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Economic Analyses Of New Therapies Useful In Phase III Studies, Trialists Say

By Kirsten Boyd Goldberg

NCI should provide support for economic analyses of experimental therapies in conjunction with phase III trials, three clinical trials experts said to an institute advisory board.

"Cost effectiveness analysis" provides a standardized methodology for comparing benefits and costs of health interventions, Scott Ramsey, an oncologist and health economist at Fred Hutchinson Cancer Research Center, said to the NCI Clinical Trials Advisory Committee at its meeting June 15.

These studies try to answer the question, "Is the new treatment strategy cost-effective compared to standard care?" Ramsey said. Ideally, the studies are developed and conducted at the same time as a phase III trial, enabling researchers to track insurance reimbursement and resource utilization on the

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Capitol Hill:

A Provision Of The EARLY Bill Is Inserted Into House Appropriations For Labor, HHS

By Paul Goldberg

A key provision of the controversial legislation that would promote breast cancer screening to women under 40 has been inserted into the spending bill passed by the House Committee on Appropriations.

The appropriations bill for fiscal 2010 directed the Centers for Disease Control and Prevention to spend $5 million on "breast cancer awareness" for women under 40.

The measure mandates CDC to collaborate with HHS, NCI, and the Agency for Healthcare Research and Quality in developing "evidence-based initiatives to advance understanding and awareness of breast health and breast cancer among women at high risk for developing breast cancer, including women under 40."

The provision was included in response to a request by Rep. Debbie Wasserman Schultz (D-Fla.), a breast cancer survivor, a rising start in the Democratic Party and an appropriations committee member who has introduced a related stand-alone bill that proposes creating a CDC program that would teach breast self-exams to girls as early as in junior high school.

Critics—who include mainstream experts in public health and evidence-based medicine—say that such programs could do harm since there is no

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Economic Analysis Provides Cost Data Of Therapy A vs. B

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experimental and control groups as part of the trial.

At the trial's conclusion, a cost effectiveness analysis will provide the "incremental cost-effectiveness ratio" between two therapies. This is the ratio that is the result of total cost for therapy A minus total cost for therapy B, divided by outcome of the therapy A group minus the outcome of the therapy B group.

In the mid-1990s, NCI and its clinical trials cooperative groups became interested in doing these types of studies. "This is a field that sort of got off the ground, maybe a little ahead of its time," Richard Schilsky, professor of medicine at University of Chicago, said in introducing the discussion at the CTAC meeting. "There were committees formed in the cooperative groups to develop such studies."

With Congress recently appropriating $1 billion for comparative effectiveness research, "the time seemed right to revisit an issue that has been ongoing for quite some time in the context of clinical trials, and that is the potential role and utility of doing economic analyses as part of clinical treatment trials," Schilsky said.

Cost effectiveness analyses are conducted in conjunction with phase III trials, which seek to evaluate "efficacy" of therapies in rigidly controlled settings. This differs from comparative effectiveness research, which seeks to assess therapies in standard clinical practice (The Cancer Letter, July 3).

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Schilsky said that in recent years NCI lost interest in supporting cost effectiveness analyses. "There are many recent examples where cost analysis components [of trials] have been turned down, either on the basis that it was self-evident that one arm would be more costly than the other because one arm included an expensive new drug compared to the standard therapy, or the view that the NCI [Cancer Therapy Evaluation Program] no longer considered cost analysis to be part of their portfolio of research," said Schilsky, who is also a CTAC member. "No other sector within NCI has stepped up as far as I can tell to express a willingness to support these sorts of studies.

"In view of where we are now in the debate on health care reform and the cost of care, it seemed it might be good for this committee to revisit this issue, with the goal of understanding what the potential value added is of doing economic analyses as part of clinical trials, and some discussion of whether or not these types of analyses should be supported by NCI, and under what circumstances, in the context of what types of trials, and if there was a sense of this group that this is an area of research that should be supported, and how will it best be supported by NCI, and how might NCI create funding mechanisms to support this kind of work," Schilsky said.

Ancillary studies to trials can be difficult to fund. "This is not different conceptually from having a pivotal quality of life question, or a pivotal biological question, but they each have to be funded in their own right," Schilsky said.

