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Research Community Mourns Death, Celebrates Life of Judah Folkman

One of the most highly praised and respected cancer researchers, Dr. Judah Folkman of Harvard University and Children's Hospital Boston, died last week from a heart attack. He was 74.

In the wake of his unexpected death, leading researchers praised his groundbreaking work on the role of angiogenesis in tumor development, calling him a pioneer who almost single-handedly altered how cancer is viewed and treated.

"Dr. Folkman championed and led the field of angiogenesis," said NCI Director Dr. John E. Niederhuber. "His dedicated leadership has created the ultimate legacy: a legion of students and fellows, many of whom are now important scientists and scientific leaders in their own right."

Dr. Folkman first came to national prominence in 1971, when he published a paper in *The New England Journal of Medicine* in which he proposed that tumors required a dedicated blood supply to form and grow, and that they orchestrated the formation of new blood vessels for this express purpose. Disrupting this

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Cancer Research Highlights

Two Studies Identify Drivers of Metastases

A study published in the January 10 *Nature* has pinpointed several microRNAs (miRNAs)—tiny RNA strands that regulate gene expression—that help suppress breast cancer metastases.

Researchers from Memorial Sloan-Kettering Cancer Center examined miRNAs in breast cancer cell lines that were highly metastatic to bone and lung compared with control breast cancer cell lines. They chose to focus further studies on the six miRNAs whose expression was most decreased in the metastatic cells.

Restoring the function of three of these miRNAs—called miR-335, miR-206, and miR-126—by gene therapy significantly reduced the

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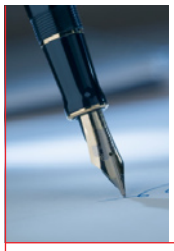

Guest

Director's Update

Addressing Cancer Health Disparities with Science and Hope

Yesterday marked the national observance of Dr. Martin Luther King, Jr.'s birthday, and with it an opportunity to reflect on his work to raise awareness of inequality and injustice in our country.

Even now, almost 40 years after his untimely death, the impact of Dr. King's work is still being felt, inspiring research that has given us a better understanding of the disparities that still exist in this country and programs at all levels that can address them. One example is NCI's Center to Reduce Cancer Health Disparities (CRCHD), formed in 2001 with the sole purpose of better understanding and eliminating disparities in cancer through research-based and diversity training programs around the country, and which I have been proud to be part of since 2005.

We are showing tangible signs of progress in cancer disparities research. But as a study that appeared earlier this month in *Cancer* demonstrated, we are up against significant obstacles. The study found that disparities in cancer treatment did not abate between 1994 and 2002 in the areas of colorectal, prostate, and breast cancers, regardless of socioeconomic status.

The reasons for cancer health disparities can be complex and unique to specific communities. That's why CRCHD is funding a broad range of activities, including the CURE Program, Minority Institution/Cancer Center Partnership Program, Community Networks Program, and Patient Navigation Research Program. These programs build local partnerships and infrastructure so that the information gathered from these communities is accurate and can better inform the social, behavioral, and educational interventions we are developing and testing to eliminate disparities.

Dr. Sanya Springfield, Director, NCI Center to Reduce Cancer Health Disparities

And despite shifts in the national budget, we are developing important new programs, namely the Advanced and Emerging Technologies Initiative, which will dovetail with existing NCI programs to train minority students from high school, college, and postbaccalaureate in fields such as nanotechnology, clinical proteomics, and bioinformatics; and the Geographical Management Program, which will build regional hubs to support cancer health disparities research, training, and infrastructure.

We are also focused on collaboration. Last November, CRCHD co-sponsored a cancer health disparities conference with the American Association for Cancer Research that included presentations on incidence, risk behaviors, and new interventions, as well as the influence of genetics and the environment on disparities.

Studies that are a part of NCI's Cancer Genetic Markers of Susceptibility initiative, in fact, should greatly inform our understanding of the role of genetic variation in cancer disparities. Recent genome-wide association studies have identified specific single nucleotide polymorphisms, or SNPs, that may provide important insights into the more aggressive nature of prostate cancer in African American men. NCI also is working in collaborative studies with other groups to do specific scans in African American populations to identify unique SNPs that may contribute to risk.

In addition, several studies have now suggested that there may be unique genetic factors that influence breast cancer risk in African American women, including a recent study conducted in the United Kingdom that found an increased risk of "triple-negative" breast cancer in African American women.

Along those same lines, relying on data from several large studies, NCI recently published a revised breast cancer risk assessment model that provides better estimates of the number of breast cancers that would develop in African American women 50 to 79 years of age. The model is now available on the NCI Web site for clinicians to use in advising their female African American patients.

