

## Genomic medicine advisory group holds first meeting

**S**ecretary of Veterans Affairs James Nicholson personally welcomed the VA's Genomic Medicine Program Advisory Committee at its inaugural meeting on Oct. 16. The committee, composed of internationally recognized scientists and veterans' advocates, was established to advise VA on emerging issues in genomic medicine. It will assess the potential impact of a genomic medicine program on patient care and make recommendations on policies and procedures for tissue collection, storage and analysis, as well as on issues regarding privacy and security of the information.

The goal of the genomic initiative is to use genetic information to optimize clinical care of veterans and further the study and development of diagnostic tests and treatments for diseases

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## Probing the benefits of green tea

For many centuries, green tea has been consumed and used medicinally in India, China, Japan and other Asian countries. Today, millions worldwide not only drink green tea but look for it in their sunscreen, shampoo and even toothpaste. The website of one popular nutrition-supplement retailer lists no fewer than 740 products consisting of or containing green tea.

But is green tea really a health elixir, as many believe? And, of particular interest to many scientists: Can it fight cancer?

After studying the topic for 16 years, VA scientist Santosh Katiyar, PhD, MS, is convinced that green tea, because of its rich polyphenol content, is among the

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Illustration courtesy of Missouri Botanical Garden



Photo by Peter Guitton

Michael Fallon, DVM, PhD, is VA's chief veterinary medical officer.

## VA veterinary chief cited for leadership in Web-based training

Michael T. Fallon, DVM, PhD, VA's chief veterinary medical officer, has received the 2006 Joseph J. Garvey Award from the American Association for Laboratory Animal Science (AALAS) for his leadership in developing educational programs both for VA and the wider research community. The award includes a plaque and \$2,000 honorarium.

Fallon, who has been with VA since 1989 and in his current post since 1998, has spearheaded the development of Web-based animal-research training for VA staff and members of institutional animal care and use committees (IACUCs), which are required by federal law at any site with animal research. His program, accessible at [www.researchtraining.org](http://www.researchtraining.org), allows users to

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## Update from Health Services Research and Development

## State-of-the-art conference helps forge chronic-care research agenda

By Shirley Meehan, MBA, PhD, acting director

More than 120 million people in the U.S. have a chronic health condition, and 24 percent of those have three or more conditions, according to estimates in the Sept. 2004 update of “Chronic Conditions: Making the Case for Ongoing Care,” a publication of the Partnership for Solutions project of Johns Hopkins University and the Robert Wood Johnson Foundation.

The challenge to VA and other health care organizations is how best to serve the needs of patients with these complex chronic-care needs. To this end, VA’s Health Services Research and Development Service (HSR&D) hosted a two-day state-of-the-art (SOTA) conference on “Managing Complexity in Chronic Care” in Arlington, Va., in September.

More than 80 VA and non-VA policy-makers, researchers, managers and clinicians met to develop policy recommendations for VA and the larger healthcare community, and to help shape a research agenda to address the current knowledge gaps in managing complex chronic care.

The SOTA planning committee, chaired by Kevin Weiss, MD, MPH, director of



Kevin Weiss, MD, MPH.

HSR&D’s Midwest Center for Health Services and Policy Research, developed the conference agenda and commissioned seven papers as background for the SOTA deliberations, providing participants with a common base of knowledge to stimulate discussion.

In the keynote address, titled “Developing a Factual Basis for Caring for Veterans with Multiple Chronic Conditions,” Gerard Anderson, PhD, of Johns Hopkins University, said there is a lack of scientific evidence on treating people with chronic conditions because they are often not included in clinical trials. He stressed the need to include this important patient population in future trials, and to incorporate the care of multiple chronic conditions in physician training.

After the keynote talk, SOTA participants were divided into six workgroups. Each focused on a topic related to managing complex chronic care, such as the identification of patients with complex chronic illness; patient self-management; and informatics for complex chronic care. After a day of deliberations, each group presented

its findings and recommendations. On the second day of the conference, a panel discussion was led by Joseph Francis, MD, VA’s acting deputy chief research and development officer. Also taking part were Joel Kupersmith, MD, VA’s chief research and development officer; Madhulika Agarwal, MD, chief patient care services officer; Ira Katz, MD, PhD, deputy chief patient care services officer for mental health; and Robert Petzel, MD, director of the VA Midwest Health Care Network.