Ramsey, who spoke to the committee by phone, said cost effectiveness analyses, when conducted concurrently with clinical trials, can provide more reliable data than post hoc analyses. Since cost effectiveness results would be produced simultaneously with clinical results, physicians, patients, and policymakers would receive more complete information on new treatments.

Piggybacking these analysis on to a randomized clinical trial requires modification of consent forms as well as staff time to design and collect health care utilization information and administer quality-of-life surveys.

"We don't need to do cost effectiveness studies alongside every clinical trial," Ramsey said. "We need to make choices about which ones are important to do this and which ones we don't have to worry about so much."

An example of a cost effectiveness analysis in conjunction with a clinical trial was Southwest Oncology Group's 9509, a randomized trial in untreated patients

with stage IIIb and stage IV non-small cell lung cancer, testing paclitaxel plus carboplatin (PC) vs. vinorelbine plus cisplatin (VC). The pharmaceutical companies sponsoring the drugs supported the cost effectiveness analysis in equal dollar amounts, Ramsey said.

The trial was started in 1996. Ramsey's paper on the economic analysis was published by JNCI Feb. 20, 2002.

Overall two-year survival in the PC group was 15 percent, compared to 16 percent in the VC group, with p=0.73, not a statistically significant difference. A quality of life analysis at 25 weeks also found no statistically significant difference.

In the PC group, the lifetime average cost was $43,522, compared to $33,209 for the VC group.

"This turned out to be an usual outcome, with quality of life and survival the same, what was left was comparing the cost," Ramsey said.

Schilsky noted that although paclitaxel didn't change the outcome or quality of life, and was more expensive, it has become the standard of care in this indication.

To select trials in which to perform cost effectiveness analysis, it would be important to look at burden of disease and the cost of the therapies, particularly if a potential new therapy is much more costly than the old therapy, Ramsey said. A new therapy that is much more effective might justify the cost. Also, if therapies have side effects that are costly to take care of, then the total cost might be different over the remainder of a patient's life.

"You might ask, is there a way to formally put all this together in terms of deciding which study should receive a cost effectiveness analysis, and there actually is an approach, called a 'value of information analysis,'" Ramsey said. "It's an exciting technique. I would expect if you undertook this for a lot of cancer clinical trials, you would find some that have extraordinary payoff in terms of the value of information."

Oncology spending is rising 15 percent annually, faster than total health care spending, Ramsey said. Much of the cost increase in oncology is driven by three factors: replacement of less expensive with more expensive treatments; more aggressive use of treatment and treatment combinations; and prolongation of the period of treatment.

To cope with increases in the cost of cancer drugs, health plans are instituting "tier 4 insurance," which increases co-payments for cancer drugs to 25 or 30 percent.

"The health plans are doing this simply based on the cost of the drugs, not on the value of drugs, and as a result, the patients who are undergoing treatment that might be very useful and might be cost-effective, are being punished just because the up-front cost of the drugs is so high," Ramsey said. "We view that as a problematic outcome in our current system and one that cost effectiveness analysis might address."

The financial cost of cancer can be substantial even among patients with health insurance, Ramsey said. A Kaiser Family Foundation study found that 25 percent of insured cancer patients use up all or most of their savings, 13 percent borrow from relatives, 7 percent receive public assistance, 7 percent have to take out a loan or another mortgage, and 3 percent declare bankruptcy, as a result of medical bills. In patients who lacked insurance at any point during treatment, 46 percent used up their savings, 30 percent borrowed money from relatives, and 6 percent declared bankruptcy.

"We think these trends are going to continue if we allow the current cost curves to continue for cancer," Ramsey said.

Ramsey pointed out two common misperceptions of cost effectiveness. "Just because something is costly doesn't necessarily mean it's not cost effective. An expensive treatment can be very cost effective if it provides a lot more life or better quality of life. Correspondingly, an inexpensive treatment can be a bad value if it doesn't add a lot to quantity or quality of life.

"Just because something is cost effective doesn't mean it is inexpensive. In fact, if we adopt cost effective therapies, we can increase our health care spending. It isn't necessarily going to bring our budget down to parity, but it could lessen the use of very expensive treatments that don't have high value.