So, clearly, our understanding of disparities has vastly improved and

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process, he suggested, could be an effective cancer treatment.

"As a surgeon, I had seen tumors and handled them, and saw that the blood vessels converging on the tumor by the thousands, and coming from a long distance, appeared to be new," Dr. Folkman recounted in a 2001 interview, discussing the often intense, decades-long skepticism toward his angiogenesis theory.

By the mid-1990s, with a growing cadre of researchers investigating his theory in lab and animal model studies—including seminal work by Dr. Folkman and his laboratory colleagues—it became evident that his 1971 proposal was correct.

In February 2004, bevacizumab (Avastin) became the first specifically designed anti-angiogenesis agent to receive FDA approval, for the first-line treatment of metastatic colorectal cancer. Other agents have followed, including sunitinib (Sutent) and sorafenib (Nexavar), both approved for the treatment of kidney cancer, and at least 50 angiogenesis inhibitors are in clinical trials around the world.

More recently, angiogenesis research has taken many interesting twists, including clinical trials using low-dose, frequent chemotherapy as an anti-angiogenic treatment and using anti-angiogenesis agents to "normalize" the vasculature of brain tumors in order to more effectively deliver chemotherapy.

According to Children's Hospital Boston, in fact, more than 1,000 laboratories worldwide are studying angiogenesis. One of those is headed by Dr. Steve Libutti, head of the Tumor Angiogenesis Section in the Surgery Branch of NCI's Center for Cancer Research (CCR). Much of Dr. Folkman's success, Dr. Libutti says, was driven by his persistence and infectious enthusiasm.

"He was able to take very complicated concepts and explain them in a way that could allow anyone, regardless of their background or specific interest, to understand what he was talking about," he says. "If you went to one of his lectures, you always came out of it motivated to go cure cancer."

Dr. Folkman's work extended well beyond cancer, Dr. Libutti adds, spurring important new insights into and treatments for other conditions and diseases in which the vasculature plays a critical role, including macular degeneration, diabetic retinopathy, and ischemic heart disease.

As much as anything, Dr. Folkman is most warmly remembered as the quintessential mentor. Dr. Kevin Camphausen, a branch chief in the CCR Radiation Oncology Branch who worked in Dr. Folkman's lab from 1999 to 2001, recalls that while the lab had a competitive atmosphere and Dr. Folkman had high expectations, he was generous with his time.

"He was a great mentor, incredibly kind, intelligent, and humble," Dr. Camphausen says. "He always took time to sit with you if you asked. He was willing to help everybody."

In addition to receiving numerous awards and honors, Dr. Folkman was highly supportive of NCI, most recently working closely with the NIH Trans-Institute Angiogenesis Research Program and, just 2 weeks ago, speaking to young investigators at the NCI Intramural Scientific Retreat.

Dr. Folkman is survived by his wife, Paula, and two daughters, Laura and Marjorie. ◆

By Carmen Phillips

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we are developing and testing important new interventions. I invite you to visit the CRCHD Web site, where you can read more about recent disparity-related research, get updates on research conferences, and learn how to register for our Cancer Health Disparities Summit 2008.

Our passionate hope is that all people will have access to education in health care and science, access to jobs in our academic research departments, and access to the latest scientific advances used to fight cancer in the communities where they live. We will continue to pursue NCI's mission of sharing progress against cancer equally. Because, as Dr. King once said, "We must accept finite disappointment, but we must never lose infinite hope." ◆

Funding Opportunities

For a complete listing of current NCI funding opportunities, please go to the HTML version of today's *NCI Cancer Bulletin* at http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_012208/page5. ◆

Cancer Research Highlights

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formation of bone metastases in mice implanted with the breast cancer cell lines. Rare cells that did metastasize had decreased expression of the three miRNAs.

To measure the expression of these miRNAs in human tumors, the investigators used archived tissue samples from 11 women with metastatic breast cancer and 9 women whose cancer did not metastasize. They found that patients whose primary tumors had low expression of the three miRNAs "had a shorter median time to metastatic relapse."

In particular, low levels of miR-335 or miR-126 "were associated with very poor overall metastasis-free survival compared to the group whose tumors expressed a high level of these miRNAs." Further studies identified genes regulated by miR-335 that are directly associated with relapse.

A second study published in the January 11 *Science* identified a specific contribution of cells in the tumor microenvironment involved in the angiogenic switch—the generation of a tumor blood supply—and the associated progression of lung micrometastases to deadly macrometastases.