Several products will be developed and disseminated based on findings from the conference. One product already under way is a special supplement of the *Journal of General Internal Medicine*. Papers to be submitted for the supplement will cover topics such as developing the evidence base for managing patients with complex chronic illness; improving systems to achieve this goal; and linking system and patient strategies. In addition, a research agenda will be developed to generate knowledge that will help VA provide the best possible care to veterans dealing with chronic illness.

## VA statisticians’ group

The VA Statisticians’ Association, formed in 2005, invites VA-affiliated statisticians to join. Email your contact information to Laura Rabuck at [Laura.Rabuck@va.gov](mailto:Laura.Rabuck@va.gov). More details are available on the VA HSR&D website at [www.hsrd.research.va.gov/for\\_researchers/vasa](http://www.hsrd.research.va.gov/for_researchers/vasa).

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most potent tumor-inhibitors that nature provides. In general, he is a feisty proponent of the Hippocratic maxim “Let food be thy medicine and medicine be thy food.”

In the Oct. 16 online edition of the *Journal of Nutritional Biochemistry*, Katiyar reviewed the latest biomedical findings on green tea and skin cancer, including those from his own animal studies at the Birmingham VA and University of Alabama. He outlined five mechanisms through which green tea’s most prevalent and active polyphenol—a robust antioxidant called epigallocatechin-3-gallate, or EGCG—appears to protect the skin from ultraviolet (UV) radiation and prevent tumor formation.

### Green tea boosts interleukin-12

One of those pathways was recently elucidated for the first time in an article published by Katiyar’s group in *Cancer Research*. They showed that EGCG prevents UV-induced cancer in mice through a DNA-repair mechanism involving interleukin-12, an important immune-system chemical.

Experts believe most skin cancer is caused by solar UV light that penetrates the skin’s top layer and strikes DNA molecules in the chromosomes, causing harmful mutations. The process is aided by oxidative stress and inflammation.

“The polyphenols in green tea have strong antioxidant and anti-inflammatory properties,” said Katiyar, “but more importantly, they enhance the production of interleukin-12, which has a role in DNA repair. If green tea polyphenols can repair DNA, then they can prevent skin cancer.”

In their experiments, Katiyar’s team exposed two groups of mice to UV radiation and measured the DNA damage that occurred. Then, they treated one group with a topical application of EGCG and left the



Santosh Katiyar, PhD, Birmingham, has found that administering green-tea polyphenols to mice in their drinking water protects against solar ultraviolet-induced skin cancer. He has also helped elucidate the mechanisms responsible for the effect.

other group untreated. In the treated mice, the formation and spreading of tumors were markedly reduced. Furthermore, DNA damage was resolved more quickly in these mice. However, when the same treatment was given to mice lacking the gene that codes for interleukin-12—IL-12 knockout mice—EGCG’s protective effect disappeared.

These and other lab results may be compelling, but as far as the U.S. Food and Drug Administration is concerned, the jury is still out, pending stronger clinical evidence. A 2005 statement appear-

ing on the FDA website asserts, “Existing evidence does not support qualified health claims for green tea consumption and a reduced risk of [prostate, breast or] any other type of cancer.”

Katiyar suggests that some epidemiologic and clinical studies on green tea and cancer may have failed to adequately control for variables such as climate, race, diet and frequency of tea consumption, which can dramatically influence green tea’s effects.

### Preparing the perfect cup

A native of India who became a U.S. citizen in the 1990s, Katiyar drinks two cups a day of green tea. He says people with fairer skin, who are at higher risk for skin cancer, may need to drink up to six cups per day to derive benefit.

For the perfect cup of tea, he advises that people boil water, remove it from the heat, and then steep the leaves, covered, for four or five minutes. “In that time, most of the polyphenols will dissolve in the warm water. If you boil it with the leaves in it, the

### What is green tea?

The three main types of tea—black, green, and oolong—all come from the same plant: *Camellia sinensis*. The difference among them is how they are processed. Black tea is fully fermented, oolong is partially fermented, and green is unfermented. Research suggests that each type of tea may possess unique beneficial compounds.



# Brain-rehabilitation innovator receives VA's Magnuson Award

**L**eslie Gonzalez Rothi, PhD, program director of VA's Brain Rehabilitation Research Center (BRRC) in Gainesville and professor of neurology at the University of Florida, has received this year's Magnuson Award. The award is VA's highest honor for rehabilitation investigators.

