'm on your show is a big step forward and that's really why I wanted to come because we need to get the word out there. We need to really talk about the successes we've had in terms of treating breast cancer. It really is not a death sentence anymore, but we still have challenges, challenges like the type of breast cancer that Sheryl had which grows fast and can rapidly become aggressive.

Because it affects Black women in a way that is different, I think that we need to get the word out there. You know, when a young Black woman feels a lump, instead of blowing it off and saying, "Well, you know, I'm too young to get breast cancer," they need to be running to find a doctor.

You know, it's not even just Black women who develop triple negative breast cancer. Any woman can develop this type of breast cancer and

that's why we're emphasizing that we've all got to come together. We can't say that breast cancer is curable now and so let's not worry about it.

We have to find out what the different types of breast cancers are, how it affects people from different race ethnic backgrounds and we have to get Black women to become a little bit more engaged in the research process so that we can study more of them. By studying more of them, they will become part of the solution.

**Tavis:** What's your sense of how this conversation fits into the larger conversation about healthcare for all Americans?


**Dr. Olopade:** Well, it's really very important to me because I work on the south side of Chicago and it's really amazing how many women without insurance come through our emergency room to be treated for breast cancer and often it's too late by the time they show up in the emergency room.

If family care doctors know about breast cancer, if women who are high-risk can get access to a fam-

ily care doctor or a family doctor who will know about their family history - I have women whose mother died of breast cancer at 34 and they just sit there waiting to get breast cancer because they have no insurance. They just graduated out of college.

So I think it's really important to begin to get everyone to have access to family care. We as the oncologists need to work with family care doctors to train them on how to identify individuals who are high-risk because breast cancer, if you actually catch it early, is still curable.

**Tavis:** She's one of the leading experts in the country on breast cancer focusing specifically these days on what killed our dear friend, Sheryl Flowers, triple negative breast cancer. She's connected with the University of Chicago Medical Center. Her name, Dr. Olufunmilayo Olopade. Dr. Olopade, nice to have you on the program. Thanks for all your research and thanks for sharing your insight on this program tonight.

**Dr. Olopade:** Thank you. 

# MacArthur Grant Winner: Helps Save Lives

**CBS Chicago**

**September 22, 2009**

It is one of the most prestigious and lucrative honors for excellence. On Tuesday, it was announced 24 people have won the so-called 'Genius Grants' from the Chicago-based MacArthur Foundation.

They each get a half million dollars to spend any way they would like. Among them, a popular Engineering Professor at the University of Illinois, Urbana-Champaign, John Rogers.

Four years ago, a University of Chicago Physician and Professor won a MacArthur grant for her work in breast cancer research. CBS 2's Jim Williams talked to Dr. Funmi Olopade.

Dr. Olopade's life and work have changed dramatically since she received the big award. She tells this year's MacArthur grant winners to get ready, life is about to change."

"They can kiss anonymity goodbye," she says. Four years ago,

the physician, Professor and Researcher won the MacArthur half million dollar genius grant and received all the publicity that comes with it.

"It does have tremendous cache. Even your children now start teasing you," Dr. Olopade said. "Anything you do now is looked upon in the context of being a genius."

All kidding aside, the MacArthur grant has had an enormous impact on Dr. Olopade's groundbreaking work in breast cancer research.

"Because of the grant, I was able to get more grants," she said. The attention from the MacArthur Foundation helped generate millions of dollars in new grant money for Dr. Olopade to study the most aggressive forms of breast cancer and why some women get it.

"I have been able to get money from the National Institute of Health. I've been able to get other foundations to come looking for me, asking me to do work with them be-

cause they know that we're going to put the money to good use and we're going to really make a difference," Dr. Olopade said.

She said it's fair to say that as a result of the MacArthur grant, lives will be saved. Recipients of the Genius Grants are free to spend the half million dollars in any way they would like. Dr. Olopade is now able to see her mother in her native Nigeria much more frequently.

"That's precious, because my mother is going to be 90, and so I can just get on a plane and go see her whenever I can," she said.

Dr. Olopade also admits getting a new kitchen.

She says the biggest challenge since she won the Genius Grant is learning how to say "no." She gets more invitations to events than she can attend.

