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Antiangiogenic Agent Shows Promise against Glioblastoma

An experimental antiangiogenesis drug may improve the treatment of the most common and deadly type of adult brain cancer, researchers from Massachusetts General Hospital and Harvard Medical School reported this week at the American Association for Cancer Research (AACR) annual meeting in Los Angeles.

The promising clinical results were buttressed by imaging and biomarker analyses that support a theory that the value of antiangiogenic agents may not be limited to halting the development of blood vessels that feed tumors, but that the drugs also can "normalize" them to the point where the delivery of standard treatments to the tumor may be improved.

The research team presented updated data from a phase II clinical trial involving 31 patients with glioblastoma that had recurred after standard treatment of chemotherapy and radiation. Daily use of the experimental agent, AZD2171, an inhibitor of vascular endothelial growth factor (VEGF) receptors, improved

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More AACR research highlights can be found on pages 7 and 8. ◆

Director's Update

Supporting Quality Research Remains NCI's Top Priority

I had the opportunity once again to provide the NCI Director's update at the American Association for Cancer Research meeting in Los Angeles.

It was an honor as a long-standing member of the organization to participate in the annual meeting as the NCI Director. I am pleased to see the significant growth and outstanding progress made by our organization.

During my talk, I took the opportunity to discuss some areas of research that I find particularly intriguing—including cancer stem cells and potential diagnostic applications of chromosome location mapping, for example—and to address some of the issues that are part of the conversation in the scientific community about the NCI budget and its potential impact on the future of cancer research.

For even the most venerable cancer researchers, the current budgetary environment is a cause for anxiety. And that concern is understandable. Because of increased costs for

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progression-free survival compared with what is historically seen in patients with recurrent glioblastoma, 111 days vs. 63 days. The drug had a more modest improvement in overall survival compared with historical controls, 211 days vs. 179 days. In addition, 9 of the first 16 patients achieved partial responses as measured by at least a 50-percent reduction in tumor contrast enhancement by imaging.

"The results are encouraging," said the study's lead investigator, Dr. Tracy Batchelor, chief of neuro-oncology at Massachusetts General Hospital Cancer Center. "All of the arrows are pointing in the right direction."

Even so, Dr. Batchelor warned, this was a small number of patients in a nonrandomized trial, so the results should be interpreted with an abundance of caution.

According to Dr. Percy Ivy of NCI's Cancer Therapy Evaluation Program, the study also reached another important metric: 27.6 percent of patients were alive and with no signs of disease progression at 6 months, compared with a historic benchmark of approximately 15 percent with standard therapy. That suggests further studies are warranted.

"This is exciting because, as a single agent, [AZD2171] has shown some evidence of activity in a disease that is uniformly fatal," Dr. Ivy said. "And the evidence is sufficient to start exploring combinations and determining if this represents a new advance in treatment."

In addition to the improved survival results, in some patients the use of AZD2171 remedied a significant problem associated with glioblastoma: swelling in the brain caused by fluid retention, known as edema. As a result, many of the patients were able to reduce or halt altogether the use of steroids to treat the edema, which carry their own debilitating side effects.

The drug's impact on edema, said study team member Dr. Rakesh K. Jain, was one of several pieces of evidence that the drug very rapidly creates a window of "vascular normalization" in the tumor. In addition to blocking the formation of small, weak blood vessels that feed the tumor, explained Dr. Jain, the study showed that, as soon as 24 hours after the first dose, AZD2171 also improved
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everything from rent to utilities, an essentially flat budget since 2004 has translated into a 12-percent reduction in NCI's purchasing power over that time period. That has real consequences for NCI, its employees, and the researchers who rely on our support.

NCI remains committed to finding ways to fund quality research.

Yet, NCI remains committed to finding ways to fund quality research. The success rate of competing RPGs, which has fallen considerably since the end of the doubling of the NIH budget in 2003, is largely attributable to a tremendous spike in the number of applications. It's important to stress that the number of awards has remained stable.

To understand the competing grant funding picture as completely as possible, I took a closer look at the ultimate success rate of all applications. Looking at competing grant applications initially submitted in 2002—the most recent year for which we have complete data—the ultimate success rate was approximately 61 percent. This rate appears to be fairly consistent through 2005.

