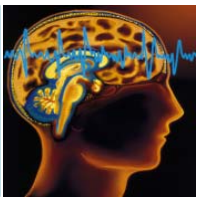
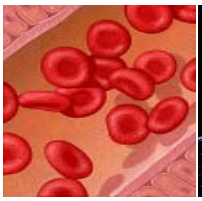
VA RESEARCH CURRENTS

NEWS FOR THE RESEARCH COMMUNITY OF THE U.S. DEPARTMENT OF VETERANS AFFAIRS • JULY 2006

VA team unlocks key to promising brain drug

Researchers at the San Francisco VA Medical Center have identified the mechanism by which minocycline, a medication being studied for the treatment of Parkinson's disease and other neurodegenerative conditions, protects brain and nerve cells. In a cell-culture study, the team determined that the drug blocks the action of poly(ADP-ribose) polymerase-1 (PARP-1), a protein that can trigger inflammation and cell death.

The way in which minocycline works had been unclear, according to lead investigator Raymond A. Swanson, MD, chief of neurology and rehabilitation at the San Francisco VA, and professor and vice chair of neurology at the University of California, San Francisco. "Minocycline turns out to be an extraordinarily good PARP inhibitor, better than most of the drugs that are marketed as PARP inhibitors," he said.

The paper appeared in the June 20 issue of the *Proceedings of the National Academy of Sciences.*

Swanson said the new findings link two previous observations. The first is that PARP-1, a protein found in every cell, becomes activated whenever a cell's DNA is damaged. Depending on the nature and extent of the damage, PARP-1 can trigger either DNA repair, an inflammatory response, or apoptosis—so-called cell suicide. "In stroke or neurodegenerative diseases, inflammation is basically a bad

see **DRUG** on pg. 6

'FRAC' members reflect on progress, challenges

"Communication, communication, communication."

That's how Rita Young, PhD, succinctly describes the value of VA's Field Research Advisory Committee (FRAC) as it enters its third year. Young, associate chief of staff for Research at the Charleston VA Medical Center, says among the FRAC's specific accomplishments have been "redoing the R&D Handbook, and affirming the importance of non-clinicians in VA research and recommending how to maintain their presence without squeezing out clinician investigators."

Young represents non-clinician investigators on the nine-member panel, formed in July 2004 to facilitate communication between the field and Central Office, provide input on issues affecting VA research, and help with strategic planning. The group also includes five associate chiefs of staff for research; two center-of-excellence directors; and a Cooperative Studies Program study chairman *(see box for roles and affiliations)*. Also taking part in the group's quarterly meetings are Service directors and the chief research and development officer (CRADO). Jay Freedman, PhD, special assistant to the CRADO, coordinates the effort.

According to veteran and outgoing members, the FRAC has made huge gains in its first two years, but also faces significant challenges.

see **FRAC** on pg. 5

Robert Pollet, MD, PhD, chief of R&D at the Atlanta VA Medical Center and an outgoing FRAC member, says the group has helped establish "an atmosphere of genuine cooperation" in support of research.

Study highlights collaborative care for bipolar disorder

In a three-year randomized controlled trial involving 306 veterans with bipolar disorder, those receiving care through a new collaborative model had better clinical and functional outcomes than those in usual care, with no added costs. The study, funded by VA's Cooperative Studies Program and conducted at 11 VA medical centers, is published in a two-part report in this month's issue of *Psychiatric Services.*

At the core of the collaborative model were "specialty teams" of psychiatrists and nurse care coordinators. Nurses enrolled patients in group psychoeducation to improve their self-management skills, and worked to ensure prompt access to medical care and proper follow-up. Team psychiatrists relied on a simplified version of VA clinical guidelines for bipolar disorder, designed to aid effective prescribing.

Over three years, veterans treated through the collaborative model had 6.2 fewer weeks in an affective episode, compared with usual care. The biggest improvement was a reduction in manic episodes. Compared to those in usual care, these patients also showed more functional gains, and reported higher mental health quality of life and treatment satisfaction.

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Mark S. Bauer, MD (facing camera), of the Providence VAMC and Brown University, chaired a VA study on bipolar disorder.

