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NCI Creates Gene Expression Database of Normal Human Organ Tissue

Researchers at the National Cancer Institute (NCI) Center for Cancer Research (CCR) today unveiled a publicly available Web site that provides a detailed catalogue of the genes that are actually expressed in most of the body's major organs. The database, also discussed in the March *Genome Research*, offers a one-of-a-kind tool that all cancer researchers can use to better define potential drug targets and anticipate their impact elsewhere in the human biosystem.

"The Normal Organ Database democratizes access to information that many, until recently, considered esoteric data for geneticists only," says Dr. Javed Khan, leader of CCR's Pediatric Oncology Branch oncogenomics team that developed the database. Today gene expression profiles are becoming widely available and widely used, Dr. Khan continues, in part because microarray technology now lets researchers run high-throughput assays for thousands of genes at once. "The challenge now is to isolate meaningful results for small numbers of specific genes within these large datasets," he adds. "More intuitively, one needs a true working definition of 'normal' against which to measure disease. This tool makes this far easier." Use of

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Director's Update

Reaching Out to Minority Investigators at NCI

In 2000, Dr. Alexzander Asea was at the Dana-Farber Cancer Institute when, with a colleague, he was the first to report that heat shock protein-70 (Hsp70), a well-known chaperone protein (a guardian of other proteins) could also act as a cytokine, helping trigger and orchestrate immune responses to, among other things, cancer cells. This and other heat shock proteins are now under intense investigation, including their potential as vehicles for delivering cancer vaccines. Dr. Asea, a native of Uganda, was able to make this discovery thanks in part to a grant he received from NCI's Comprehensive Minority Biomedical Branch (CMBB). The discovery, published in *Nature Medicine*, and subsequent publications enabled him to get his first NCI R01 grant, establishing him as an independently funded investigator and helping obtain a position as an assistant professor of medicine at Boston University School of Medicine.

Dr. Asea's ascension through the research ranks since he first began as a postdoctoral research fellow 10 years ago is exactly the kind of result envisioned by NCI leaders who established CMBB 30 years ago. Although its name has changed slightly, CMBB's mission has not: cultivating culturally

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the database (http://home.ccr.cancer.gov/oncology/oncogenomics) is not limited to cancer biologists, but is also open to those involved in developing new drugs for a wide range of diseases such as heart disease and autoimmune disorders. It may elucidate the pathological processes in these diseases as well.

Each of the 19 organs tested in the *Genome Research* study revealed a distinctive expression pattern or genetic fingerprint, even though the sources of human postmortem tissue samples used in the study were biologically diverse. By using so many samples (158) from many different regions of each organ, Dr. Khan's team engineered a generic database that is statistically sound. "Remarkably," says Dr. Khan, "any truly random subset of 1,000 genes will distinguish one organ from another."

With this baseline of normal gene expression for a given organ now accessible on the Web site, researchers should be able to more effectively analyze tissue samples from their own work. For example, Dr. Khan's work has largely focused on neuroblastoma (NB). Using the organ database, the research team detected and identified 19 highly expressed genes from their own NB samples that seem to be crucial to the biology of the NB carcinogenic process. This information now can inform clinicians of potential "druggable" targets.

The CCR team then took that same data one step further, trying to actually predict outcomes for particular patients based only on gene expression. "Using a sophisticated computer program that relies on artificial neural networks, the team analyzed NB expression profiles from the database and developed a patentable prognostic tool that improves on the current prognosis standard in the field, developed by NCI and the Children's Oncology Group," Dr. Khan said.

"I expect this new searchable database to be heavily used by the scientific community," predicts Dr. Paul Meltzer, Molecular Genetics section chief of the Cancer Genetics Branch at the National Human Genome Research Institute. "Because now any user can extract information relevant to their own scientific interests without having to consult an expert in microarray data analysis."

The normal organ database used cDNA microarrays to profile genes. For those researchers whose data was derived from Affymetrix chips or oligonucleotide arrays, Dr. Khan intends soon to provide transformation matrices that will make the datasets fully compatible. ◆

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sensitive, well-trained, competitive minority researchers.

CMBB is unique because of its holistic approach. Efforts to recruit promising minority researchers begin in high school and continue through to the grantees' first academic appointments. As part of CMBB's innovative Continuing Umbrella of Research Experiences (CURE) program, for example, NCI-designated cancer centers can fund placement of promising minority high school and undergraduate students in their research programs. The opportunity for these students to experience firsthand the excitement of basic, clinical, and population-based cancer research can make an indelible impression and set their future career course.