Ramsey said the standard for assessment of cost effectiveness is set by the National Institute for Health and Clinical Excellence (NICE), a special authority in the United Kingdom's National Health Service.

NICE has been able to use cost effectiveness analysis in drug pricing negotiations with pharmaceutical companies, he said.

In 2008, NICE recommended that none of the four new drugs for treating advanced renal carcinoma—bevacizumab, sorafenib, sunitinib, and temsirolimus—should be used because they are not cost effective. After oncologists and patient organizations were outraged, NICE responded with a national survey to determine whether the population wants higher thresholds for treatments at the end of life.

In a related presentation to CTAC, Jane Weeks,

professor of medicine and health policy at Dana-Farber Cancer Institute and Harvard Medical School, said the first step cooperative groups would take in order to begin these studies is to determine which randomized trials would be suitable for economic analysis.

The Cancer and Leukemia Group B, developed three criteria for selection of trials for economic analyses:

—There's a reasonable possibility that the trial results could influence practice.

—A change in practice could have non-trivial cost implications.

—The expected differences in clinical outcome are likely to be relatively modest.

Weeks noted that cost effectiveness will vary with the disease setting. A small survival benefit in the adjuvant setting can result in a lot of extra life-years, which could result in greater cost effectiveness.

"In the popular press, the debate over cost effectiveness is all in the metastatic setting," Weeks said.

The metastatic setting presents greater challenges for cost effectiveness analysis, because the difference in cost between arms may be sensitive to second-line and later therapy, she said. This requires information on treatment after progression, and the capture of total costs of care. Also, quality of life during the added months is likely to be compromised, so that the value of a new therapy could be less.

Weeks said the process for targeting randomized trials for a cost effectiveness analysis would require:

—Systematic review of concepts to identify those that meet the pre-established criteria.

—Decision about whether to include an economic companion early in the protocol development process.

—True collaboration between the study chair and the individual leading the economic component.

Capitol Hill:

Appropriations Includes $5M For Breast Cancer Awareness

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evidence that would support it. The measure is called the Education and Awareness Requires Learning Young Act (The Cancer Letter, April 10, June 19).

In the House, EARLY, or HR1740, has 361 sponsors, more than enough to assure passage. However, in the Senate, the measure (S994) appears to have stalled with only 24 cosponsors.

The EARLY bill would give CDC $9 million a year between 2010 and 1014 to conduct a broader program. In a recent interview with the Minneapolis Star, Sen.Amy Klobuchar (D-Minn.), the sponsor of the Senate version of the bill acknowledged that "to get it passed, I think we're going to have to make some changes."

In the interview, Klobuchar said that the bill would target groups that are more likely to get breast cancer at a younger age. However, even in these groups, which include Ashkenazi Jews, the risk isn't high enough to justify screening at a young age.

The stand-alone bill by Wasserman Schultz and Klobuchar has run into significant opposition, triggering criticism from the National Breast Cancer Coalition as well as a flood of press reports that included the skeptical point of view. The American Cancer Society hasn't taken a formal position on the measure, but the group's chief medical officer and spokesmen have warned publicly about the potential for doing harm. The bill's supporters include Susan G. Komen for the Cure and the Young Survival Coalition.

Overall, the House bill added $38.4 billion to the President's budget proposal for CDC. This would include $5 million for the breast and cervical cancer screening program to start implementation of the mandate.

"As a member of the Appropriations Committee, Rep Wasserman Schultz requested this programmatic funding language and the Chairman included it," said Jonathan Beeton, a spokesman for Wasserman Schultz. "This does not relate to the EARLY Act, which is a separate piece of legislation that has been introduced in the House and the Senate, but has not been passed."

However, Beeton acknowledged the overlap. "The language is obviously similar in that it encourages the CDC, HHS, NCI and Agency for Healthcare Research and Quality to utilize the funds to develop evidence-based initiatives to advance understanding and awareness of breast health and breast cancer among women at high risk for developing breast cancer, including women under 40," he said.

The language of the House appropriations committee bill follows:

Breast cancer is the most commonly diagnosed cancer among women. Thare are approximately 180,000 new cases and 40,000 deaths from breast cancer annually. According to data from U.S. Cancer Statistics Report from 2001-2005, approximately five percent of all female invasive cancers are amomh women under 40 years of age. Raising awareness among providers and the public about the importance of early detection can result in improved outcomes and quality of life among cancer survivors.