Research Currents interviewed Mark S. Bauer, MD, a psychiatrist with the Providence VA Medical Center and Brown University, to learn more about the research. Bauer chaired the study and was lead author on the papers.

RC: How common is bipolar disorder among VA patients?

MB: Both bipolar disorder and schizophrenia have about a two-percent prevalence rate in the VA. The rate of bipolar disorder is likely actually higher, since it is difficult to diagnose and often misconstrued as schizophrenia. Also, there are high rates of comorbidity that complicate diagnosis—among those with bipolar disorder who have a hospitalization, over 30 percent at any given time will have comorbid substance use disorders and almost 40 percent will have a concurrent anxiety disorder. Notably, 25 percent will have PTSD, and only half of this is combat-related.

RC: How did you develop the care model used in the study?

MB: This represents a novel adaptation of an organization of care heretofore used only for chronic medical illnesses and for depression treated in primary care. This "collaborative chronic care model" had not previously been used in chronic, severe mental illnesses such as bipolar disorder. The model involves supporting patients to become better managers of their own symptoms, supporting providers through evidence-based guidelines, and improving access so that the medical-care system responds more promptly to patient needs.

RC: To what do you attribute the effectiveness of the model?

MB: We were impressed that even severely ill patients could participate

What is bipolar disorder?

Bipolar disorder, or manic-depressive illness, is a serious mental illness that affects about three percent of Americans. It involves shifts in mood, energy, and ability to function. Manic episodes are marked by unrealistic beliefs in one's abilities and powers; poor judgment; substance abuse; and provocative, intrusive, or aggressive behavior. Depressive episodes may be characterized by feelings of hopelessness or pessimism; difficulty concentrating, remembering, or making decisions; restlessness or irritability; chronic pain or other persistent bodily symptoms that are not caused by physical illness or injury; and thoughts of death or suicide.

Though medication and psychotherapy can be effective, many patients with bipolar disorder fail to receive optimal long-term treatment. According to VA's Mark Bauer, MD, "The clinical course of this disease is typically complex, and comprehensive approaches to treatment are required."

effectively in, and benefit from, the intervention. The medical chronic-care literature indicates that patient self-management skills are an essential component of effects. Thus it is likely that enhancing such skills is a key component of the collaborative chronic care model's effects. However, the model goes beyond psychotherapy interventions by supporting provider decision-making and reducing barriers to care. This orientation is very much consistent with the wellness orientation of the VA's mental health services.

RC: Why do you think the intervention had more of an effect on manic episodes than depressive symptoms?

MB: There are very few interventions of any type that improve acute depressive episodes or prevent their recurrence in bipolar disorder. Among medications, lithium and perhaps the anticonvulsant lamotrigine may help. Cognitive-behavioral therapy may help as well. In future generations of the collaborative chronic care model, we would incorporate greater focus on these modalities to achieve more impact on depressive symptoms.

RC: The paper describes the intervention as "cost-neutral," although it appears to have in fact saved about $1,000 per year per patient.

MB: These were not statistically significant changes. This is in part because of the heterogeneity of the sample, as is often the case in economic analyses. Is about $1,000 per year clinically—or economically—significant? That is for the individual administrator to determine in deciding whether to implement the program. If it were implemented on a wider scale, these cost-savings could conceivably be both statistically and economically significant.

RC: Do you foresee this collaborative-care model being adopted within VA?

MB: This trial, and a concurrent trial of a very similar intervention in an HMO setting, in which I collaborated with Dr. Greg Simon, now show the effectiveness of this approach in over 700 individuals with bipolar disorder. Thus the collaborative chronic care model is worth considering in terms of dissemination. The major issues at this point are developing the optimal dissemination strategy, and investigating applicability of the model in smaller health care venues. It is also reasonable to investigate whether the same principles can be adapted for other severe and persistent mental illnesses such as PTSD and even schizophrenia. With VA's capitated budget, a strong business case could certainly be made for adoption of the model.

RC: What are the implications of these study results beyond VA?

