



VA ResearchCurrents

Update from the Office of Research and Development...

New funding program to encourage 'bench to bedside' research

By Nelda P. Wray, MD, MPH, *Chief Research and Development Officer*

A major RAND Health study published last month in the *New England Journal of Medicine* found that Americans, on average, fail to receive recommended health care nearly half the time. The study, conducted by a team including two VA researchers, was the largest and most comprehensive examination ever conducted of U.S. health care quality.

On a related note, the Institute of Medicine pointed out in its 2001 report "Crossing the Quality Chasm" that it takes an average of 17 years to incorporate into practice the knowledge produced in clinical trials.

These two reports, along with many others, indicate that health care in the United States is seriously troubled. Important biomedical discoveries stall for years before they can be tested in human studies. The knowledge produced in clinical trials encounters numerous obstacles that keep it out of clinical care. Because of these difficulties, many Americans are not getting the health care they need.

As the nation's largest health care system, VA must take the lead in solving these problems. One new initiative we have created to meet this challenge is the Bench to Bedside Translational Research (BBETR) program. This funding opportunity is intended to speed the translation of basic science discoveries into pre-clinical and clinical studies, and to

ensure that clinical findings drive best-practice health care. The program is also designed to encourage collaborations that might not naturally develop between basic scientists and practitioners working at different ends of the translational research continuum.

The program reflects a new spirit and direction in VA research, encouraging researchers from basic, applied pre-clinical, clinical and health services

areas to collaborate on research endeavors. Investigators from these different areas are invited to develop and submit proposals together, providing a plan for an intensive exchange of ideas in which bench findings are rapidly shared with clinical researchers—and, in turn, clinicians support and even guide the efforts of bench researchers.

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VA R&D website to get facelift

By Gerry McGlynn, *Information Dissemination Program Manager*

Mountains of information have been posted to the VA Research and Development (R&D) website (www.va.gov/resdev) since it was launched in 1996. The organizational framework of the site has remained the same, with only slight modifications to comply with VA web regulations and policies.

But change is in the air. We recently acquired the needed resources to create a state-of-the-art website. Charlie Festel has been brought on as the web project manager for R&D, and working together with the Information Dissemination Program staff, he will orchestrate the redesign and content enhancement process. The goal is to better serve the VA research community and all of our web users, including policymakers, managers, veterans and the public.

Our new site will have improved navigation and accessibility and better-organized information on topics such as training, career development and funding opportunities. Some content we hope to add includes:

- searchable database of study and citation information;
- catalogue of major accomplishments of R&D findings and breakthroughs; and

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The collaborative group on BBeTR proposals must include principle investigators (PIs) from at least three of the four research areas mentioned above. Creative collaborations aimed at expediting the movement of research findings to patient care are encouraged.

Proposals will be peer reviewed for scientific merit by committees consisting of basic and clinical research scientists. Particular attention will be focused on the collaborative and translational nature of the research; the extent to which PIs will interact and evaluate the progress of the research; and the potential of the project to affect clinical practice.

Awards will be for direct costs of up to \$300,000 per year for three years. Programs that document exceptional performance and a high potential for bringing their results to the bedside may qualify for additional funding.

A Request for Proposals will be issued shortly and posted on the VA Research website with full details.

The Bench to Bedside Translational Research program is among several initiatives we are pursuing to help make evidence-based medicine a reality for veterans and all Americans, and to enable us to achieve our vision: "Today's VA Research Leading Tomorrow's Health Care." ■

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researchinfo@vard.org

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- current content, i.e., feature articles on hot research topics, researcher profiles, center initiatives, awards, summaries of R&D press coverage, etc.

By analyzing web traffic reports and talking with VA research personnel in the field, we know that researchers and administrators are a primary audience for the R&D website. Therefore it is vital that we understand your preferences concerning web content and functionality. While we cannot guarantee a response to every request, we want to meet your needs and expectations to the extent possible.

There are two ways for you to communicate your ideas to us. We have created a short and completely voluntary input form on the R&D site at www.va.gov/resdev/webinput. Please take a few minutes to let us know how you currently use the R&D website and what you would like to see on the site. Or, you can send your comments to ORD.Web@med.va.gov. If you send e-mail, please indicate "Web Input" in the subject line. Your input by Aug. 11 would be most helpful.