Within the total for breast and cervical cancer, the Committee includes $5,000,000 for breast cancer awareness for young women. The Committee encourages CDC, in collaboration with HHS, The National Cancer Institute, and the Agency for Healthcare Research and Quality to develop evidence-based initiatives to advance understanding and awareness of breast health and breast cancer among women at high risk for developing breast cancer, including women under 40.

In the Cancer Centers:

Janet Rowley Named Winner Of Gruber Genetics Prize

JANET ROWLEY, the Blum-Riese Distinguished Service Professor at the University of Chicago, a founder in the field of cancer cytogenetics, will receive the 2009 Genetics Prize of The Peter and Patricia Gruber Foundation for her research on recurrent chromosomal abnormalities in leukemias and lymphomas. A 1998 recipient of the Lasker Award and the National Medal of Science, Rowley is also being honored for her "critical national and international leadership in the biomedical research community." The honor comes with a gold medal and an unrestricted cash prize of $500,000. It will be presented on Oct. 23 in Honolulu at the annual meeting of the American Society of Human Genetics. . . . **CITY OF HOPE** and Children's Hospital Los Angeles received $600,000 in grants for research from Think*Cure*!, the official charity of the Los Angeles Dodgers. The one-year grants support research in the development of new therapies to treat brain tumors, gene therapy for lymphoma, and a vaccine for leukemia. These are the first research grants awarded by Think*Cure*. A peer-based panel of cancer researchers reviewed the grant applications. The grantees are **Hua Yu,** professor of cancer immunotherapeutics and tumor immunology at City of Hope; **Robert Seeger,** director of the Cancer Research Program at Children's Hospital; **Karen Aboody,** assistant professor of hematology and neurosciences at City of Hope; **Rex Moats,** imaging scientist and researcher at Children's Hospital and director of its Saban Institute Small Animal Imaging Core; **Behnam Badie,** director of the Brain Tumor Program at City of Hope; **John Rossi,** the Lidow Family Research Chair and chair of molecular biology at City of Hope; **Don Diamond,** director of translational vaccine research at City of Hope; and **Anat Erdreich-Epstein,** director of basic and translational pediatric brain tumor research at Children's Hospital. . . . **DONALD SMALL**, a nationally recognized leader in the research and treatment of childhood blood cancers, has been selected to head the Pediatric Oncology Division of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins. After having spent 32 years at Johns Hopkins, with the last 19 as a member of the faculty, Small has been serving as acting director of the division since September 2006. Small said he will focus on expanding the childhood cancer program, both its clinical trials and research efforts. Small and his team were the first to clone the human FLT3 receptor gene, the most frequently mutated gene in acute myelogenous leukemia. He and his team then identified small molecules capable of inhibiting the receptor and killing the cancer cells while leaving normal blood cells unharmed. The work led to the design of clinical trials using one of these drugs, first as a monotherapy, and later in combination with chemotherapy for adults with AML. Most recently, the drug has entered clinical trials through the Children's Oncology Group for children with FLT3 mutant AML and infants with acute lymphocytic leukemia. Antibodies they helped to develop against FLT3 are also now entering clinical trials for leukemia. "Don embodies the philosophy and mission of Johns Hopkins in everything he does," said **William Nelson**, director of the Sidney Kimmel Comprehensive Cancer Center. "He's a dedicated physician, teacher and mentor, and among the nation's best researchers in his field." . . . **UNIVERSITY OF CHICAGO** opened the $244 million Gwen and Jules Knapp Center for Biomedical Discovery. The 330,760-square-foot facility is a state-of-the-art home for researchers working at the interface between basic science and medicine. They will translate fundamental scientific discoveries made by biologists and other scientists into the prevention, treatment and cure of diseases. The building is one of several clinical and research structures at the northwest corner of campus. It connects via third-floor bridges with the Gordon Center for Integrative Science and the Donnelly Biological Sciences Learning Center. Across the street is the Jules F. Knapp Medical Research Center. The new Knapp Center comprises the Ludwig Center for Metastasis Research; the Beverly Duchossois Cancer Laboratories; the Kovler Diabetes Center; and the Institute for Genomics and Systems Biology. It also houses researchers from the Department of Pediatrics; the Department of Biochemistry and Molecular Biology; and the Department of Medicine's Gastroenterology, Endocrinology, and Hematology/Oncology sections. . . . **AXEL ULLRICH**, director of the Department of Molecular Biology at the Max Planck Institute of Biochemistry in Germany, whose discoveries have led to novel cancer therapies including Herceptin, is