Although the bulk of applications are approved after their initial submission, there are numerous instances where funding doesn't come until two application revisions over several years. We're going to be working with NIH to take a closer look at researchers in these situations, who may be eligible for bridge funding to keep their research programs operating during the application revision and resubmission process.

As I also have noted previously, we are particularly focused on protecting and supporting young investigators. The number of NCI-funded new investigators has continued to climb, with the payline for those grants in some circumstances extended by up to 6 percentile points. And in the last review round, in fact, I personally reviewed those applications from new investigators that fell just short upon their initial review to determine which would be selected for an exception.

As usual, AACR highlighted some of the most exciting and innovative work being done in cancer research. I'd like to congratulate the organization on reaching its 100th anniversary, and thank all of its members for everything they are doing to decrease the cancer burden. ◆

Dr. John E. Niederhuber
Director, National Cancer Institute

Missed an Update?

Go to http://www.cancer.gov/directorscorner to access all of the Director's Updates from past issues of the *NCI Cancer Bulletin.* ◆

Cancer Research Highlights

Gleevec Protects Against Recurrence of Gastrointestinal Tumors

Imatinib (Gleevec) can reduce the recurrence of gastrointestinal stromal tumors (GIST) in patients whose tumors have been surgically removed, a large, randomized clinical trial has found. The final-stage clinical trial, sponsored by NCI, was cut short after an interim analysis of the data showed that taking imatinib was associated with a decreased risk of recurrence. Imatinib was made available to all patients participating in the trial.

A network of researchers led by the American College of Surgeons Oncology Group conducted the study, which involved more than 600 patients. The interim analysis showed that 97 percent of patients who received 1 year of imatinib after surgery did not have a recurrence of their cancer compared with 83 percent of patients who received 1 year of placebo. Imatinib, which has been taken by more than 100,000 patients worldwide for GIST and chronic myelogenous leukemia, was well tolerated.

The standard treatment for primary GIST is the surgical removal of the tumor without additional therapy. Conventional chemotherapy agents have been notoriously ineffective against GIST, a type of tumor usually found in the stomach or small intestine.

"This study for the first time demonstrated that targeted molecular therapy reduces the rate of recurrence after complete removal of a primary GIST," said the principal investigator, Dr. Ronald DeMatteo of Memorial Sloan-Kettering Cancer Center. "These results have major implications for patients with primary GIST."

Palliative Radiation Extends Survival for Elderly Patients with Glioblastoma

Elderly patients with glioblastoma benefit from palliative radiation therapy, which provides significantly increased survival with no detriment to quality of life, according to a study published in the April 12 *New England Journal of Medicine*. The randomized trial, conducted by the Association of French-Speaking Neuro-Oncologists, also highlighted the feasibility of enrolling elderly patients in cancer clinical trials.

The investigators enrolled 81 patients 70 years of age or older with glioblastoma into the trial. All patients had good functional status. Forty-two received supportive care alone, including antiseizure medication, physical and psychological support, and access to a palliative care team. The other 39 patients received supportive care and radiation therapy (50 Gy in doses of 1.8 Gy per day, given 5 days a week).

Patients receiving radiation therapy had a median survival of 29.1 weeks compared with 16.9 weeks for those receiving supportive care alone. Radiation therapy produced a survival benefit regardless of the extent of surgery performed, which ranged from biopsy alone to complete resection. Physical and mental status declined over time in both groups, with no significant differences observed between the groups. Perceived quality of life also did not differ between the groups.

The authors stated that "radiotherapy increases the median survival of elderly patients with glioblastoma who have a good performance status at the start of treatment." They also noted that "the optimal dose of radiotherapy in elderly patients remains undetermined." Other studies have indicated that various other palliative radiation regimens, using different doses and fractionation schemes, may provide similar benefit.

Hispanic Breast Cancer Differences Persist with Equal Access to Care

Despite equal access to health care services, differences persist in the size, stage, and grade of breast cancer for Hispanic women compared with non-Hispanic white (NHW) women, according to results from a study published online April 9 in *Cancer*.