Researchers from Cold Spring Harbor Laboratory found that micrometastases that recruit a type of cell called a bone marrow-derived endothelial progenitor cell (EPC) to their immature blood vessels undergo development of a blood supply, in both xenograft and spontaneous mouse models of cancer.

The researchers also identified a protein called Id1 that is needed to draw the EPCs to the tumor site. When this protein was suppressed in a mouse model, the number of EPCs in the bloodstream was significantly reduced, and tumor blood vessel growth was suppressed. "These findings …suggest that the efficacy of antiangiogenic inhibitors used in clinical trials…may be a consequence of directly targeting [bone marrow]-derived EPCs, as well as the nascent tumor vasculature," conclude the authors.

Black British Women Younger at Breast Cancer Diagnosis

In the first published study of patterns of breast cancer in British black women, available online January 8 in the *British Journal of Cancer*, researchers found that black women were diagnosed with invasive breast cancer at a significantly younger median age than white women and had a higher frequency of higher grade tumors, estrogen receptor (ER)-negative, and basal-like (triple negative) tumors, similar to African American women.

The investigators from Cancer Research UK identified 102 black women and 191 white women diagnosed with invasive breast cancer between 1994 and 2005 at a hospital in East London. Black patients were diagnosed at a median age of 46, compared with a median age of 67 for white patients. An analysis of the population structures in the geographical area showed no differences between the black and white populations, "confirming that there is a true increase in the frequency of breast cancer in young black women."

Black patients also had a greater frequency of grade 3 tumors, positive lymph nodes, and ER-negative, progesterone receptor-negative, and basal-like tumors; however, only tumor grade was significantly different in all age groups. None of the results changed when adjusted for socioeconomic status.

No significant difference in overall survival was found between black patients and white patients. However, for women whose tumors were 2 centimeters in size or smaller, black patients had poorer survival. Because records showed that black women received more adjuvant therapy than white women, the authors conclude that "there is no evidence that observed differences are due to… inequalities in the receipt of therapy."

The current government breast cancer screening program in the United Kingdom begins at age 50. The authors suggest that "alterations to the screening services offered to black populations might be considered to better reflect the incidence patterns for this group."

Melanoma Study Finds, Targets Tumor Stem Cells

Researchers several years ago identified a population of cells within melanoma skin cancers that may cause resistance to chemotherapy. The researchers now say that these cells, which express the protein ABCB5, may be uniquely suited to initiate tumors and fuel their growth. Dr. Markus Frank of Harvard Medical School and his colleagues report in the January 17 *Nature* that antibodies against this protein can help prevent

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tumors from developing in animal models of the disease.

The study describes a hierarchy of cells within melanoma tumors. The capacity to self-renew and give rise to diverse cell types—the hallmarks of tissue stem cells—are concentrated in the ABCB5-positive cells, the researchers conclude. An analysis of tumors revealed greater expression of ABCB5 in more clinically advanced cases compared to less advanced cases, suggesting a link between these cells and melanoma progression.

The cancer stem cell hypothesis says that some cancers are driven by small populations of self-renewing cells. The cells have been reported in various tumor types, including brain, breast, and pancreatic tumors. Previous reports on melanoma have proposed that the proteins CD133 and CD20 may be markers of tumor stem cells.

Few studies have tested the idea that patients would benefit from the eradication of tumor stem cells. Support now comes from experiments in this study showing that antibodies against ABCB5-positive cells inhibited tumors in mice.

"This study provides validation of the hypothesis that specifically targeting cancer stem cells would inhibit tumor growth," said Dr. Frank, noting that more research is needed before the strategy could be applied to humans. Additional markers to further characterize melanoma stem cells at the clonal level are also needed because not every ABCB5-positive cell is a tumor-initiating cell.

Brain Tumor Stem Cells May Depend on Silenced Gene

Researchers have identified a gene that is improperly silenced during the development of some neural stem-like cells *in vitro*, a finding which could help explain why similar cells may result in aggressive brain tumors *in vivo*. Further experiments in a human line derived from cells taken from glioblastoma multiforme patients showed that activating the silenced gene restores its normal developmental stages, suggesting a potential strategy for treating patients.

Tumor stem-like cells, like normal stem cells, can self-renew, but unlike stem cells, they fail to differentiate into normal cell types. Instead, they give rise to dysregulated cells, which may develop into a tumor.

This new research links changes in gene regulation to the survival of stem-like cells in culture and exposes a possible Achilles' heel.

Lead investigator Dr. Howard Fine of NCI's Center for Cancer Research is collaborating with drug developers to identify compounds that could activate the silenced gene in the subset of glioblastoma brain cancers with a similar flaw. The hope is that causing neural stem-like cells to mature could stop them from developing into brain tumors.