Gonzalez Rothi, the first woman to receive the award since it was instituted in 1998, was cited, among other accomplishments, for her "ability to bring people together to work toward a common goal." She and her center's team of biomedical engineers, neurologists, therapists, and psychologists have been credited with helping to show that patients who have had a stroke or other neurological injury can continue to benefit from treatment for longer periods than were previously thought possible.

In an editorial in the May/June 2006 issue of the *Journal of Rehabilitation Research Development (JRRD)*, Gonzalez Rothi and coauthor Anna M. Barrett, MD, wrote: "In the past, clinicians and the lay public pervasively believed that stroke recovery was very limited. We are now entering an exciting period in poststroke care in which the time span and extent of continued improvement is extending incredibly. ... The articles in this issue demonstrate the powerful synergy of a scientific culture that seeks to dissolve barriers to continued progress for people with chronic poststroke deficits..."

Gonzalez Rothi, who has served as president of the International Neuropsychological Society and had a number of other leadership roles in the research and therapy community, has championed the integration of phase 1 and 2 exploratory studies into her center's research. For example, she and her colleagues reported earlier this year in *JRRD* on the partially successful results

of an intensive "phonomotor rehabilitation" program—a treatment adapted from therapy traditionally used for children with dyslexia—designed to improve the speech of a 73-year-old man who had suffered a stroke 11 years earlier.



Leslie Gonzalez Rothi, PhD

Gonzalez Rothi has also influenced basic and applied scientists to work together more closely to identify new approaches to neurorehabilitation. Her center's innovative research includes studies on physical,

speech and cognitive therapies; drug treatments; brain-imaging techniques to study changes associated with treatment; interventions to enhance daily life for patients with brain injuries; and telecommunication technology to evaluate treatments.

The Magnuson Award is named for Paul B. Magnuson, a bone and joint surgeon and chief medical director for VA in the years after World War II. The award is given annually to VA rehabilitation investigators who display entrepreneurship, humanitarianism and dedication to veterans, in the spirit of Magnuson. Winners of the award receive a \$5,000 cash prize and a plaque, along with an additional \$50,000 per year for three years to supplement ongoing peer-reviewed research.

## Career milestones

**Bruce Sangeorzan, MD**, director of VA's Seattle-based Center of Excellence in Limb Loss Prevention and Prosthetic Engineering, is this year's recipient of the Sustaining Membership Lecture Award from AMSUS, the Society of Federal Health Agencies. The award, which includes a plaque and honorarium, is given annually to a federal health practitioner for outstanding contributions to medical research.

**Theresa Pape, DrPH, MA**, a research career scientist at the Hines VA Medical Center, received the 2006 James Brady Award from the Brain Injury Association of Illinois. The award is given for contributions to increased societal awareness of brain injury. Pape, who has been funded both as a health-services and rehabilitation investigator, focuses on measurement, treatment and outcomes relating to traumatic brain injury.

**David Relman, MD**, is one of 13 recipients of the 2006 Director's Pioneer Award from the National Institutes of Health. Relman, chief of infectious diseases at the VA Palo Alto Health Care System and associate professor of microbiology and immunology and of medicine at Stanford School of Medicine, will study indigenous microbial communities that exist with the human body, with the goal of producing new insights to guide disease management and preventive care. The NIH award, which provides each winner with \$2.5 million over five years, funds scientists with creative ideas who propose novel approaches to major challenges in biomedical research. The award was characterized by NIH director Elias Zerhouni, MD, as "one way we are exploring the funding of unconventional ideas that are promising but might not fare well in the traditional peer-review system."

## New CDC guidelines on HIV screening reflect input from VA study

**T**he U.S. Centers for Disease Control and Prevention recently announced new voluntary guidelines recommending that all Americans ages 13 to 64 be screened for HIV, the virus that causes AIDS. Previous guidelines recommended testing only high-risk individuals, such as those with multiple sex partners. The new guidelines were influenced by research published last year in the *New England Journal of Medicine* (see VA press release at [www.research.va.gov/news/press\\_releases/hiv-012705.cfm](http://www.research.va.gov/news/press_releases/hiv-012705.cfm)). Senior author on that article was Douglas Owens, MD, a physician and health-services investigator with the VA Palo Alto Health Care System, and associate professor at Stanford University School of Medicine. Owens' group found that expanding HIV screening would be a cost-effective way to increase life expectancy and decrease the transmission of HIV. In a recent interview with Stanford's press office, Owens discussed his group's work and the new screening guidelines.