The study compared 139 Hispanic women and 2,118 NHW women with breast cancer who were all established members of the Kaiser Permanente Colorado health plan. The Hispanic women were diagnosed at a younger age; at a later stage of disease; with larger, higher grade tumors; and with less treatable estrogen- and progesterone-negative tumors, reported the investigators led by Dr. A. Tyler Watlington at the University of Colorado Health Sciences Center.

"The results of this study confirm those of many previous studies that breast cancer presents differently in Hispanic women," the researchers noted. Previous research has suggested that the differences may be due to socioeconomic factors, especially lack

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of or inadequate health insurance and less access to care among low-income Hispanic women. However, the current study shows that "these differences were apparent even among a group of Hispanic women with equal access to care and similar health care utilization," they added.

"The results of this study, in our opinion, lend further support to the evidence for a biologic/genetic basis for these differences," the researchers stated. Future research should more carefully explore differences in clinical presentation as well as biologic differences in tumor genotypes and phenotypes, "as different strategies for breast cancer prevention may then be warranted for Hispanic women," they concluded.

Age, Race, and Income Level Associated with Undertreatment of Ovarian Cancer

Women with ovarian cancer who are aged 70 and older, African American or Hispanic, or insured by Medicaid were less likely to receive the recommended comprehensive surgical treatment, according to study results in the May 15 *Cancer*.

Ovarian cancer is the leading cause of death from gynecologic malignancies in the United States, accounting for more than 14,000 deaths each year. Providing comprehensive surgical treatment for women with ovarian cancer, which is often diagnosed at advanced stages, is one of the most effective ways to improve survival outcomes.

Dr. Barbara Goff of the University of Washington, Seattle, and colleagues analyzed hospital admissions data of 10,432 women aged 21 and older who were diagnosed with ovarian cancer and underwent surgical removal of their ovaries (oophorectomy). Researchers identified patients across nine states from 1999 to 2002 using the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project's state inpatient databases, which contain discharge information, such as demographics, place of residence, and diagnosis.

Researchers found that 66.9 percent of the patients received comprehensive surgical treatment (oophorectomy plus surgical removal of all visible extra-ovarian tumors). Women who were 70 or older, African American or Hispanic, or Medicaid patients were all less likely to receive comprehensive surgery compared with women who were between the age of 21 and 50, Caucasian, and had private insurance. Women in hospitals with obstetrics-gynecology teaching programs were also more likely than women in nonteaching hospitals to receive comprehensive surgery. Surgeons that performed fewer than 10 ovarian cancer surgeries per year were significantly less likely to provide comprehensive surgical care.

The authors noted, "Because optimal surgery with cytoreduction is associated with improved overall survival, efforts should be made to ensure that all women with ovarian cancer, especially those who are vulnerable because of age, race, or socioeconomic status, are referred to centers or surgeons from whom they are more likely to get optimal surgery." ◆

University of Michigan Hosts Town Hall Meeting: Stopping Cancer Before it Starts

On April 11, the nonprofit Friends of Cancer Research and the University of Michigan (U-M) Comprehensive Cancer Center hosted a town hall meeting on what the most promising new developments in cancer prevention and detection research will mean for the public.

The guest panel, moderated by Susan Dentzer of the *NewsHour with Jim Lehrer* on PBS-TV, included the Hon. John Dingell (D-MI); NCI Director Dr. John E. Niederhuber; FDA Commissioner Dr. Andrew von Eschenbach; U-M Cancer Center Director Dr. Max Wicha; Dr. Stephen Gruber, director of the Cancer Genetics Clinic at U-M; Dr. Dean Brenner, professor of pharmacology and internal medicine at the U-M School of Medicine; Dr. Joseph Purvis of the pharmaceutical company AstraZeneca; and Ruth Freedman, a long-term breast cancer survivor and volunteer patient counselor at U-M Cancer Center.

NCI Director Dr. John E. Niederhuber makes a point at the University of Michigan Town Hall Meeting as Dr. Max Wicha, director of University of Michigan Comprehensive Cancer Center, is in the background.

Discussion topics ranged from recent findings on how cancer develops and how it may be prevented to how this information may influence clinical trial design, FDA regulation of new products that can prevent and detect cancer, postmarket surveillance, and the financial and other barriers affecting progress in these areas.