the winner of the 2009 Dr. Paul Janssen Award for Biomedical Research. An independent committee of scientists selected Ullrich, who on Sept. 8 will receive a $100,000 prize during a ceremony in Beerse, Belgium. . . . **TWO SCIENTISTS** at University of North Carolina at Chapel Hill School of Medicine, were named 2009 Clinical Investigators by the Damon Runyon Cancer Research Foundation: **William Kim**, assistant professor of medicine, and **C. Ryan Miller**, assistant professor of pathology and laboratory medicine. The recipients of this prestigious, three-year award are outstanding early career physician-scientists conducting patient-oriented cancer research at major research centers under the mentorship of the nation's leading scientists and clinicians. Each will receive $450,000 to support the development of his cancer research program. Kim, along with **Raj Pruthi**, professor of surgery, has been studying the role of EGFR inhibition in patients with bladder cancer. Kim will be mentored by **Charles Perou**, associate professor of genetics and pathology. Miller's research focuses on glioblastoma. Miller will work with pre-clinical molecular analyses and models to develop diagnostic tests to subtype glioblastoma with the goal of using these subtypes to develop clinical trials for specific subtypes of these tumors.. Miller will be mentored by Perou and **Terry Van Dyke**, the Sarah Graham Kenan Professor of Genetics.

In Brief:

Lawrence, Shipley To Receive ASTRO's Highest Honor

AMERICAN SOCIETY FOR RADIATION ONCOLOGY selected **Theodore Lawrence** and **William Shipley** as its 2009 Gold Medal recipients, the highest honor that ASTRO bestows. They will be presented with the awards Nov. 3, during ASTRO's annual meeting in Chicago.

Lawrence is an Isadore Lampe professor of radiation oncology, chairman of the Department of Radiation Oncology and a professor in the Department of Environmental Health, School of Public Health at the University of Michigan in Ann Arbor. He is also co-chair of the Radiation Sciences Program and head of the Experimental Irradiation Core of the University of Michigan Comprehensive Cancer Center.

Lawrence joined the faculty of the University of Michigan in 1987, following a fellowship in medical oncology and a residency in radiation oncology at NCI. He received his research degree in cell biology from the Rockefeller University in New York, followed by his medical degree from Cornell University and an internal medicine residency at Stanford University.

Lawrence serves as chairman of the NCI Board of Scientific Councilors and a member of the Institute of Medicine. He is also the editor of Translational Oncology, an editor of The Cancer Journal: Journal of the Principles and Practice of Oncology, and the associate editor of Seminars in Radiation Oncology. He is an ASTRO past president and former chairman of the board, and a past member of the ASCO board of directors.

He was also named by the ASTRO Board of Directors as one of the first general co-chairs of the of the Radiation Oncology Institute's Vision of Value fundraising campaign, which will raise money to help develop innovative ways of enhancing the profile of radiation oncology in the world cancer community and prepare the specialty for the future. His interests in the laboratory are focused on chemotherapeutic and molecularly targeted radiosensitizers, and his clinical research combines these laboratory studies with conformal radiation guided by metabolic and functional imaging for the treatment of patients with gastrointestinal and central nervous system malignancies.

Shipley is chairman of the genitourinary oncology unit at Massachusetts General Hospital and the Andres Soriano professor of radiation oncology at Harvard Medical School, both in Boston. He earned his M.D. from Harvard Medical School and completed a surgical internship and residency at Massachusetts General Hospital. Shipley then completed a residency at the Harvard Medical School Joint Center for Radiation Therapy, where he served as chief resident.