Through CURE, CMBB also offers other opportunities to researchers further along in their careers. Qualified minority researchers, for instance, can receive career development awards that provide protected time to develop and receive support for their initial independent cancer research work. The award helps smooth out what can be a difficult transition for postdoctoral research scientists leaving the confines of their mentored work to become full-fledged independent researchers.

CMBB also supports efforts to develop minority researchers on a broader scale, including the Comprehensive Minority Institution/Cancer Center Partnership program to develop and fund partnerships between NCI-designated cancer centers and institutions that serve a large minority population. These partnerships—54 awards have been funded since this program began 5 years ago—are increasing the minority-serving institutions' cancer research capabilities as well as improving the cancer centers' effectiveness in developing and sustaining activities that address the well-documented disparities in cancer care.

In the spring, Dr. Asea will leave Boston to become the holder of the Cain Centennial Chair in Clinical Pathology and chief of the Division of Investigative Pathology at the Scott & White Clinic and Texas A&M University College of Medicine. There, he will continue his research as well as another of his pursuits: mentoring young minority researchers. "Many minority researchers lack the established network and role models that other younger researchers take for granted," he says. With the right assistance, these researchers can "bring unique cultural perspectives to the research environment and enrich and reshape the future of scientific research."

CMBB grantees are bringing the Branch's work full circle. It's that self-sustaining desire that will continue to make this program a success. More information is available at http://minorityopportunities.nci.nih.gov. ◆

Dr. Andrew C. von Eschenbach
Director, National Cancer Institute

Spotlight

Cancer Stem Cells: An Overview

When a tumor disappears during treatment and later recurs, the question is always: Why? One theory to be tested in the coming years blames such recurrences on a small but hardy population of cells inside tumors that can withstand an attack by drugs and then reconstitute a tumor. These cells, known as cancer stem cells, resemble traditional stem cells in their ability to perpetuate themselves while giving rise to different types of cells.

Stem cells in tumors are not the same cells that, early in human development, give rise to all the tissues of the body. But tumors are like other tissues in that they develop according to certain rules. Research on cancer stem cells aims to understand how this process unfolds and the roles of stem cells in that process. At the moment, cancer stem cells appear to be the driving force behind the development of some tumors, but beyond that there are more questions than answers.

"This field is in its infancy right now, and the cells themselves have only recently been described," said Dr. Michael Clarke of the University of Michigan Medical School in Ann Arbor, who led a team that identified cancer stem cells in breast tumors. His laboratory is trying to refine the techniques for isolating stem cells in human tumors so that researchers might one day routinely detect the rare cells in any tumor, if they are present.

The potency of cancer stem cells was illustrated recently in a study led by Dr. Peter Dirks of the University of Toronto. After isolating stem cells in human brain tumors, his team showed that these cells alone were able to initiate new brain tumors when transplanted into mice. The vast majority of brain tumor cells could not "seed" new growth, the researchers reported in the Nov. 18, 2004, issue of *Nature*.

If current notions about cancer stem cells are correct, then some chemotherapy and cancer drugs may be missing their most important targets, nearly wiping out whole tumors but leaving stem cells intact. Leading stem cell researchers, including Dr. Clarke and Dr. Irving Weissman of the Stanford University School of Medicine in California, believe that in order to cure cancer it is necessary to locate and kill tumor stem cells.

The hypothesis that stem cells may play a role in cancer is an old one, going back decades. But no one had been able to isolate the cells from tumors until 1994, when they were found in patients with acute myeloid leukemia. In recent years, cancer stem cells have been isolated in tumors of the breast and the brain and found in cancer cell lines, sparking new interest among researchers.

"The evidence that there are now identifiable cancer stem cells in solid tumors is, to my mind, revolutionary," commented Dr. Michael Dean of the Laboratory of Genomic Diversity, NCI-Frederick. "The concept of cancer as a stem cell disease could dramatically change our understanding of the disease and lead to new targeted approaches for treatment."

Dr. Dean and his collaborators have begun to investigate the mechanisms of drug resistance in cancer stem cells. The goal is to identify agents, such as the drug cyclopamine, that might prevent cancer stem cells from replicating.

Drs. Clarke and Weismann expect eventually to find cancer stem cells in most of the tumors they examine. The cells isolated to date have certain proteins on their surfaces that can serve as "markers" for tracking the involvement of cancer stem cells throughout a disease.