A videocast of the meeting is available online at: http://ummedia02.rs.itd.umich.edu/cccmc041107. ◆

Spotlight

Mammogram Study Evaluates Computer-Aided Detection

Researchers are reporting that a computer system created to help radiologists interpret mammograms may not be helping after all. The system, known as computer-aided detection, or CAD, uses software to mark suspicious spots on mammograms that could be overlooked by radiologists.

In the first large-scale study of how well the technology works in the clinic, the researchers found that it did not improve the detection of breast cancer. Rather, the use of CAD led to significantly more false-positive mammograms than when radiologists relied on their own experience.

With the technology, 20 percent more women had biopsies than when the system was not used, even though most of these women did not have breast cancer. Dr. Joshua J. Fenton of the University of California, Davis, and his colleagues reported their findings in the April 5 *New England Journal of Medicine* (*NEJM*).

"Our goal was to see how computer-aided detection is working in clinical practice, and this study tells us that it's probably not working the way we expected," says co-author Dr. Stephen Taplin of NCI's Division of Cancer Control and Population Sciences (DCCPS).

The findings will surprise and disappoint most mammographers, says Dr. Ferris Hall of Beth Israel Deaconess Medical Center in an accompanying editorial. He points out that the use of CAD not only failed to increase the cancer-detection rate, but also was harmful because it increased the number of false-positive mammograms, which resulted in more testing and biopsies.

"Our goal was to see how computer-aided detection is working in clinical practice, and this study tells us that it's probably not working the way we expected."

CAD systems, which cost between $50,000 and $175,000, are increasingly common in relatively large mammography centers. The Food and Drug Administration approved the technology in 1998 based on limited data, and Medicare began to pay for CAD soon after. Within 3 years of FDA approval, 10 percent of U.S. mammography facilities had adopted CAD, and others have followed.

It is unfortunate, Dr. Fenton notes, that the technology has come into widespread use before researchers could be certain of its clinical benefits. His team and Dr. Hall have called for larger studies to determine whether the routine use of CAD does more good than harm.

The researchers analyzed 429,000 mammograms and 2,351 cases of cancer detected at 43 facilities of the Breast Cancer Surveillance Consortium between 1998 and 2002. During this period, seven of the facilities implemented CAD, which allowed the researchers to compare results before and after. The other facilities were the control group.

The study did not evaluate whether CAD might save lives. But the results reinforce the need to resolve a major controversy in breast cancer: the clinical implications of detecting ductal carcinoma *in situ* (DCIS), a precancerous condition that may lead to invasive cancer, but also may never cause harm. It is not possible to identify which ones will lead to invasive cancer at this time.

The use of the technology increased the detection of these lesions, but it did not identify more invasive cancers. This raises the question of whether detecting more DCIS will save lives. The editorial suggests that it may not substantially reduce deaths, because detecting DCIS accounts for only about 10 percent of the reduction in deaths associated with screening.

"The critical question is whether detecting more DCIS helps save lives, and we do not have an answer right now," says Dr. Taplin.

The researchers estimate that with CAD, 157 women would be recalled (and 15 would undergo a biopsy) in order to detect 1 additional case of cancer, which might be DCIS. This

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scenario could increase the national costs of mammography screening by approximately $550 million annually.

In addition to the economic costs, a false-positive mammogram can have long-term effects on a woman's health. Women who receive false-positive mammograms tend to become more anxious and worried about breast cancer, and the concerns can linger for many years, researchers reported in the April 3 *Annals of Internal Medicine*.

"Receiving a false-positive mammogram can have an enduring effect on a woman's behavior and her well-being," says Dr. Noel Brewer of the University of North Carolina, Chapel Hill, who led the study.

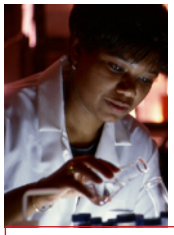
For many women in the *NEJM* study, the result of a false-positive mammogram was not just some anxiety, but also a biopsy. "These women are not just getting a false-positive and becoming worried—they're also having a procedure," says Dr. Taplin. "We need to understand the implications of this."