### **Question: Why does this new policy matter?**

**Owens:** The policy is a profound change because it advises that all individuals ages 13 to 64 be screened for HIV. It matters because it will identify people who have HIV but don't know it. They will benefit because they'll have access to life-prolonging drugs that they otherwise might not have received until very late in the course of HIV disease. The rest of the community will also benefit, through reduced transmission of HIV.

### **Q: How did your findings contribute to the CDC adopting the new guidelines?**

**Owens:** First, we found that widespread screening provides a substantial health benefit to HIV-positive people who are identified through screening and receive anti-retroviral treatment earlier than they



Photo by Chard Rappell

Research by a team led by Douglas Owens, MD, of the Palo Alto VA and Stanford University, helped guide the Centers for Disease Control and Prevention in updating its recommendations on HIV screening.

would have otherwise. Early treatment added about a year and a half of life expectancy for these people. Second, we found a substantial potential benefit to the community because of reduced transmission of HIV. Transmission is reduced because many people cut down on risky behaviors when they're identified as having HIV, and because anti-retroviral treatment makes a person less infectious. Our key finding was that screening is cost-effective even if only one in 2,000 people who are screened has HIV. This means HIV screening is cost-effective in a much broader group than recognized previously.

### **Q: Did you and your colleagues play a role in the decision-making?**

**Owens:** CDC officials made this change because they saw mounting evidence that the prior approach to screening wasn't working. If you test people based on risk behavior, you miss many people who have

HIV. We also know that most people who have HIV are diagnosed very late in the disease, when they can't fully benefit from anti-retroviral therapy. Our involvement in the decision-making was to help assess the prevalence of HIV at which routine screening would be recommended. Through several conference calls with CDC officials, we presented our work and explained the issues related to cost-effectiveness and prevalence. Based on those results and the results of a similar study from Yale, the agency went in the direction of lowering the threshold for screening quite substantially—to 1 in 1,000 from a prior threshold of 1 in 100.

### **Q: Will most physicians follow the new guidelines?**

**Owens:** That's the big question. The previous CDC screening guidelines were not widely adopted. The new recommendations

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of particular relevance to veterans. The advisory committee may also make recommendations concerning the development of a research agenda and approaches by which research results can be incorporated into routine medical care.

Joel Kupersmith, MD, VA's chief research and development officer, emphasized to committee members that their input will be crucial in guiding the scope of the program. He also said he looked forward to establishing a structure that would bring together the most knowledgeable experts to assure the success of the program.

During the meeting, the committee identified unique advantages of VA that should allow it to successfully initiate a genomic medicine program: the altruism of veterans; the electronic health record; and the integration of care and research within the Veterans Health Administration. The group approved of the development of appropriate collaborations with other federal agencies, and with academia, foundations, and industry. They also stressed the need to maintain the highest ethical standards, and to meticulously protect veterans' privacy and avoid the misuse of their genomic data. They also noted the importance of establishing and maintaining effective dialogues with veterans to promote understanding about the advantages of genomic medicine.

In addition, committee members emphasized the pressing need for large prospective studies to elucidate phenotype and genotype associations. The group recommended that VA pay close attention to the work of other institutions addressing questions related to genomic medicine, and review and adapt recommendations for VA use where appropriate. In the future, the committee plans to develop working groups and recruit additional input and expertise to address specific issues. ■

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are much easier to adopt, because they don't depend on clinicians' determining the prevalence of HIV in their patient population. Still, it will take a lot of follow-up to make sure physicians implement the guidelines. One key obstacle will be getting payers to reimburse for HIV testing. That's a critical issue, which the CDC is aware of.

**Q: Some HIV/AIDS advocates object to the new guidelines because they recommend removing two requirements that some states have: mandatory, signed consent forms and counseling before testing. Would removing the two requirements be a big problem?**

**Owens:** It's important to emphasize that the new guidelines say people should always be informed before testing and should be able to decline. Informed consent and pretest counseling had become important barriers that were preventing people from being tested. Everyone agrees that no one should be tested without their knowledge, but that doesn't mean you need a separate consent form. Of course, the confidentiality of the test results should continue to be carefully protected. I would also note that some states have laws that require informed consent—whether they will change these laws is not clear. ■

## Rapid testing for HIV may boost screening rates

Standard HIV screening tests require patients to return several days later for their results and post-test counseling. However, according to research, as many as 3 in 10 of those who test positive and 4 in 10 of those who test negative for HIV never come back for their results.