"Many people years ago thought that stem cells and cancer cells were similar because they self-renewed, but no one could test the role of stem cells in cancer because they had not been isolated," explained Dr. Weissman. "When you finally get to the point of isolating stem cells then you can begin to use markers to look at the stages of disease to see where stem cells are involved."

The origins of cancer stem cells are not clear. One theory holds that cancer stem cells were originally normal stem cells that acquired genetic mutations over time, predisposing themselves to becoming cancerous under certain conditions. Normal stem cells that maintain adult tissues such as bone marrow and skin have long life spans; they could accumulate the necessary mutations over decades.

Another theory says that cancer stem cells are actually adult cells that acquired the ability to self-renew through genetic changes. "There may be evidence for both theories," said Dr. Clarke. ◆

Cancer Research Highlights

Genetic Signature Associated with Breast Cancer Relapse

Scientists have identified a genetic "signature" associated with breast tumors that recur years after treatment. The signature is based on the activity of 76 genes and could potentially be a diagnostic tool for identifying patients at risk for relapse before they are treated, according to a study in the February 19 issue of *Lancet*.

Dr. John Foekens of Erasmus MC, Rotterdam, Netherlands, and his colleagues profiled gene activity in 286 tumors from patients with lymph-node-negative breast cancer who had not received hormone or chemotherapy after their initial treatment. Using DNA microarrays, they tracked nearly 18,000 genes, eventually pinpointing 76 that strongly correlated with the risk of recurrence. The researchers tested the signatures of those genes in 171 patients and accurately identified 93 percent of those who had relapsed within 5 years of treatment.

The ability to use genetic signatures to recognize tumors that are likely to recur after treatment could allow doctors to tailor treatment plans accordingly, sparing patients with good prognoses unnecessary therapy. Currently, there are no reliable diagnostic tools to predict which patients are likely to relapse.

Several recent studies have generated candidate signatures for breast tumors, but the authors of an editorial accompanying the new study observe that there is a "complete lack of agreement" among the lists of suspect genes. "Much larger numbers of observations" are needed to develop reliable consensus signatures, write Dr. Tor-Kristian Jenssen of PubGene AS, Vinderen, Norway, and Dr. Eivind Hovig of Norwegian Radium Hospital, Montebello, Norway.

Chronic Myeloid Leukemia Vaccine May Boost Remission Rate

A multicenter, observational study of 16 patients with chronic myeloid leukemia (CML) identified a vaccine that holds promise as an adjuvant therapy to imatinib (Gleevec) and interferon, the current treatments of choice for CML, according to a report in the February 19 issue of *Lancet*.

The study's authors, led by Dr. Monica Bocchia from Siena University in Italy, emphasized that the vaccine treatment was designed to further reduce any residual disease—after remission effects from one of the other drugs had leveled off—as well as to increase the number of patients able to reach complete cytogenic remission. The vaccine—known as CMLVAX100—is a multipeptide compound. It targets malfunctions at the p210 fusion point by generating peptide-specific CD8 and CD4 cells.

The study patients had all experienced varying degrees of remission while on chemotherapy with either imatinib or interferon; however, all had some residual disease at the molecular level. Their disease conditions had also stabilized for a median of between 10 months (imatinib) and 17 months (interferon), as indicated by bone marrow assessment for Philadelphia chromosome-positive cells, the marker traditionally used to measure CML at the cellular level.

After 6 vaccinations in 3 months, 15 of the 16 patients experienced further reductions of their disease, with 7 progressing to complete cytogenic remission. In addition, some of those who did progress to complete remission showed no detectable transcripts of the *BCR-ABL* gene, which encodes the p210 protein.

In an accompanying editorial, researchers at the Beckman Research Institute, City of Hope National Medical Center, noted that while imatinib had "revolutionized the therapy of CML," drug resistance and other factors would make a vaccine a welcome addition to the treatment arsenal.

New Biomarker May Improve Early Detection of Liver Cancer

Patients who have liver cirrhosis, an antecedent to liver cancer, can undergo frequent screening to catch cancer early, if it develops. But the current screening procedures for liver cancer, including ultrasound and blood tests (one of which detects alpha fetoprotein, or AFP), are not very reliable. However, researchers have identified a blood protein—des-gamma-carboxyprothrombin (DCP)—that may solve this problem, and NCI has launched a new clinical trial, led by Dr. Jorge Marerro of the University of Michigan and coordinated by Dr. Paul Wagner of NCI's Cancer Biomarkers Research Group, to determine whether an assay that detects DCP will improve the accuracy and sensitivity

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of liver cancer screening over the methods currently available.