When we have made some progress with design and content, we will conduct focus groups to check how we are doing. If you are interested in participating in a focus group, please indicate that in your message to us.

Initial work on the redesign has already begun, and our expected launch for the new site is early 2004. We will keep readers of *VA Research Currents* posted on our progress, and we look forward to your input and feedback. ■

Cleveland FES Center receives \$7.9 million grant from Ohio

The Cleveland FES Center, a VA-cosponsored program that has pioneered the use of functional electrical stimulation to restore motor function to those with paralysis and other disorders, has received \$7.9 million from Ohio as part of an initiative to advance the state's biotechnology industry.

The FES Center is a consortium of the Louis Stokes Cleveland VA Medical Center, Case Western Reserve University and the MetroHealth Medical Center, with additional funding from the National Institutes of Health and other sources. Under the directorship of P. Hunter Peckham, PhD, the center pioneered the development of "Free-hand," an artificial nerve system that enables a user with upper-limb paralysis to grasp objects. The center earlier this year implanted a diaphragm stimulator system in actor Christopher

Reeve to help him breathe for extended periods without a ventilator.

The new grant is part of a \$24.5 million package from Ohio's Biomedical Research and Technology Transfer Commission's Partnership Award program, designed to link academic research programs with commercial partners. Two other grants will support applied research in stem cell and regenerative medicine and advanced magnetic resonance imaging. The FES grant will partner the FES Center with two firms—NDI Medical and Johnson and Johnson Corp.—to develop and market FES technologies for patients with spinal cord injury, bladder and bowel disorders, sleep apnea, dysphagia and other conditions. The new collaboration will be called the Ohio Neurostimulation and Neuromodulation Partnership. ■

Selected findings

Studies confirm poorer cognitive performance in Gulf War veterans

Veterans deployed to the Persian Gulf in 1990 and 1991 scored worse overall on neuropsychological tests than non-deployed veterans in a series of studies by researchers at the Boston Environmental Hazards Center, part of the VA Boston Healthcare System. The five studies appear in the June 2003 *Journal of Psychopathology and Behavioral Assessment*.

In one study, Gulf-deployed veterans performed significantly worse than their non-deployed cohorts on tests of attention, visuospatial skills, visual memory, and mood. Among the deployed veterans, those who reported having taken pyridostigmine bromide—a pill given to some 250,000 Gulf War personnel as a preventive treatment against possible attack with the nerve gas soman—performed worse than those who had not taken the pill.

Past research on Gulf War veterans has shown they are at higher risk for a vague cluster of symptoms known as Gulf War illness, involving chronic fatigue, musculoskeletal problems, asthma, post-traumatic stress disorder, depression, memory loss, poor concentration and other health problems. However, there is still no definitive answer on the cause. Theories point to stress and other psychological factors; exposure to chemical or infectious agents or other environmental toxins; or side effects of anti-nerve gas agents.

Another of the five studies showed that symptoms of post-traumatic stress disorder were more prevalent in Gulf-deployed veterans, and that these symptoms were associated with poorer neuropsychological performance.

According to Roberta F. White, PhD, collaborator on four of the articles and author of the fifth—a review of existing research—there appear to be multiple causes of Gulf veterans' health problems: "The neuropsychological and health symptom sequelae of Gulf War zone service are multi-determined and cannot easily be explained on the basis of simplistic models of causation," wrote White. "Psychological, historical, and exposure parameters must be considered in the scientific evaluation of this problem."

Since 1994, the departments of Defense, Veterans Affairs, and Health and Human Services have spent \$213 million on 224 research projects relating to the health effects of military deployment. VA plans to spend up to an additional \$20 million in this area by the end of fiscal 2004.

Researchers inhibit spread of breast cancer in mice

Researchers at the San Francisco VA Medical Center have used modified version of a naturally occurring human protein to decrease the spread of human breast cancer implanted in mice. The findings appeared in the June issue of *Clinical Cancer Research*.

"We were able to significantly reduce the spread of the disease and decrease tumor growth without any evidence of toxicity," said senior author Gary Jarvis, PhD, a VA microbiologist and associate professor of laboratory medicine at the University of California, San Francisco.