MB: First, the fact that individuals with this severe mental disorder can collaborate effectively in their care and be good "self-managers" breaks down the stigma that has traditionally separated chronic mental illnesses from chronic medical illnesses. Second, as Medicaid becomes increasingly cost-conscious, its administrators have decided to focus on "disease management" strategies, and this provides one example of the type of method that will become increasingly important to them. ■

Update from Clinical Science Research and Development...

Cooperative Studies Program launching six new trials

By Grant Huang, MPH, PHD, deputy director, CSP; and Timothy J. O'Leary, MD, PHD, director, CSR&D

The Cooperative Studies Program (CSP) conducts multi-site clinical trials and epidemiological studies to provide definitive scientific evidence on prevalent diseases that impact our veteran population. This summer, CSP is launching six new clinical trials. These collaborative research studies are listed below along with brief descriptions.

1) Prostate Cancer (CSP #553)—chaired by Drs. R. Bruce Montgomery and Daniel Lin, Seattle. This study will evaluate early adjuvant therapy as compared to the current standard of care in patients who have had radical prostectomy but are at a high risk for relapse.

2) Mental Health/Schizophrenia (CSP #555) — chaired by Drs. Robert Rosenheck and John Krystal, West Haven. This trial aims to determine the effective-

see CSP on pg. 8

Cyber-security guidance on ORD website

VA researchers looking for the latest policies and procedures regarding cyber security and privacy can visit: www.research.va.gov/resources/policies/cybersecurity.cfm.

This newly updated page on the VA research website contains recent memos from ORD and VHA leadership, as well as many pertinent VA Handbooks and Directives, such as Handbook 1605.1 on the "Privacy and Release of Information" and Directive 2004-002 on commercial or external Web-hosting services.

Among the recent communications found on the page are a July 10 memo on "Researcher Contacts with Veterans," and a June 12 memo titled "Research Responsibilities for Protecting Sensitive Information."

Recent publications and presentations by VA investigators

Below is a sampling of recent publications and presentations by VA investigators, based on notifications received by R&D Communications (see reporting requirements at www.research.va.gov/resources/policies/pub_notice.cfm.) Every attempt is made to present a cross section of investigators, topics and medical centers. Only VA-affiliated authors are listed here, due to space constraints.

"Basis for the Failure of Francisella Tularensis Lipopolysaccharide to Prime Human Polymorphonuclear Leukocytes." Jerrold Weis, PhD; Michael A. Apicella, MD; William M. Nauseef, MD. **Iowa City.** *Infection and Immunity*, June 2006.

"Chronic Central Overexpression of Leptin Elevates Blood Pressure Despite Extreme Hypoleptinemia." Nihal Tumer, PhD. **Gainesville**. *XIV International Symposium on Atherosclerosis*, June 20, 2006.

"Comparison of Rates of Potentially Inappropriate Medication Use According to the Zhan Criteria for VA versus Private Sector Medicare HMOs." Mitchell J. Barnett, PharmD, MS; Jodi D. Langstaff; Peter J. Kaboli, MD, MS. **Iowa City.** *Journal of Managed Care Pharmacy*, June 2006.

"Cost-Effectiveness of Hernia Surgery: Implications for Practice." Denise Hynes, PhD, RN. **Hines**. *Academy Health Annual Research Meeting*, June 26, 2006.

"Developing a Bio-Terrorism Preparedness Campaign for Veterans – Using Focus Groups to Inform Materials Development." Drew Helmer, MD, MS; John Fotiades, MD. **East Orange, Bronx.** *Health Promotion Practice*, June 2006.

"Effect of Calcitriol on Prostate-Specific Antigen in Vitro and in Humans." Tomasz M Beer, MD; Mark Garzotto, MD; David Sauer, MD; Kristine Eilers, MD. **Portland, Hines.** *Clinical Cancer Research*, May 2006.

"Effect of Cell Culture Conditions on the Anticytomegalovirus Activity of Maribavir." Sunwen Chou, MD. **Portland**. *Antimicrobial Agents and Chemotherapy.* July 2006.

"Factors Affecting Compliance With Diabetes Hypertension Guidelines." Julie C. Lowery, MHSA, PhD; Sarah L. Krein, PhD. **Ann Arbor**. *Academy Health annual meeting*, June 26, 2006.