A study funded by VA's Quality Enhancement Research Initiative (QUERI) and presented at the 16th International AIDS Conference in August 2006 found that rapid testing for HIV, which has become increasingly available in the past few years, may not only increase the percentage of patients who collect their results, but sway more patients to get tested in the first place. Rapid testing most often involves an oral swab, and results can be available in 20 minutes.

The study, which included 189 veterans at the West Los Angeles VA, found that those who were referred to a nurse for a rapid HIV test and streamlined counseling were far more likely to get tested and retrieve their results than those prompted to ask their doctor about testing, or those referred to a nurse for standard testing. ■

## Will the new guidelines change VA practice?

VA already offers voluntary HIV testing, with written consent, for all patients and provides documented pre- and post-test counseling, as required by federal law. Will the new CDC guidelines (*see story starting on pg. 5*) change VA practice?

In a memo to VHA clinicians after the latest CDC guidelines were released in September, Ronald Valdiserri, MD, MPH, chief consultant for VA's Public Health Strategic Healthcare Group, reiterated the "importance of offering every veteran under VA care the opportunity to have a voluntary HIV test." He added that VA "will continue to promote efforts to reduce barriers to diagnosing HIV in a timely manner." However, he pointed out that "the new CDC recommendations do not supersede current VA regulations." In an interview, Valdiserri stressed that VA "encourages all veterans to talk with their providers about the importance of routine HIV testing." Full details about VA's HIV testing program are available at [www.publichealth.va.gov/hiv\\_testing.htm](http://www.publichealth.va.gov/hiv_testing.htm).



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self-register, take courses and exams, and print certificates. In addition, local research administrators can view and print records of staff participation. The site now boasts more than 75,000 registered users, more than 90 percent of whom are employees with VA or its university affiliates.

Coded by programmer Stephanie Manuel of Fallon's office, the software has also been adapted by AALAS for its own online training programs, and licensed to the Collaborative Institutional Training Initiative (CITI)—a program based at the University of Miami—for use in training some 20,000 healthcare workers each month in human-subjects protection.

### From fish to ferrets

According to AALAS past president and Seattle VA veterinarian Cynthia Pekow, DVM, who nominated Fallon for the award, he is highly qualified to develop veterinary training programs because of his rich experience in the field. Since getting involved with animal research in the late 1970s, Fallon has filled diverse roles: animal caretaker, bacteriology technician, veterinarian, principal investigator, text author, administrator, instructor, and IACUC member.

"The breadth of experience Mike has in the lab animal field ... has allowed his keen understanding of what types of training and educational programs are needed in our field, and what approaches are likely to be successful," said Pekow.

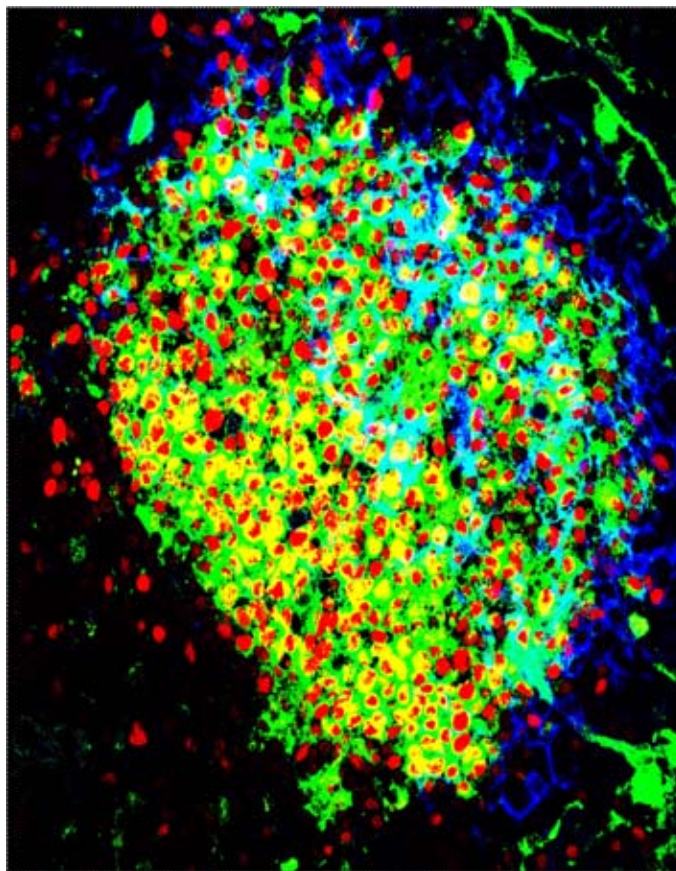
Fallon, whose office includes a part-time staff scientist and full-time programmer, is involved in more than education. In fact, most of his time is spent providing consultation to IACUCs, investigators and support staff at the 76 or so VA sites with animal-research programs. These sites house creatures ranging from Zebra fish, frogs and ferrets to chickens, cats, and even primates—in addition, of course, to lots of mice, rats and rabbits.