DCP, a precursor to the protein prothrombin, is produced by the liver to help blood clot. DCP levels start to rise in patients with liver cancer, and this trend can be monitored through a blood test. The test kit, which was developed by Eisai Company and is being supplied to the study free of charge by this company, has shown 90 percent accuracy in detecting DCP.

Now the validity of that test will be measured through the EDRN-established phase II clinical validation trial conducted at six centers across the United States: University of Michigan; Mount Sinai Hospital in New York City; University of Pennsylvania; Mayo Clinic; St. Louis University; and Stanford University. Over the course of 2 years, researchers will monitor 450 patients who have liver cancer, 170 of whom are early stage, and a control group of 450 patients who have cirrhosis but not cancer. Data are expected in early 2007. "If DCP is proven as an early biomarker alone or as an adjunct to AFP," says Dr. Sudhir Srivastava, chief of NCI's Cancer Biomarkers Research Group, "it will trigger early intervention leading to a much needed effective clinical management of the disease."

NCI Researchers Improve Efficacy of Anti-Cancer Immunotoxin

NCI researchers have improved the anticancer immunotoxin HA22 by simply changing one amino acid in this protein. The researchers, led by Dr. Ira Pastan, increased HA22's toxicity to cancer cells over two-fold without producing any additional harmful side effects in mice. These results appear in the February 15 *Clinical Cancer Research* and demonstrate that genetic engineering can be used to increase the efficacy of immunotoxins and other drugs, allowing researchers to create the most effective drugs before clinical testing.

Immunotoxins, which are emerging as promising cancer treatment agents, are hybrid proteins comprising an antibody portion that selectively bind targets on the surface of cancer cells and a toxin that kills the cancer cell once it is internalized. The immunotoxin HA22's antibody component targets the surface protein CD22, which is expressed on many B-cell lymphomas and leukemias. Dr. Pastan and colleagues mutated the toxin's arginine 490 residue to an alanine, hypothesizing that altering this exposed portion of HA22 might increase its half-life in the blood and make it more resistant to degradation.

Interestingly, the engineered HA22 (R490A) did not have an increased half-life, but was still more effective than HA22. HA22 (R490A) was two to three times more toxic to several different B cell lymphoma cell lines and was also about twice as effective in reducing tumors in mouse models. At therapeutic doses, HA22 (R490A) was well tolerated in mice, causing some weight loss but no other adverse effects.

Higher PSA Yields More Biopsies, Early PLCO Data Show

Rates of biopsy among men with abnormal prostate-specific antigen (PSA) and digital rectal exam (DRE) tests show wide variance, according to some early data from the prostate cancer screening arm of the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial. Published in the March issue of the *Journal of Urology*, the study shows that at 3 years, of the 2,717 men who had a baseline positive PSA (greater than 4 nanograms per milliliter based on results from a central laboratory) at study entry, 41 percent had a biopsy within 1 year and 64 percent had a biopsy within 3 years. PSA scores of 7 ng/ml or higher were associated with significantly higher biopsy rates. Biopsy rates were lower among men who had positive DRE results but negative PSA results, with 27 percent of the 4,449 men in this category obtaining a biopsy within 3 years.

Diagnostic follow-up of PLCO participants was not included in the trial design, meaning that after screening, the decision for participants to undergo a biopsy or not was left to the discretion of treating physicians. Given the "large, geographically diverse sample of American men" participating in PLCO, said study lead author Dr. Paul F. Pinsky from NCI's Division of Cancer Prevention, "these results suggest that the experience of PLCO men in terms of follow-up biopsy is generally representative of current practice patterns in the United States."

A related commentary in the journal criticized the PLCO design for not requiring that participants undergo "effective therapy if cancer is found." In the study authors' published response, they explained that the design was necessary because "study investigators…work within a medical system of physician patient/autonomy, particularly those regarding the choice of diagnostic follow-up procedures or therapies." In addition, they argued, the study data "indicate that the medical community at large does not view immediate biopsy as the standard of care for all men with positive prostate cancer screens" and "clearly show that physicians are using clinical judgment in determining who should be biopsied." ◆

A Conversation with Dr. Javed Khan

Dr. Javed Khan is head of the Oncogenomics Section of NCI's Pediatric Oncology Branch. He trained at Cambridge University and came to the National Institutes of Health (NIH) in 1995. He joined NCI in 2001 and has made a number of contributions to the field of gene expression profiling while also focusing on the translation of these new discoveries into useful clinical tools. *(See story on page 1.)*

How does gene expression profiling work?