"Heart Failure, Chronic Diuretic, and Increase in Mortality and Hospitalization: An Observational Study Using Propensity Score Methods." Ali A. Ahmed, MD; Louis J. Dell'italia, MD; Richard M. Allman, MD. **Birmingham**. *European Heart Journal*, June 2006.

"Likelihood of Home Death Associated With Local Rates of Home Birth: Influence of Local Area Healthcare Preferences on Site of Death." Maria J. Silveira, MD, MA, MPH; Laurel A. Copeland, PhD, MPH. **Ann Arbor, San Antonio**. *American Journal of Public Health*, May 30, 2006.

"Outcomes with Porcine Graft Placement in the Anterior Vaginal Compartment in Patients Who Undergo High Vaginal Uterosacral Suspension and Cystocele Repair." Kathryn L. Burgio, MD. **Birmingham**. *American Journal of Obstetrics Gynecology*, May 2006.

"Predictors of Hearing Protection Use Between Hispanic and Non-Hispanic White Factory Workers." David L. Ronis, PhD, MA. **Ann Arbor**. *Research and Theory for Nursing Practice: An International Journal*, Summer 2006.

"Race Differences in Diagnosis and Surgery for Occupational Low Back Injuries." Elena M. Andresen, PhD. **Gainesville.** *Spine*, May 2006.

"Secreted Proteins from Mycobacterium Tuberculosis Gain Access to the Cytosolic MHC Class-I Antigen-Processing Pathway." David M. Lewinsohn, MD, PhD. **Portland**. *Journal of Immunology*, July 2006.

"Sequential Combination of Flavopiridol and Docetaxel Reduces the Levels of X-Linked Inhibitor of Apoptosis and AKT Proteins and Stimulates Apoptosis in Human LNCaP Prostate Cancer Cells." Carlos Perez-Stable, PhD. **Miami.** *Molecular Cancer Therapeutics*, May 2006.

"The Cancer and Leukemia Group B Cancer in the Elderly Committee: Addressing a Major Cancer Need." Harvey Jay Cohen, MD. **Durham**, *Clinical Cancer Research*, June 2006.

"The Standard Gamble vs. Willingness to Pay: Examining Older Adult Health Preferences for Functional Dependence across Methods of Valuation." Mary K. Goldstein, MD. **Palo Alto.** *American of Health Annual Meeting*, June 24-26, 2006.

"Veterans Health Administration Patients' Use of the Private Sector for Coronary Revascularization in New York: Opportunities to Improve Outcomes by Directing Care to High-Performance Hospitals." William B. Weeks, MD, MBA; Stacey L. Campbell, MPH; Steven M. Wright, PhD; Elliott S. Fisher, MD, MPH. **White River Junction**, **Providence, Washington, DC.** *Medical Care*, June 2006.

"Violent Criminal Behavior and Perspectives on Treatment of Criminality in Opiate Treatment." Darren M. Mays; Adam J. Gordon, MD, MPH; Mary E. Kelley, PhD; Steven D. Forman, MD, PhD. **Pittsburgh.** *Substance Abuse*, 2006. ■

See notification procedure at:
www.research.va.gov/resources/policies/pub_notice.cfm

FRAC (from pg. 1)

"This committee has been critical in establishing field input and communication at the highest levels of VA research leadership," said Robert Pollet, MD. "This ongoing dialog and access, both formal and informal, has led to an atmosphere of genuine cooperation in facilitating … regulatory compliance at our VAMCs and reducing the negative impact of potential barriers to our research program."

Fred Wright, MD, agreed. "It's a forum for a really fruitful exchange of information, where investigators can learn about the political and financial constraints that leaders in Central Office have to deal with, and the Central Office leaders can get ideas and feedback from investigators about what is working and what isn't."

Members cite successes, frustrations

FRAC members offered several examples of recent accomplishments in the Office of Research and Development (ORD) that they say relied heavily on input from their group. These include reworking the R&D Handbook; ensuring that adequate numbers of proposals are funded; and resolving issues concerning VA's Technology Transfer Program and the nonprofit research corporations that help support VA research.