Since 1974, he has worked in various academic appointments for Harvard Medical School and in various hospital appointments at Massachusetts General Hospital; he also served as a visiting scientist at the Institute of Cancer Research at the Royal Marsden Hospital in Surrey, England, for two years in the early 1980s. Shipley is active in medical societies in the U.S. and abroad and has held committee appointments with several of these organizations, including the International Congress of Radiation Oncology, the International Society of Radiation Oncology, the National Bladder Cancer Group and the Radiation Therapy Oncology Group.

He was named a fellow of the American College of Radiology in 1988 and an ASTRO Fellow in 2006. Shipley has been involved with ASTRO's International Education Subcommittee since 2003, and in 2006, organized the first ASTRO-led international scientific

and educational meeting in the Philippines, which was designed to help strengthen ASTRO's involvement in radiation oncology abroad and collaborate with related specialty societies in other countries.

MELANOMA RESEARCH ALLIANCE announced nearly $2 million in grants to fund 13 individual scientists. For its second grant cycle, the MRA received 80 proposals from seven countries. Since MRA was founded in November 2007, it has awarded $8 million to 30 research programs.

Young Investigator Awards of $100,000 over two years: Zhen Cheng, Stanford University; Sanjev Kumar, University of Michigan; and Patrick Ott, New York University.

Established Investigator Awards of $225,000 over two years: Martin McMahon, University of California, San Francisco; Lynda Chin, New York University; TC Wu, Johns Hopkins University; F. Stephen Hodi, Dana-Farber Cancer Institute; Alexander Levitzki, Hebrew University of Jerusalem; and Roya Khosravi-Far, Beth Israel Deaconess Medical Center.

Pilot Awards of $100,000 over two years: Sancy Leachman, University of Utah; Maria Wei, North California Institute for Research and Education, University of California San Francisco; and Xue-Zhong Yue, Moffitt Cancer Center.

Development Award of $50,000 for one year: Nallasivam Palanisamy, University of Michigan.

MULTIPLE MYELOMA RESEARCH CONSORTIUM, a network of 15 academic institutions across North America, announced preliminary data from an analysis showing that clinical trials opened through its clinical trials network were activated 30 to 40 percent faster than comparable clinical trials in oncology.

Based on the implementation of specific business solutions, particularly scientific leadership, standardized clinical contracts and on-site project management resources, the MMRC has been able to decrease by an average of 100 days the time from the development and finalization of the trial's protocol to actual patient enrollment.

"This accelerated activation rate may help make myeloma more attractive from a development process as well as de-risk the process for our industry partners," said Susan Kelley, chief medical officer of the MMRC. "With so many new investigational agents in cancer clinical trials and escalating pressures to speed the time to completion of clinical trials, the MMRC is committed to sharing risk with the companies and investigators focused on myeloma to ensure that new treatments are delivered to patients as quickly as possible."

"The MMRF and MMRC provide an end-to-end solution for biotech firms and pharmaceutical companies partners seeking to advance promising drug leads into clinical trials," said Susan Molineaux, founder and chief scientific officer of Proteolix Inc., which has collaborated on two trials in the MMRC clinical trials network. "These new data underscore what Proteolix has already experienced in collaborating with the MMRC– speed, efficiency, and results."

Data on key activities related to clinical trial start-up were collected and analyzed from 12 phase I and II clinical trials conducted within the MMRC clinical trials network from May 2006 to March 2009. The analysis demonstrated that the trials initiated during 2007-2008, following the implementation of business solutions, were able to open to patient enrollment in an average of 158 calendar days, down from an average of 257 calendar days for trials initiated earlier in the history of the MMRC and consistent with published data about conventional experience with trial activation (Dilts and Sandler, JCO, 2006). This acceleration represents a 30 to 40 percent time-savings in the rate at which clinical trials were activated. Data will be submitted for presentation at an international scientific meeting later this year.

NCI News:

Method Tested To Screen Biomarkers In Patient Samples

A team of researchers has demonstrated that a new method for detecting and quantifying protein biomarkers in body fluids may ultimately make it possible to screen multiple biomarkers in hundreds of patient samples, to try to ensure that only the strongest biomarker candidates advance down the development pipeline.

The researchers developed a method with the potential to increase accuracy in detecting real cancer biomarkers that is highly reproducible across laboratories and a variety of instruments so that cancer can be caught in its earliest stages.