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FDA Update

FDA Issues Pain Warning for Bisphosphonates

On January 7, the U.S. Food and Drug Administration (FDA) issued an alert to health care providers and patients regarding bisphosphonate drugs, which prevent and treat bone-density problems in patients who have cancer-related hypercalcemia, Paget disease, multiple myeloma, or bone metastases from solid tumors, as well as osteoporosis.

The agency warns that this class of drugs—which includes Fosamax, Didronel, Boniva, Aredia, Actonel, Skelid, Reclast, and Zometa—can cause severe musculoskeletal pain beginning days, months, or years after starting use. Patients have characterized the pain as extreme and disabling, to the point that they could no longer continue normal activities, such as walking.

When patients first begin using bisphosphonates, particularly if the drugs are given intravenously, they may develop fever, chills, or bone, muscle, and joint pain, but these symptoms tend to resolve within a few days. In some cases, however, the pain is severe and does not resolve unless the drug is stopped.

Though the risk factors for severe musculoskeletal pain associated with bisphosphonate use are still unknown, FDA has issued this warning so that health care providers are aware of the relationship and can address patients' needs more quickly. "Prescribers should consider discontinuing the bisphosphonate if severe pain symptoms occur," the statement says. "Alternative causes of the musculoskeletal pain should be considered if symptoms do not lessen or resolve following withdrawal of the bisphosphonate."

The agency will continue to evaluate reports of the trend in the coming year and post updates on its Web site as they become available. ◆

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As reported in the January *Cancer Cell*, the silenced gene is the *bone-morphogenetic protein receptor 1B* (*BMPR1B*), which is involved in cell differentiation. The silencing occurs through an epigenetic change known as methylation in which the gene is chemically modified.

A surprise was that even though the brain cancer stem-like cells had genetic flaws as well as the epigenetic change, the single step of reactivating the *BMPR1B* receptor caused the cells to grow and differentiate normally. "We may be able to use a drug to differentiate these tumor stem cells without having to treat all the other genetic abnormalities," noted Dr. Fine. "One could argue that the stem-like cell pathways may trump the classic oncogenic pathways."

The findings also suggest that all cancer stem-like cells do not have the same flaws. Rather, to treat the disease it may be necessary to identify the specific pathways that are disrupted in individual cancer cells. The researchers estimate that the *BMPR1B* gene is silenced in 15 to 20 percent of glioblastoma cases.

Newly Discovered Virus Linked to Aggressive Skin Cancer

Researchers have identified a previously unknown virus and linked it to Merkel cell carcinoma, a rare but usually rapidly fatal skin cancer. The researchers, led by Drs. Yuan Chang and Patrick Moore of the University of Pittsburgh Cancer Institute, say it is too soon to know whether the virus causes the cancer, but their evidence suggests that it may be a contributing factor.

The virus, which they named Merkel cell polyomavirus (MCV), was reported in *Science* on January 17. It is related to a group of polyomaviruses, which has long been known to cause cancer in animals.

Merkel cell carcinoma has been linked to sun exposure and a weakened immune system, though its causes are not known. Approximately 1,500 cases are diagnosed in the U.S. each year. The incidence has been rising, particularly among individuals whose immune systems are compromised by AIDS or immunosuppressant drugs.

The researchers detected MCV DNA in 8 of 10 Merkel cell tumors they tested. By comparison, it was found in 5 of 59 (8 percent) control tissues from various body sites and 4 of 25 (16 percent) control skin tissues. It is not clear why most—but not all—Merkel cell tumors are infected with the virus.

Experiments indicated that the virus had infected human cells before the cells became malignant. In addition, the viral DNA was integrated in six of the eight tumors. This suggests that the virus plays a role in the tumor, the researchers note on a Web site describing the findings. They used a technique called digital transcriptome subtraction to isolate a viral DNA sequence that was similar to but distinct from all known viruses.

If MCV is shown to play a role in the cancer, investigators will have new leads to explore for understanding and treating the deadly disease. The discovery could have implications for other cancers, noted Dr. Kishor Bhatia of NCI's Center for Cancer Research.

In 1994, Drs. Moore and Chang discovered the virus that causes Kaposi sarcoma, the most common malignancy in AIDS patients and the most common cancer in Africa.

Comorbidities May Limit Benefits of Combination Prostate Therapy

The addition of androgen suppression therapy (AST) to radiation therapy (RT) improved overall survival in men with localized prostate cancer and risk factors for disease recurrence, but the survival benefit may apply only to men who do not have moderate to high levels of other illnesses, researchers report in the January 23 *Journal of the American Medical Association.*

Previous observational studies and pooled analyses of randomized trials have suggested that AST may be associated with an increased risk of heart attacks and other cardiovascular events in older men.