One concern that he and others are investigating is whether breast biopsies may distort breast tissue and affect the interpretation of future mammograms. ◆

By Edward R. Winstead

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_041707/page7. ◆



Featured Clinical Trial

Reactivating Tumor Suppressor Genes

Name of the Trial
Phase I Study of 5-Fluoro-2'-Deoxycytidine and Tetrahydrouridine in Patients with Advanced Solid Tumors (NCI-06-C-0221). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-06-C-0221.

Principal Investigator
Dr. James Doroshow, NCI CCR and DCTD

Dr. James Doroshow

Why This Trial Is Important
A drug called 5-fluoro-2'-deoxycytidine (FdCyd) may be effective in blocking a cellular process called DNA methylation, which is believed to play an important role in the development of many cancers. Excessive methylation (hypermethylation) may silence, or "turn off," genes that suppress tumor formation, thereby allowing abnormal cells to proliferate.

Preclinical studies have shown, however, that FdCyd is rapidly broken down in the body, and the breakdown products do not block methylation. Another drug called tetrahydrouridine (THU) may help prevent FdCyd breakdown when administered with it. THU may allow FdCyd to remain intact long enough to reduce the hypermethylation of tumor suppressor genes and possibly allow them to be reactivated.

This is the first clinical trial to test the combination of FdCyd and THU in humans. Researchers are interested in establishing the maximum tolerated dose and determining how this regimen affects the methylation of certain genes. They will also determine the toxicity of this treatment, and examine its effects on levels of proteins that are important for the progression of cancer.

"FdCyd/THU is being developed collaboratively by researchers at the City of Hope Comprehensive Cancer Center and the NCI," said Dr. Doroshow. "So far, patients in the trial have tolerated the combination well, and we have seen some clinical responses.

"Our hope is to develop the regimen as an orally available combination that will safely and effectively deliver repetitive doses of these tumor-suppressor gene-activating agents to patients."

Who Can Join This Trial
Researchers will enroll up to 60 adult patients with advanced solid tumors that have not responded to standard treatment. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/NCI-06-C-0221.

Study Sites and Contact Information
This study is taking place at the NIH Clinical Center in Bethesda, MD, and at study sites in California. See the list of study contacts at http://cancer.gov/clinicaltrials/NCI-06-C-0221 or call the NCI Clinical Trials Referral Office at 1-888-NCI-1937. The toll-free call is confidential. ◆

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

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the structure and function of some larger, leaky vessels—normalizing them—for at least 28 days. In some cases, this normalization lasted up to 4 months.

Evidence for normalization was acquired through a novel application of imaging studies that allowed a careful comparison of blood vessels on the unaffected side of the brain with vessels in and around the tumor. Molecular biomarker analyses, meanwhile, showed that the expression of two proteins, bFGF and SDF1α, correlated with tumor progression and reversion of vessel diameter to an abnormal, enlarged state during treatment.

These findings, Dr. Jain continued, suggest that bFGF and SDF1α are pro-angiogenic reinforcements called to action to help tumors escape anti-VEGF treatment. Although animal model studies had indicated bFGF was likely involved in angiogenesis, SDF1α's involvement is a new finding.

Based on these results, NCI has approved an early-phase clinical trial to evaluate AZD2171 in combination with standard therapy of radiation and temozolomide in newly diagnosed glioblastoma patients. And Dr. Batchelor will lead a randomized phase III trial supported by AstraZeneca that will test AZD2171 in combination with chemotherapy in patients with recurrent glioblastoma. That trial has been submitted to the FDA for approval, Dr. Batchelor said, with the hope of enrolling patients by the end of the year. ◆

By Carmen Phillips

HPV Vaccines Demonstrate Long-Term Protection

New data presented at the AACR annual meeting today on the longer term effectiveness of two human papillomavirus (HPV) vaccines demonstrate strong protection against the two HPV types linked to more than 70 percent of cervical cancers as well as the precancerous lesions associated with them.

Data from the ongoing evaluation of participants in a phase II trial testing a still-experimental vaccine manufactured by GlaxoSmithKline (GSK) called Cervarix showed that more than 98 percent of the 776 participants for whom extended follow-up data are available maintained protection against HPV types 16 and 18—considered the two most oncogenic HPV types—for more than 5 years.