The results of the Clinical Proteomic Technology Assessment for Cancer study, sponsored by NCI and partner organizations, appeared online June 28 in Nature Biotechnology.

"These findings are significant because they provide a potential solution for eliminating one of the major hurdles in validating protein biomarkers for clinical use," said NCI Director John Niederhuber. "Thousands of cancer biomarkers are discovered every

day, but only a handful ever makes it through clinical validation."

The multi-institute nature of this work was critical because many other technologies have yielded test results that vary greatly from one laboratory to the next. NCI's Clinical Proteomic Technologies for Cancer (CPTC) program was established to help solve this problem. The five institutes that participated in this research include the Broad Institute of the Massachusetts Institute of Technology and Harvard; Vanderbilt-Ingram Cancer Center; University of California, San Francisco; Purdue University; and Memorial Sloan-Kettering Cancer Center.

The current biomarker discovery process typically identifies hundreds of candidate biomarkers in each study using small numbers of samples, leading to very high rate of invalid biomarkers. The biomarkers that are actually valid—that is, true biomarkers—must be culled from lengthy lists of candidates, a time-consuming and not always accurate process.

The CPTAC center network study demonstrates that new applications of existing proteomic techniques show promise of greater accuracy. The findings suggest that two technologies—multiple reaction monitoring (MRM) coupled with stable isotope dilution mass spectrometry (SID-MS), which is a technique used by protein scientists to measure the abundance of a particular protein in a sample—may be suitable for use in preclinical studies to rapidly screen large numbers of candidate protein biomarkers in the hundreds of patient samples necessary for verification.

MRM provides a rapid way to determine whether a candidate biomarker is detectable in blood. This is important for clinical use, as well as in being able to assess whether changes in a candidate biomarker correspond with the presence or stage of a disease. A sophisticated type of mass spectrometry, MRM is designed for obtaining the maximum sensitivity for quantifying target compounds in patient samples.

"Our work demonstrates that this technology has the potential to transform how candidate protein biomarkers are evaluated. SID-MRM-MS, combined with complementary techniques, could provide the critical filter to assess protein candidate performance without the immediate need for other detection or quantification tests. This would provide the critical missing component for a systematic biomarker pipeline that bridges discovery and clinical validation," said senior author Steven Carr, director of the Proteomics Platform at the Broad Institute. "This is an important step forward for the field of proteomics, one that would not have been possible without the collaborative efforts of the CPTAC partners."

The researchers demonstrated that MRM is highly sensitive and specific, important characteristics that ensure the detection of real disease-specific biomarkers. In addition, using common samples and standardized protocols, they found that MRM is highly reproducible across laboratories and technology platforms. Clinical Proteomic Technologies for Cancer will make common samples and standardized protocols available through its reagents data portal, which can be accessed at http://proteomics.cancer.gov.

This new work grew from a memorandum of understanding between the NCI (through Clinical Proteomic Technologies for Cancer) and FDA to accelerate proteomics technology development and application in clinical settings.

CPTAC's goal is to empower the research community with the tools and methods needed to translate proteomics from laboratory research to clinical utility.

Funding Opportunities:

Status of Applications and Awards under the New NIH Guidelines for Human Stem Cell Research http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-123.html

Building Interdisciplinary Research Careers in Women's Health (K12) (RFA-OD-09-006) http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-09-006.html

Development of New Technologies Needed for Studying the Human Microbiome (R01) (RFA-RM-09-008) NIH Roadmap Initiatives http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-008.html

Development of New Technologies Needed for Studying the Human Microbiome (R21) (RFA-RM-09-009) http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-009.html

Diet, Epigenetic Events, and Cancer Prevention (R01) (PA-09-234) http://grants.nih.gov/grants/guide/pa-files/PA-09-234.html

Diet, Epigenetic Events, and Cancer Prevention (R21) (PA-09-235) http://grants.nih.gov/grants/guide/pa-files/PA-09-235.html

AHRQ Grants for Health Services Research Dissertation Program (R36) (PAR-09-212) http://grants.nih.gov/grants/guide/pa-files/PAR-09-212.html

Improving Diet and Physical Activity Assessment (R21) (PAR-09-225) http://grants.nih.gov/grants/guide/pa-files/PAR-09-225.html

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