In brief, the idea is to see the forest for the trees. We have discovered that only about 3 percent of the human genome actually codes for some 25,000 genes that build specific proteins. How do you find which genes are on and which are off in cells? Even more importantly for clinicians, how does this affect the function of that cell?

Specifically?

We create small "chips" made of DNA fragments representing most of the genes in the human genome. In our new normal sample database, this means nearly 19,000 genes. Scientists then label the genes they are studying with fluorescence, and the DNA from those cells finds its match on the chip and lights it up. We know which gene it is because we built the coordinates of the chip map. Once you have a target organ or disease, you look for active genes with unusual expression profiles. We've built artificial neural networks that actually have "learned" to predict, correlating profiles to disease outcome better than the clinicians could.

Where do you see the field of oncogenomics headed?

I think the era of personalized medicine is on the horizon. Nanotechnology could one day replace the chemical nature of our microarrays with electronics, essentially hard-wiring a chip that would yield a definitive diagnosis from a small number of biopsy samples. If such nanodevices could be combined with sophisticated neural networks, they could be used both as diagnostic tools and as probes to look for specific biomarkers. Compared with current clinical approaches, these new nanodevices should be smart enough to yield profound results. ◆

Notes

NCI 2006 Budget Proposal Available on Web

NCI recently launched the HTML version of *The Nation's Investment in Cancer Research: A Plan and Budget Proposal for Fiscal Year 2006* online at http://plan.cancer.gov. On this site, users can take advantage of an enhanced search capability and click on links to other Web sites to view additional information on programs and topics highlighted in the document. This professional judgment plan and budget outlines NCI's vision for the future and the collective judgment of NCI staff, its advisory groups, and representatives of the cancer research and advocacy community regarding those activities and resources that will most effectively move NCI toward its Challenge Goal to eliminate the suffering and death due to cancer. The plan is built around seven strategic areas for new investment designed to help deliver the promise of improved patient care and public health for all. NCI will publish a companion progress report in the next few months to update the community on achievements in each of these strategic investment areas. Users can also download the document as a PDF from this site; hard copies can be ordered by sending an e-mail request to cisocc@pop.nci.nih.gov.

NCI Voted One of Best Work Sites for Postdocs

The NCI campuses in Maryland were named as the third-best work environment for postdoctoral researchers in the life sciences in the United States, according to the third annual Best Places to Work for Postdocs survey by *The Scientist* magazine. The Environmental Protection

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Agency campus in Research Triangle Park, N.C., and the Fred Hutchinson Cancer Research Center in Seattle, Wash., received first- and second-place honors respectively.

More than 3,500 postdoctoral fellows responded to the survey and cited a valuable training experience, access to research equipment and library resources, and good mentoring relationships as the ingredients that make for a good workplace. Full survey results are available in the February 14 issue of *The Scientist*.

In the United States, government institutions and private research centers accounted for 11 of the top 15 work environments. Institutions in Canada, Scandinavia, and the Netherlands occupy 11 of the top 15 spots for non-U.S. institutions.

PBS Documentary Features NCI

An hour-long documentary, *Cancer Cures?: Sesno Reports*, features interviews and footage of NCI leaders, as well as cancer patients being treated at the NIH Clinical Center. Hosted by former CNN reporter Frank Sesno, the program includes interviews with NCI Director Dr. Andrew C. von Eschenbach, Dr. Steven Rosenberg, Dr. Lee Helman, Dr. Harold Freeman, and others. A number of cancer survivors, including NPR Political Analyst Cokie Roberts, relate their personal stories, describing how they learned about their disease and how they found ways to cope and survive. The program focuses on medical progress against the disease, as well as new therapies under development.

The program will air on public television stations through the rest of the year. Check local listings for the air date and time.

NLM Lecture Focuses on Cultural Perceptions of Cancer

Dr. Keith A. Wailoo, Rutgers University history professor, with several published works on the history and sociology of science, spoke last week at the National Library of Medicine (NLM) about "Race, Science, and Cancer," a talk adapted from his upcoming book. In tracing the phenomenon of cancer, both within the African American community and the larger society in 20th century America, Dr. Wailoo illustrated why shifting perceptions—driven by cultural and technological events—have contributed to reasons why certain ethnic groups and special populations may not easily accept the cancer awareness message as it is often presented. For most of the century—for a variety of demographic, commercial, technological, and cultural reasons—cancer messages were tailored and directed primarily to white populations. This may have prevented the messages from being clearly translated into other groups' cultural contexts. A VHS tape of the lecture may be viewed at NLM or by contacting the NLM directly at (888) 346-3656.