The vaccine, reported the study's lead investigator, Dr. Stanley Gall from the University of Louisville, provided near complete protection against HPV types 16 and 18 incident infection (98 percent), 100-percent protection against 6- and 12-month persistent infection, and protection against most instances of HPV-associated precancerous growths. Although it's only designed to protect against HPV types 16 and 18, the GSK vaccine also demonstrated protection against incident infections of HPV type 45 (88 percent) and HPV type 31 (54 percent), which together account for approximately 10 percent of cervical cancers, Dr. Gall explained.

GSK applied to the FDA for marketing approval for Cervarix on March 29.

Longer term data also were presented on more than 12,000 women in a phase III trial testing Gardasil, the HPV vaccine approved by the FDA last year. Dr. Darron Brown of the Indiana University School of Medicine reported that, 3 years after completion of the three-shot vaccine regimen, Gardasil provided virtually complete protection against precancerous lesions associated with HPV types 16 and 18, and HPV 16 and 18 antibody levels continue to be significantly elevated.

In the 241 women for whom 5-year follow-up data are available, Dr. Brown reported, Gardasil provided 100-percent protection against HPV 16- and 18-related precancerous lesions. A preplanned substudy of vaccine cross-protection against other HPV types has been completed, Dr. Brown added. Although the final results are not ready for presentation, he said, the available data are "very encouraging."

Engineered Virus Delivers Killer Protein to Prostate Cancer Cells

Researchers from Columbia University have developed a novel gene therapy technique that uses a virus engineered to replicate only within cancer cells and produce a protein toxic to those cells. The results of their laboratory studies, presented at the 2007 AACR annual meeting, showed complete eradication of both primary and distant tumors in a mouse model of prostate cancer.

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The investigators built their system around a gene called *mda-7/IL-24,* which produces the cytokine IL-24, a signaling protein important to the immune response, that kills cancer cells when expressed at high levels. They engineered an adenovirus carrier for the gene, which can multiply within cancer cells. The virus was altered to replicate in response to transcription factors found only in cancer cells. When the virus enters a cancer cell, the researchers explained, it replicates millions of copies of itself and produces IL-24, which kills the cell and releases a flood of virus into the bloodstream to infect and kill other cancer cells.

After *in vitro* experiments confirmed that viral replication was confined to cancer cells and induced growth inhibition and cell death, the investigators tested their gene therapy system in a xenograft mouse model of therapy-resistant prostate cancer. The virus completely eradicated not only the primary tumor but also distant tumors, explained the study's leader, Dr. Devanand Sarkar from Columbia University.

An earlier version of the therapy has already been tested in a phase I clinical trial, producing a significant clinical response in several of the patients who completed one 28-day treatment cycle. Experiments to test the next-generation treatment in mice with fully functional immune systems are ongoing, Dr. Sarkar said.

Risk of Colon Cancer in African Americans Linked to Genetic Variants

Any one of four DNA variants in a gene involved in mediating inflammation may significantly increase the risk of colon cancer in African Americans, according to the results of an ongoing study presented at the AACR annual meeting. The risk is even further heightened in African American men who have two copies of all four variants, the research team found.

The finding may provide some insight into the higher colon cancer incidence and mortality in African Americans seen over the past three decades when compared with Caucasians, according to Dr. Krista A. Zanetti, a Cancer Prevention Fellow, and Dr. Curtis C. Harris, chief of the Laboratory of Human Carcinogenesis in NCI's Center for Cancer Research (CCR).

Despite the small sample size of African American cases and controls, "These results are particularly robust," Dr. Zanetti said. The variants are single nucleotide polymorphisms (SNPs), which are places in the genome where a single unit of DNA may vary from one person to the next.

The team conducted a case-control study that included 261 individuals with colon cancer and 537 healthy individuals, all from the greater Baltimore area. Of these, African Americans represented 103 cases and 201 controls. In African Americans, four SNPs in the *MBL2* gene increased the risk of colon cancer at least three- to fourfold compared with African Americans without the genetic variants. In African Americans with two copies of all four *MBL2* variants, there was a nearly sixfold increased risk. These associations were not seen in Caucasians.