Regarding funding, Michael Davey, MD, PhD, pointed to the group's recommendation that ORD strive to fund 25 percent of all investigator-initiated-research proposals. "This was felt to be the minimum needed to sustain an intramural program and leave mentors in place for career development."

see **FRAC** on pg. 6



Joining VA's Field Research Advisory Committee this year are (from left) Frank Lederle, MD; Mohamed Boutjdir, PhD; and Warren D. Blackburn, MD.

Who's on the FRAC?

FRAC members are elected by their VA peers for three-year terms, with one-third of the members rotating off annually. Current members include:

ACOS/R&D: Northeast—**Mohamed Boutjdir, PhD,** New York (replacing Fred Wright, MD, West Haven); Mid-Atlantic—**Donald H. Rubin, MD,** Nashville; South—**Warren D. Blackburn, MD,** Birmingham (replacing Robert Pollet, MD, PhD, Atlanta); Midwest—**Theodore Goodfriend, MD,** Madison; West—**Michael Davey, MD, PhD,** Portland.

Center Directors: Rehabilitation R&D: **Stephen A. Fausti, PhD,** Portland; Health Services R&D: **Stephan D. Fihn, MD, MPH,** Seattle.

Cooperative Study Chairman: **Frank Lederle, MD,** Minneapolis (replacing Steven Goldman, MD, Tucson).

Non-Clinician PhD Scientist: **M. Rita I. Young, PhD,** Charleston.

The rich history of VA research

Pre-World War II visions of veteran-focused research

The following is an excerpt from "VA Research, 1925 – 1980," a history compiled by Dr. Marguerite Hays, who directed VA's Medical Research Service during the 1970s. The complete text is expected to be available in print or on CD by early next year.

Support of medical research in the 1920s and 1930s came from researchers themselves and from foundations, universities, industry and, lastly, the government. Each of these sectors was represented on the [Veterans' Bureau] Medical Council's Group on Research.

Foundations were the most important funders. From 1937 to 1940, American foundations' annual support of medicine and public health was estimated to be in the range of $12.25 to $13.5 million. Foremost of the foundations was the Rockefeller Institute, founded in 1902. The Institute was the site of basic and clinical research in infectious diseases, cardiology and other prevalent medical problems. …

With regard to governmental support, [Alan Gregg, Rockefeller Foundation Director for the Medical Sciences] warned that: "The usual reservation regarding research under governmental control is that political preferment or unenlightened parsimony may spoil the quality of the work." And while these factors may have kept the VA research program small before 1946, the VA was not alone in receiving little governmental funding. As

see **HISTORY** on pg. 7

FRAC (from pg. 5)

On a related issue, Theodore Goodfriend, MD, cited FRAC support for the decision to "hold down the Merit Review per-grant funding ceiling so that the number of grants can be as large as possible."

On the negative side, Davey expressed frustration over what he said has been slow progress in obtaining federal approvals for an ORD policy on financial conflicts of interest. But he underscored the FRAC's attempts to speed the process so VA investigators could have clear, firm guidance as early as possible.

Stephan Fihn, MD, MPH, acknowledged that "given the pace and complexity of issues in CO, it is often difficult for FRAC members to have sufficient knowledge … to have the level of involvement they seek."

Steven Goldman, MD, said the group would benefit from the perspective of "more young people and more women," and suggested there is an ongoing need within the FRAC and VA's research community at large to move from a "silo" mentality—in which researchers and administrators seek to "protect their own turf"—to a more cooperative, less competitive culture.

Leadership during difficult times

According to Pollet, the most critical issue facing the FRAC in the next year or two is helping VA implement its genomic-medicine research program, which he said promises to propel VA into the forefront of American medicine.

Fihn pointed to the challenge of "providing leadership and support to the field during what is certainly going to be a difficult period in terms of funding and regulation." He added that FRAC members will continue to have a crucial role to play in communicating the worth of VA research,

see **FRAC** on pg. 8

Drug (from pg. 1)

thing, because it damages cells," Swanson noted. "And cell suicide is not necessarily the best thing for the whole organism."

Swanson cautioned, though, that blocking PARP-1—and thereby interfering with DNA repair—could have a downside. "In blocking DNA repair you conceivably increase the risk of cancer. In clinical trials where people are taking minocycline for months at a time, I think that investigators need to take this into consideration—although for someone with a serious neurodegenerative disease like ALS, it could be a reasonable tradeoff. But you want to have your eyes open."