In the current study, researchers randomly assigned 206 men with localized prostate cancer and a high risk of recurrence to either RT alone or RT plus AST for 6 months. The men, whose average age was 72.5, were classified into subgroups based on the severity of their other illnesses, such as diabetes or a previous heart attack.

After 7.6 years median follow-up, estimated 8-year survival was 74 percent for men randomized to RT plus AST compared with 61 percent for men assigned to RT alone. A total of 74 men had died—44 of those assigned to RT alone and 30 assigned to RT plus AST.

Among the 157 men with only minor comorbidities, 31 of those treated with RT alone had died, compared with 11 of those in the RT plus AST group. Among the 49 men with moderate to severe comorbidities, however, 19 of those randomized to RT plus AST had died, compared with 13 of those assigned to RT alone.

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Spotlight

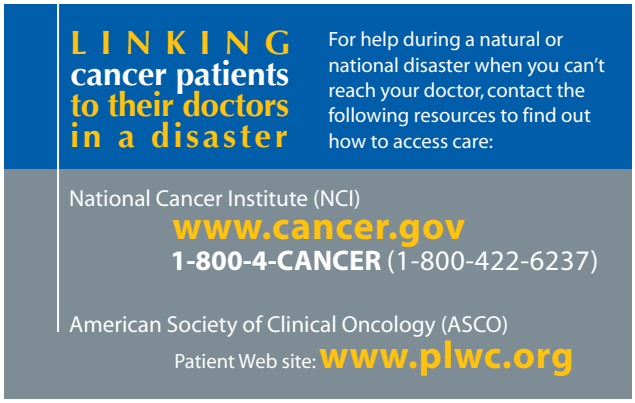
NCI and ASCO Develop Wallet Card for Gulf Coast Cancer Patients

NCI and the American Society of Clinical Oncology (ASCO) have developed a wallet card that is being piloted with oncologists in the Gulf Coast states. The wallet card guides displaced cancer patients to ASCO's patient information Web site and NCI's Cancer Information Service (CIS) national toll-free number (1-800-4-CANCER), *LiveHelp* instant messaging service, and e-mail service available at www.cancer.gov/help.

Using this nationwide electronic and telecommunication infrastructure, patients and physicians can access and share information in the event of a disaster. The card also provides space to write the patient's name, diagnosis, and treatment to communicate vital information to health care providers.

"Connecting patients from all over the country to cancer information and clinical trials is what NCI's CIS does every day," said Madeline La Porta, former deputy director of CIS and current associate director of the Office of Dissemination, Initiatives, and Partnerships in NCI's Office of Communications and Education. "Our collaboration with ASCO will help reconnect displaced patients and doctors after a natural disaster so they can get the information they need."

This collaboration builds upon a successful partnership in 2005 in response to the devastation caused by hurricanes Katrina and Rita. NCI and ASCO worked closely to provide the toll-free CIS phone number and Web-based resources to help displaced doctors and their cancer patients contact each other to ensure continued care.



"Continuity of care is crucial to the health and well-being of people with cancer," said ASCO President Dr. Nancy E. Davidson. "ASCO is pleased to partner with NCI to ensure that people with cancer across the United States can access the high-quality care that they need, no matter what the circumstance."

Before developing the card, ASCO conducted a formative evaluation of the concept and prototype of the wallet card among oncologists and oncology nurses who attended the Oncology Nursing Society Annual Congress, the ASCO Annual Meeting, and an ASCO Committee Meeting. ASCO staff reported that all of the attendees surveyed at their annual meeting agreed that such a resource would be valuable for their patients.

The card will be piloted over the next year to include the 2008 hurricane season with oncologists in the Gulf Coast states. An evaluation of the pilot will help determine whether the program is expanded to cover other geographic areas or other potential disasters.

"When I received the e-mail about this program, I was very excited," says Coleen Booker, a registered nurse and coordinator for the GI Oncology Center at the University of Florida Shands Cancer Center in Gainesville. She recalls how after Hurricane Katrina, cancer patients from New Orleans came to Florida. Their medical records had been destroyed, and sometimes the patients didn't know how to spell their doctor's name, making it difficult to determine their true diagnosis, medical history, and best course of treatment. "But it's not just about catastrophes," she says. "With this program, if people come to Florida on vacation or as snowbirds to live for half of the year, these cards will make it much easier for us to help them."