Additional studies are needed to clarify and validate these findings, Dr. Zanetti explained.

"Given the lower frequency of these SNPs in Caucasians than African Americans in this study, we may need a larger number of samples to see if this association exists in Caucasians as well," Dr. Zanetti said. They are investigating this by using case and control samples from the ongoing, NCI-funded Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. ◆

Featured Meetings and Events

A calendar of scientific meetings and events sponsored by the National Institutes of Health is available at http://calendar.nih.gov ◆

The *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads the national effort to eliminate the suffering and death due to cancer. Through basic, clinical, and population-based biomedical research and training, NCI conducts and supports research that will lead to a future in which we can identify the environmental and genetic causes of cancer, prevent cancer before it starts, identify cancers that do develop at the earliest stage, eliminate cancers through innovative treatment interventions, and biologically control those cancers that we cannot eliminate so they become manageable, chronic diseases.

For more information on cancer, call 1-800-4-CANCER or visit http://www.cancer.gov.

NCI Cancer Bulletin staff can be reached at ncicancerbulletin@mail.nih.gov.

Notes

NCI Scientists and Advisor Receive AACR Awards

Drs. Douglas R. Lowy and John T. Schiller of NCI's CCR received the Dorothy P. Landon-AACR Prize for Translational Cancer Research for their work leading to the development of the human papillomavirus vaccine. Dr. Lowy is chief of the Laboratory of Cellular Oncology (LCO) and Basic Research Laboratory; Dr. Schiller is a senior investigator in LCO and head of the Neoplastic Disease Section. The international prize is one of the largest awards offered to cancer researchers from a professional society of their peers.

Dr. Harold P. Freeman, senior advisor to the NCI director, received the second annual AACR-Minorities in Cancer Research-Jane Cooke Wright Lectureship for his work on the Patient Navigator Program. This community-based effort to reduce cancer disparities led to the development of the Patient Navigation Research Program, a grant program funded by Congress that is administered by NCI's Center to Reduce Cancer Health Disparities.

The awards were presented at the 2007 AACR annual meeting in Los Angeles.

Collins to Give Kaplan Lecture at Harvard

Dr. Jerry M. Collins, associate director of the Developmental Therapeutics Program in the Division of Cancer Treatment and Diagnosis (DCTD), will present the 13th Annual William D. Kaplan Lecture at Harvard Medical School on April 24.

Dr. Collins, an expert clinical pharmacologist, will share his views on positron emission tomography (PET) imaging in a talk titled: "Beyond FDG: Facilitating the Next Generation of PET Imaging Probes." The lectureship is named after Dr. William Kaplan, who was the first chief of oncologic nuclear medicine at Dana-Farber Cancer Institute and professor of radiology at Harvard Medical School.

Free Telephone Workshop for Cancer Survivors

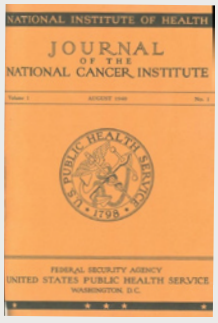
Cancer*Care*, in collaboration with NCI, the Lance Armstrong Foundation, Intercultural Cancer Council, Living Beyond Breast Cancer, and National Coalition for Cancer Survivorship, presented the first of a three-part telephone education workshop series on April 17, "Cancer Survivorship: Living With, Through, & Beyond Cancer."

This free series offers cancer survivors, their families, friends, and health care professionals practical information to help them cope with concerns and issues that arise after treatment ends.

Part I of the series focused on "Neuropathy and Joint Aches: New Post-Treatment Challenges." Part II, "My Treatment Is Over: Why Do I Feel so Alone and Sad?" is scheduled for May 15. Part III, "Finding Hope and Meaning After Treatment" is scheduled for June 19. All workshops take place from 1:30 to 2:30 p.m., EDT.