Photo by Ed Caballero

Raymond Swanson, MD, San Francisco, and colleagues studied the mechanisms of the drug minocycline, now being studied for ALS and other neurodegenerative conditions.

The second observation, said Swanson, was made a decade ago by study coauthor Tiina M. Kauppinen, PhD, currently a neurology research fellow at the San Francisco VA and UCSF, when she was a graduate student in Finland. Kauppinen found that minocycline, an antibiotic derived from tetracycline, prevents inflammation and apoptosis in cultured brain cells.

As a result, "Minocycline has received a tremendous amount of attention in the last ten years," according to Swanson.

Next ORD field conference calls:

Monday, Aug. 21 • 1:30 pm (EST)

Monday, Sept. 18 • 1:30 pm (EST)

Dial 1-800-767-1750

(access code: 17323)

Currently, he said, there are clinical trials under way testing minocycline as a potential treatment for Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis (ALS), all of which cause brain and nerve cell degeneration as a consequence of inflammation.

Swanson credited the study's lead author, Conrad Alano, PhD, also of VA and UCSF, with the insight that the action of minocycline closely resembles the action of previously studied PARP-1 inhibitors. This perception led to "a simple experiment – putting cells in a dish, doing things to the cells that would activate PARP-1, and seeing what the effect of minocycline was."

Swanson characterized the result of the experiment as "absolute black and white." Minocycline, at extremely low concentrations, inhibited PARP-1 in cell culture and reduced cell death by more than 80 percent, compared to cells not given minocycline.

"This doesn't exclude the possibility that it has other actions," said Swanson, "but as far as we can tell, the only way it blocks inflammation is by blocking PARP-1."

The study was funded by VA, the American Heart Association and the National Institutes of Health. ■

History (from pg. 5)

late as 1945, the National Institute of Health (as it was then known) spent only three million dollars on medical research, while foundations contributed some $16 million.

Before World War II, VA hospitals were not affiliated with medical schools, but this probably was not the key factor keeping the research program small. Only a few of the most prominent medical schools, especially those with full-time clinical faculty, had significant clinical research programs. …

Important basic research, funded mostly by foundations, was being done at a few places, such as the Rockefeller Institute, the Mayo Clinic and a few medical schools, but such studies were not expected of the Veterans' Bureau. Rather, the clinical research the Medical Council urged was closely associated with the patient. It endeavored to bring systematic observation and scientific method to bedside treatment. …

'Research based on practicability'

The Medical Council's view of research appropriate to the Veterans' Bureau emphasized standardization of practice and records and statistical studies. Members also emphasized the importance to the Veterans' Bureau of clinical researchers, particularly those that studied outcomes. As Chairman [Ray Lyman] Wilbur said in a 1926 address:

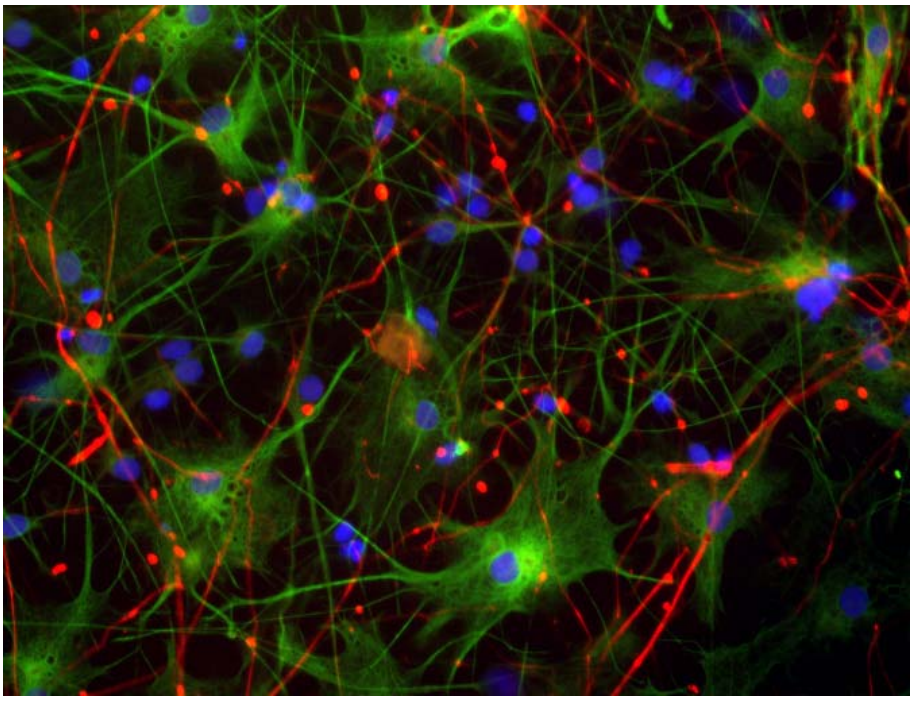
"If we can get the best medical brains of this country concerned with the neuropsychiatric veteran, not only to study him but to get him back 'on the job,' and also trace through over a period of years just what actually does happen, keeping alive a constant scientific interest in the problem, we will have done a real service in the advance of medicine."