Oncology practices in the Gulf States can order copies of the card by calling CIS at 1-800-4-CANCER (1-800-422-6237). Quantities may be limited. ◆

By Brittany Moya del Pino

A Closer Look

Countering Tobacco Use Among Young Adults: New Approaches Needed

For the tobacco industry, a 22-year-old who isn't a smoker represents a challenge but also an opportunity.

The reason: While most—but by no means all—smokers start as teenagers, only about one-third are fully addicted smokers by age 18. Young adulthood, typically defined as ages 18 to 25, is when many transition from light smokers to heavy smokers—or quit. If smoking hasn't taken root by age 25, studies show, chances are good it's not going to.

This young adult period, tobacco control researchers point out, is one of transitions in roles, responsibilities, and behaviors. Many of the barriers to smoking are gone: High school is done, many people leave home for college or go to work and, for the first time, have an income and are able to purchase tobacco products legally.

These facts haven't escaped the tobacco industry, which in 2005 spent more than $13 billion to market tobacco products. Their efforts have not been in vain: At slightly below 25 percent, 18- to 25-year-olds have the highest smoking rate of any adult age group.

Tobacco control researchers have concluded that new approaches are urgently needed to reach young adults with smoking prevention and cessation messages and interventions. The importance of this task is magnified because, as numerous studies show, the best way for a smoker to avoid the enormous health risks of smoking, including cancer, is to quit at a young age.

Smoke-free events sponsored by Urban Fuel in Las Vegas are popular with young adults.

Fortunately, results from a number of recent studies have provided a more complete dossier of young adult smokers, with new data that suggest some potentially promising avenues for influencing young adults' tobacco use behavior.

A Clearer Picture

Socioeconomics are critical to smoking behavior. It's now well established, for example, that young adults with less education and, often, lower incomes, are far more likely to smoke. In one recent study, 48 percent of survey respondents with only a high school education or less smoked—nearly twice the rate of respondents with at least a college education.

Several studies also have reported that less educated young adults try to quit as frequently as their more highly educated counterparts. However, physicians are less likely to advise young adult smokers to quit, compared with older smokers.

Several things are abundantly clear, says Dr. C. Tracy Orleans, a Distinguished Fellow at the Robert Wood Johnson Foundation. First, programs aimed at young adults with lower levels of education and income have to become a high priority.

"That represents one of the most important challenges for tobacco control," Dr. Orleans says, particularly because socioeconomic disparities have expanded over the past several decades.

And second, to better reach young adults—and all smokers, in truth—the packaging and delivery of anti-smoking messages and cessation interventions has to improve.

To do so, explains Dr. Orleans, a member of the public-private Youth Tobacco Cessation Collaborative, tobacco control and public health officials might want to take cues from an unlikely source, the tobacco companies.

"We have to use the same viral marketing strategies [as the tobacco industry], get online, develop connected communities, use the same approaches tailored to psychographics," she says.

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Psychographics, explains Dr. Stanton Glantz, director of the Center for Tobacco Control Research and Education at the University of California, San Francisco, underlie much of tobacco industry marketing.

"They do these extensive surveys that ask many different questions," says Dr. Glantz, who, along with his colleague Dr. Pamela Ling, has studied thousands of pages of tobacco industry documents made available to the public as a result of litigation against the tobacco industry. "They would be viewed as unscientific questions: What kind of music do you like? What's your favorite movie? Do you fix your own car?"

Using statistical techniques, Dr. Glantz continues, the tobacco companies sift through the data "looking for clouds of people, who they are and what their smoking behavior is, and their marketing and messages are built around that."

And just as the tobacco industry uses psychographics to deliver its messages directly to targeted populations—via magazines, sporting events, the Internet, and bars and clubs—the tobacco control community needs to do the same, says Dr. Orleans.

New Approaches

Some small but encouraging changes are already happening. Researchers in New Zealand and the United Kingdom, for instance, have reported some success with smoking cessation programs for young adults that incorporate one of their new favorite pastimes, cell phone text messaging.

On the other end of the spectrum, in Las Vegas, a program sponsored by the Clark County Health Department called Urban Fuel sponsors regular "Smokefree and Sexy" events at

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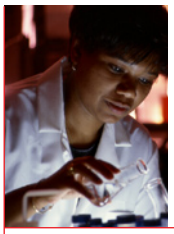

Featured Clinical Trial

Inhibiting Tumor Angiogenesis in Children

Name of the Trial

Phase I Study of Cediranib in Pediatric Patients with Refractory or Recurrent Extracranial Malignant Solid Tumors or Acute Myeloid Leukemia (NCI-06-C-0152). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-06-C-0152.