No phone charges apply, but preregistration is required. To register or to access an archived workshop, go to www.cancercare.org/TEW. ◆

70 YEARS OF EXCELLENCE IN CANCER RESEARCH



If Memory Serves…

The first issue of the *Journal of the National Cancer Institute* was published in August of 1940. The journal's Editor in Chief was NCI's Director Dr. Carl Voegtlin. The first few volumes of the journal featured articles on stomach cancer, a predominant cancer of the era, and mostly contained papers written by NCI staff members. (Read more)

For more information about the birth of NCI, go to http://www.cancer.gov/aboutnci/ncia.

CCR Grand Rounds

April 24: Dr. Merrill J. Egorin, Professor of Medicine and Pharmacology, University of Pittsburgh Cancer Institute. "The Relevance of Old-Fashioned Clinical Pharmacology to Modern Anticancer Chemotherapy."

May 1: Dr. Stephen J. Elledge, Gregor Mendel Professor of Genetics and Medicine, Harvard Medical School. "The Phosphoproteomics of the DNA Damage Response."

CCR Grand Rounds are held 8:30 to 9:30 a.m. at the NIH campus in Bethesda, MD, in the Clinical Center's Lipsett Amphitheater. ◆

A Closer Look

Breast Cancer in the News

Several high-profile reports about breast cancer have received media coverage in recent weeks, including work on magnetic resonance imaging (MRI), computer-assisted detection, and screening mammography recommendations. With research often reduced to sound bites and headlines, it can be a challenge to distinguish the key points and understand the implications. To help, here are summaries of three recent publications.

MRI Detects Contralateral Breast Cancers

What: After a woman is diagnosed with cancer in one breast, MRI can help detect unsuspected cancers in the other (contralateral) breast.

Where: Published in the March 29 *New England Journal of Medicine.*

Target audience: This study is about breast cancer detection and applies only to women who have been newly diagnosed with breast cancer and want to know whether they have cancer in both breasts.

Findings: MRI plus mammography can help identify hard-to-detect cancers that might be missed by mammography alone. By detecting cancer in both breasts at the same time, women could potentially be treated for both cancers simultaneously rather than having to go through treatment again in the future.

Bottom line: When used in combination with physical examination and mammography, contralateral breast MRI will identify the vast majority of contralateral cancers at the time of diagnosis in women who have an indication such as having very dense breasts or being at high risk for breast cancer.

MRI Screening, Mammograms Urged for High-Risk Women

What: The American Cancer Society (ACS) is recommending MRI scans along with screening mammograms once a year for high-risk women starting at age 30.

Where: Published in the March/April *CA: A Cancer Journal for Clinicians.*

Target audience: This report provides consensus guidelines developed by experts and applies only to women who are at high risk of developing breast cancer.

Findings: In certain groups of high-risk women, conducting both annual MRI scans and screening mammography increases the likelihood of early detection. "High risk" is defined in these guidelines as women who have a 20- to 25-percent lifetime risk of developing breast cancer. This is a very substantial increased risk. Only 1 to 2 percent of women have a risk of breast cancer this high. Risk can be estimated with a risk-assessment tool, and more information can be found on the ACS Web site.

Bottom line: Women should talk to their physicians about whether they fall into the high-risk category and might benefit from MRI scans along with screening mammography.

Comment: "These two publications confirm earlier reports that MRI is a very sensitive technology for detecting breast cancer, and they give us a little more information about when it should be used, including for women who have just been diagnosed with breast cancer and for women who are at high risk," says Dr. Daniel Sullivan, associate director of the Cancer Imaging Program, NCI's Division of Cancer Treatment and Diagnosis.

Mammogram Study Evaluates Computer-Aided Detection

What: A computer system used to interpret mammograms may reduce the accuracy of screening rather than enhance it.

Where: Published in the April 5 *New England Journal of Medicine.*

Target audience: Researchers and clinicians. This study raises questions about software used at some mammography facilities but does not alter recommendations for women about screening mammograms.

Findings: This was a large-scale analysis of screening mammography performed between 1998 and 2002 at 43 U.S. facilities, some of which adopted computer-aided detection, or CAD. CAD increased the detection of ductal carcinoma *in situ* but not invasive cancer. It also increased the number of evaluations that resulted in biopsy compared with the period when CAD was not available.

Bottom line: Larger, carefully designed studies are needed to determine whether the potential benefits of CAD outweigh the potential harms. ◆