As a way of targeting metastasis, coauthor Constance John, PhD, had proposed modifying a human protein known as galectin-3, a member of the family of proteins called lectins, which bind to sugar molecules on the surfaces

of cells. Galectin-3 is known to play multiple roles in cancer formation, including the promotion of cell-to-cell adhesion, or sticking. "The idea was to break that contact and inhibit secondary cancer formation," Jarvis said.

The researchers left the sugar-binding region of galectin-3 intact, but removed the part of the protein that normally allows cells to stick to one another. They then implanted portions of human-derived breast cancer tumors into the chest pads of nude mice, mice having a low-functioning immune system. Once the tumors were established, the researchers injected the experimental animals with truncated galectin-3. The control mice were given sham injections.

After 90 days, the team found that cancer had spread to lymph nodes or other organs in 4 of 20 experimental mice versus 11 of 20 control mice. In addition, the post-treatment growth of the implanted tumor fragments was significantly less in the nude mice than in the control animals. The modified protein did not cause any apparent adverse effects or death in the mice.

Jarvis believes that the modified version of galectin-3 was able to interfere with the breast cancer cells' ability to stick to one another and to the healthy cells of other organs. "The data support the hypotheses that truncated galectin-3 inhibits the process of metastasis," he said. ■

Epilepsy and aging explored

The Miami VA Medical Center is a cosponsor of the upcoming International Geriatric Epilepsy Symposium, to be held Sept. 12 – 14 in Coral Gables. Among the presenters will be James A. Rowan, MD, chief of neurology at the Bronx (NY) VAMC, and staff neurologist R. Eugene Ramsay, MD, of the Miami VAMC. For more information visit www.iges2003.com.

Cooper receives Magnuson Award

Rory Cooper, PhD, director of VA's Pittsburgh-based Center for Wheelchair and Related Technology, last month received the 2003 Magnuson Award from VA's Rehabilitation Research and Development service. The Magnuson Award, the highest award for VA rehabilitation researchers, is presented annually to an investigator who exemplifies entrepreneurship, humanitarianism, and dedication to veterans.

A leading authority on mobility, Cooper was recognized for pioneering work in wheelchair and related technology and for his role in building the careers of young VA scientists. Cooper has designed manual and electric-powered wheelchairs, developed wheelchair standards, promoted the understanding of secondary disabilities among wheelchair users, and improved the social integration of people with disabilities.

The department chair of rehabilitation science and technology at the School of Health and Rehabilitation Sciences, University of Pittsburgh, Cooper has authored or coauthored more than 300 publications and lectured at institutions around the world. He and his students have collaborated with assistive-technology professionals abroad—in India, Russia, Vietnam, Zimbabwe and several other countries—to support the development and local manufacture of affordable, high-quality wheelchairs. Cooper also received VA's Olin Teague Award in 2002 for research accomplishments on behalf of veterans with service-connected problems.

The Magnuson Award was established in 1998 in honor of Paul B. Magnuson, MD, a bone and joint surgeon and chief medical director for VA in the years after World War II. He initiated VA's university-affiliation model and was known for his dedication to finding innovative and individualized solutions for patients with disabilities. Magnuson Award winners receive a \$5,000 cash award and a plaque, along with an additional \$50,000 per year for three years to support a currently funded, nationally peer-reviewed research project. ■

Health services investigator featured in newsletter

Lisa V. Rubenstein, MD, MSPH, a VA health-services researcher who directs the Sepulveda-based Center for the Study of Healthcare Provider Behavior, was profiled in the June issue of *AcademyHealth Reports*. The newsletter is published by AcademyHealth, a 4,000-member Washington-based professional society for researchers, analysts and others involved in health policy.

Rubenstein is recognized nationally for designing and evaluating systems to improve health care, both in VA and non-VA settings. The recipient of VA's 2001 Under Secretary's Award for Outstanding Achievement in Health Services Research, she is credited with aiding VA's shift in the mid-1990s from hospital-based care to primary and ambulatory care. Rubenstein played a key role in the landmark Pilot Ambulatory Care and Evaluation (PACE) project, which helped make the Sepulveda VA Medical Center a national model for the transition.

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