Principal Investigator

Dr. Elizabeth Fox, NCI Center for Cancer Research

Why This Trial Is Important

Great progress has been made in the treatment of childhood cancers over the past 30 years, thanks primarily to advances in chemotherapy and a high level of participation in clinical trials by pediatric patients. This progress, however, is in danger of stalling without new treatment advances.

One approach that has shown effectiveness in the treatment of some adult cancers is inhibiting the growth of new blood vessels to tumors (i.e., blocking tumor angiogenesis). Without angiogenesis, solid tumors are unable to grow beyond a few millimeters in size. Because drugs that inhibit angiogenesis may cause different side effects in children than they do in adults, it is important to carefully test their use in pediatric cancer patients.

In this trial, researchers are testing an angiogenesis inhibitor called cediranib in pediatric patients who have solid tumors (except brain tumors) or acute myeloid leukemia (AML), a type of blood cancer. Although solid tumors are not formed in AML, there is evidence that a protein known to be important in tumor angiogenesis (i.e., vascular endothelial growth factor, or VEGF) may also be important for the growth of AML cells. Cediranib blocks all three known receptor proteins for VEGF.

"Solid tumors in children tend to be highly vascular, and adult AML patients with elevated levels of VEGF typically don't survive as long as those with lower levels," said Dr. Fox. "So, there's a strong rationale for using VEGF inhibitors for these cancers. However, it is vitally important to assess the toxicities and establish the appropriate dosage of cediranib for pediatric patients.

"Furthermore, we plan to study how cediranib affects a number of markers related to cancer progression and, at least preliminarily, determine tumor responses to cediranib in these patients," she added.

For More Information

See the list of eligibility criteria and contact information at http://cancer.gov/clinicaltrials/NCI-06-C-0152 or call the NCI Clinical Trials Referral Office at 1-888-NCI-1937. The call is toll free and confidential. ◆

An archive of "Featured Clinical Trial" columns is available at http://cancer.gov/clinicaltrials/ft-all-featured-trials.

Notes

Bennett Named CCR Deputy Director

Dr. L. Michelle Bennett has been named Deputy Director of NCI's Center for Cancer Research (CCR). She previously served as CCR's Associate Director for Science. As Deputy Director, Dr. Bennett will be involved in strategic planning, program integration, and scientific communications.

Dr. Bennett trained at the McArdle Laboratory for Cancer Research where she focused on the genetic susceptibility of inbred strains of mice to liver cancer. She completed a postdoctoral fellowship at the National Institute of Environmental Health Sciences in Research Triangle Park, NC, where—among other achievements—she contributed to the identification and characterization of the human *BRCA1* gene. While at the Lawrence Livermore National Laboratory, she focused on the mechanisms associated with the etiology of breast cancer in rodents. Dr. Bennett joined CCR in 2002 and has been involved in a broad range of projects and activities, including the development and implementation of CCR's strategic plan, the introduction of new Centers of Excellence as hubs for collaboration, and the restructuring of CCR's communications activities.

Stinchcomb Named Branch Chief

David Stinchcomb has accepted the position of chief of the Cancer Statistics Branch in the Surveillance Research Program (SRP) of NCI's Division of Cancer Control and Population Sciences. Mr. Stinchcomb joined SRP in 2004 as a geographer with extensive experience in computer science. During his tenure, he has become the scientific coordinator and technical lead for the nationally recognized State Cancer Profiles interactive Web site. He is the senior surveillance expert on geocoding technology and information systems, as well as an expert on issues involving geography, population estimates, and socioeconomic data for SEER and other scientific databases.

UICC to Mark World Cancer Day with Smoke-Free Childhood Campaign

On February 4, World Cancer Day, the International Union Against Cancer (UICC) will launch the "I love my smoke-free childhood" campaign.

About 700 million children—almost half of the world's children—breathe air polluted by tobacco smoke, particularly at home. The message to parents is: "Second-hand smoke is a health hazard for you and your family. There is no safe level of exposure to second-hand smoke. Give your child a smoke-free childhood."

The goal of the campaign is to raise public awareness through a global media campaign; engage member organizations and partners to promote changes in smoking behavior in the environment of children within their communities; and mobilize citizens, schools, communities, and coalitions of voluntary associations around local initiatives to create smoke-free environments for children.

More information is available at http://www.worldcancercampaign.org/. ◆

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some of the most popular clubs on the Vegas strip. And, says Malcolm Ahlo, Urban Fuel's 26-year-old program director, its largest event, called "Nasty Habits," has become so popular that tickets have to be purchased well in advance through a major ticketing firm.