### Building networks among veterinary staff

"Most of my job is providing support and answering questions that come in by email or phone," said Fallon. He also helps people network: "We're essentially creating a self-supporting community of people who can share information and ask each other questions."

But it's mainly the training piece that has gained him recognition from AALAS. Partly because of his experience as a PI, Fallon saw the need early-on for an efficient way for VA physician-investigators—and others with tight schedules—to complete their required training.

## The 'art' of science



### Immune insights

This image was produced through immunofluorescent staining of mouse spleen tissue in the Birmingham VA lab of rheumatologist Robert Carter, MD, as part of the group's research on B cells, a type of lymphocyte that makes antibodies and presents antigens to other immune cells, among other roles. The slide shows that germinal center B cells (shown in green) undergo cell division (indicated by the proliferation marker Ki67, in red) in and outside the area of follicular dendritic cells (blue), another type of antigen-presenting cell. One aim of Carter's work is to explore the depletion of B cells as a potential therapy for autoimmune diseases.

"When we started," said Fallon, "you could find a lot of programs that people were using for college classroom situations, but no one had software focused on researchers who simply wanted to go in, do their compliance training, take their test, and be done."

Fallon noted that federal and VA regulations concerning animal research have become more stringent in recent years. And while he acknowledges that not everyone in the field might agree with him, he thinks lab animals—and the quality of the research—are benefiting as a result. "It's dramatic. I see tremendous improvement

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in the care of animals and the quality of the oversight. There's more awareness of the ethical issues, and more consideration of what's best for the animal in terms of housing, pain relief, surgical support, anesthesia."

### 'Walking a tightrope'

Those involved with animal research are not oblivious to the controversy surrounding their work. But Fallon and other lab veterinarians point to a long list of lifesaving medical advances that would not have been possible without tests on animals.

"The veterinarians' oath not only requires them to protect the health of animals, but to support the investigation of new knowledge that benefits mankind, and to serve the public health," explained Fallon. "So a lot of animal research is at the intersection of those two ideas. There's always a tension between what is best for the animal and what might be best for science. That's the tightrope we and the IACUCs have to walk."

He described animal caretakers, who account for many of his training website's clientele, as "unsung heroes" who play a critical role in this research effort.

"Animal research simply cannot be performed unless the caretakers are doing their job every day," said Fallon. "If the animals are not fed and watered, and they're not clean, the experiments are going to be altered. We would lose public confidence in what we're doing. The quality of the science depends on the animal caretakers as well as the investigators."

Fallon's greatest satisfaction, he said, is seeing his work and that of his veterinary colleagues facilitate advances in health care. "The thing that gives me the most pleasure is to make life easier for the investigators and administrators—to help them do their jobs and conveniently meet their training needs. Because those are the folks who are actually making the breakthroughs that help our veterans." ■

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polyphenols may get oxidized and polymerized and reduce their activity."

The researcher, who has been funded by VA as well as the National Center for Complimentary and Alternative Medicine and National Cancer Institute, believes military personnel may be at special risk for skin cancer, given their increased exposure to sunlight. That is part of what motivated him to join VA in 2003 and conduct research on behalf of veterans. More than a decade earlier, his initial passion for exploring natural cancer therapies had centered on quite a different population: mothers.

"I lost my mother to breast cancer," shared Katiyar. "I had done my PhD in nutrition, and I realized that my parents had devoted a lot of time and energy to my education. Yet, I could not help my mother. So I resolved to do something to help all the other mothers who are still here. I decided I would work on cancer—how it can be prevented, particularly by dietary supplements and nutrients." ■