Yeh to Speak at International Women's Day Celebration

On Tuesday, March 8, the NIH's Fogarty International Center and Office of Research on Women's Health will sponsor an International Women's Day celebration from 4:00–5:30 p.m., in Wilson Hall, Building 1, at the NIH Campus in Bethesda, Md. The celebration will feature panel discussions from international women scientists at NIH discussing their research and career paths. Among the featured speakers will be Dr. Grace Yeh, chief of CCR's Cellular Defense and Carcinogenesis Section in the Laboratory of Metabolism.

More information can be found at http://www.fic.nih.gov.

Polymer Engineering Leads to Drug Delivery Advances

Dr. Robert Langer, professor of chemical and biochemical engineering at the Massachusetts Institute of Technology, gave a talk on February 24 as part of NCI's Nanotechnology Seminar Series. Dr. Langer discussed the use of chemically engineered polymers to provide sustained release of a wide range of drugs and genes to treat cancer and other diseases.

Dr. Langer highlighted more than 30 years of work that, at nearly every step, has successfully challenged scientific dogma and produced new scientific insights into how to successfully deliver therapeutically important molecules in the human body. His initial work was instrumental in the discovery of angiogenesis inhibitors. Dr. Langer's work has lead directly to the development of therapeutics that millions of patients use every day.

Some of the examples he discussed included the development of chemotherapy wafers that can be implanted in the brain to slowly release a drug used to treat glioblastoma or implanted in the prostate gland to treat prostate cancer.

More information on the Nanotechnology Seminar Series can be found at: http://nano.cancer.gov/events_nanotech_seminar_series.asp ◆

Community Update

ACRIN Trial May Reveal a Definitive Role for Virtual Colonoscopy

Concurrent with the sixth annual National Colorectal Cancer Awareness Month in March, the American College of Radiology Imaging Network (ACRIN), a cooperative group funded by NCI, is launching a clinical trial to test the efficacy of computerized tomographic colonography (CTC), or virtual colonoscopy, as a screening tool for detection of colorectal cancer (CRC) at 15 centers across the United States. The National CT Colonography Trial is being led by principal investigator Dr. C. Daniel Johnson of the Mayo Clinic.

The slow, progressive nature of CRC permits detection and treatment of precancerous and localized cancers. Therefore, an enormous opportunity exists to save lives with early detection. Currently accepted CRC screening tools have limitations including poor sensitivity and specificity performance, patient risk, and compliance barriers. "Our goal is to validate a more acceptable and high-performance examination that will translate into higher patient compliance, more patients undergoing the screening exam, and consequently reducing overall colon cancer mortality," says Dr. Johnson.

While CTC is now technically feasible, there is conflicting evidence about its role compared with colonoscopy for CRC screening. Designed to assess CTC's performance versus the "gold standard" of colonoscopy and to address other pertinent CTC questions, trial data are expected to provide a balanced appraisal of the value and practicality of this promising screening tool.

The aims of the study address important clinical applications. These include:

- Assess the sensitivity and specificity of CTC to detect polyps or cancers of at least 1 centimeter, using colonoscopy as the reference standard.
- Evaluate inter-observer variability including any benefits of either a primary 3D read or an independent second interpretation.
- Describe the effects of different colon preparations on the accuracy of CTC.
- Measure patient acceptance of CTC as compared with colonoscopy.
- Estimate the accuracy of CTC to detect flat lesions and describe their various morphological features, distribution, and frequency.
- Report the prevalence and clinical significance of extra-colonic abnormalities detected by CTC.
- Assess differences in the various CTC software platforms by evaluating user preferences and performance differences.
- Develop a database of CTC case material for future studies including data appropriate for computer-aided detection development.
- Assess the cost-effectiveness of CTC as compared with other CRC screening tests.

For more information about the National CT Colonography Trial including a protocol summary and list of participating sites, visit http://www.acrin.org/6664_protocol.html.

The American Cancer Society has officially endorsed the trial to assist with patient recruitment efforts. ◆

Featured Meetings and Events

A comprehensive calendar of cancer-related scientific meetings and events sponsored by NCI and other scientific organizations is available at: http://calendar.cancer.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.

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