Surveys at Urban Fuel's smaller, weekly events show that most attendees prefer the smoke-free environments. "Even the smokers," says Mr. Ahlo.

And the companies that manufacture smoking cessation medications also are catching on. GlaxoSmithKline (GSK), for example, now sponsors NASCAR events and has counseling booths at races where it also promotes its products. GSK also recently introduced Cinnamon Surge, a new flavor of its Nicorette nicotine gum. Cinnamon Surge has bright red, flashy packaging, a catchy tag line ("Fight Fire with Fire"), and a Web site with pictures of young adults that, when clicked on, lead to tips for how to best use the product and quit smoking. ◆

By Carmen Phillips

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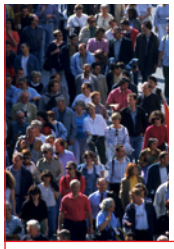
"Preexisting comorbid illness may increase the negative effects of specific anticancer treatments such as AST," conclude the researchers, who were led by Dr. Anthony V. D'Amico of Brigham and Women's Hospital in Boston. They recommend that follow-up clinical trials be designed to further assess this interaction and identify which illnesses in particular may shorten life expectancy among men undergoing treatment with AST. ◆



Community Update

Duke Forging Research Ties in China

For nearly a decade, the Duke Comprehensive Cancer Center has been exploring the world's most populous country, talking to Chinese leaders and researchers, "looking for ways to collaborate on our common goal—eradicating cancer," said Dr. H. Kim Lyerly, center director. In 2007, Duke entered into a formal partnership with the Peking University Health Science Center, which includes a hospital focused exclusively on cancer larger than most general hospitals in America, with 800 beds and treating more than 150,000 patients a year.

Yet how many of these Chinese receive the chemotherapy and biological agents that have been approved by the U.S. Food and Drug Administration? "In a timely manner? Not very many," said Dr. Wei Chen, a cancer researcher on the faculty at Duke who was born in China.

China has its own regulatory body, the State Food and Drug Administration. For various reasons, neither country has accepted the results of most research done by its counterpart. Dr. Chen hopes that the Duke/Peking University partnership will begin a process that might eventually break down that wall.

The partners think they can provide the government agencies in both countries with a groundbreaking example of collaborative research that will meet the standards and expectations of each. "We plan to identify some pressing and pertinent problems," said Dr. Chen, "and attack them synergistically, taking advantage of the strengths and assets of each institution's medical system."

One of the first initiatives will probably be a breast cancer treatment trial, sponsored by Duke, with Peking University Health Science Center serving as a remote site. Drs. Lyerly and Chen visited Beijing last September, along with Dr. Ken Buetow, director of the NCI Center for Bioinformatics, to begin preparations for caBIG.

NCI's Cancer Biomedical Informatics Grid (caBIG) provides the electronic environment and platforms to connect cancer researchers so they can communicate data and work seamlessly. This project will be caBIG's first overseas application.

Merging electrons is one thing, but "it's far more challenging to bring the medical cultures and practices of two major medical systems into synch," said Dr. Chen. This month, six clinical researchers from the Peking Cancer Hospital are at the Duke Medical Center, getting formal training in the procedures and protocols expected by the FDA for the conduct of clinical trials.

The Chinese clinicians will return to China with the know-how to run the trial, but "modifying the culture of current Chinese medicine that is practiced at even advanced medical centers will require a lot of persuasion and dialogue," noted Dr. Chen. As the trial nears, researchers from Duke will travel to China to provide advice and convey the rationale at the crux of the partnership.

An enormous evidence-based literature has accumulated in the West, explained Dr. Chen, "but as scientists we really can't say whether these data apply to the Chinese," given differences of race, environment, and different therapies. Tissue banking, pharmacogenomics, and clinical trials like this one will begin to establish the foundation for truly consensual data that the partners hope can bring regulators and governments in both countries together.

Even though breast cancer incidence is lower in Asia than in the West, with a population of 1.3 billion, China has more patients than the U.S. or any other country. Among people over the age of 65, "cancer is their number one killer," explained Dr. Lyerly, and "with 110 million people older than 65, [that is] twice the number here. Breast cancer is a huge problem," and is growing as much as 3 percent each year.

"The opportunities are tremendous from this large pool of patients," said Dr. Lyerly. "As we increasingly consider providing and testing treatments for certain types of cancer based on a specific marker or genetic fingerprint, we will need to be able to rapidly access large populations of cancer patients with those characteristics." So the benefits clearly run in both directions. "It's a win-win," he explained, "and serves to illustrate the opportunities for the sorts of collaborations we think will be crucial to address the looming issues of global health care in the 21st century." ◆

By Addison Greenwood