In 1926, Dr. [Philip B.] Matz, chief of research at Bureau headquarters, described his view of that component of the agency's mission:

"It must be clearly understood at the outset that research work in our service must show that upon consummation it will result in the betterment of the treatment of the beneficiary. It is not within the province of the Veterans' Bureau to carry on research work of a purely academic character; there are other governmental agencies for this line of endeavor; ours must be research based on practicability—something akin to the research work carried on by the large commercial corporations of the country. Our research work must eventually result in larger percentages of recoveries and reduced mortality rates of the beneficiaries of the United States Veterans' Bureau. …"

Next month's installment: "Affiliation with medical schools: The concept" ■

The 'art' of science



Tri-color immunostained neural cells in culture, courtesy of Micheline McCarthy, MD, PhD, of the Miami VAMC.

Miami lab probes HIV's effects on nervous system

The image above was produced as part of a VA-funded study titled "Neurogenesis and Neuronal Survival in HIV-1 Infection." Co-principal investigator Micheline B. McCarthy, MD, PhD, and her team at the Miami VA Medical Center used an immunofluorescent staining technique to explore the effects of Human Immunodeficiency Virus (HIV) on the development and survival of human neurons in culture.

"This particular image is a control—cells incubated without any virus present," explained McCarthy. "This image tells us that the human neuroepithelial progenitor population will differentiate into mature astrocytes—the green cells—and neurons—the red cells. Images like this are used as a basis for comparison with cultures that have been exposed to virus." (The blue parts of the image are cell nuclei, added McCarthy.)

FRAC (from pg. 6)

especially in an era when policymakers and the public are "frustrated by the lack of major breakthroughs despite the massive investment over the last decade" and "perplexed by the constant barrage of conflicting claims and counter claims in the press that lead them to question the fundamental value of medical research."

A couple of veteran FRAC members said another constant challenge is making sure the group keeps a high profile in ORD decision-making.

"Our biggest challenge is to avoid being ignored," said Goodfriend. "We need to be convincing in our recommendations." Added Goldman, "The FRAC has to be relevant and provide [the CRADO] with information and feedback."

Overall, FRAC members voiced satisfaction with the group's ongoing positive impact on communication between ORD and the field.

Said Wright, "I think it is essential that both groups continue to take advantage of the opportunity to listen and inform." ■

CSP (from pg. 3)

ness of an injectable antipsychotic agent on schizophrenia symptoms and hospitalization compared to standard oral antipsychotic treatment.

3) Cardiovascular Surgery/Diabetes (CSP #557) — chaired by Drs. Masoor Kamalesh and Thomas Sharp, Indianapolis. This study will compare coronary artery bypass graft surgery to percutaneous coronary intervention with drug-eluting stents to determine whether one approach can better prevent death or myocardial infarction in diabetics with severe ischemic heart disease.

4) Mental Health/Post-Traumatic Stress Disorder (PTSD) (CSP #504) — chaired by Drs. John Krystal and Robert Rosenheck, West Haven. The trial will examine whether risperidone reduces PTSD symptoms in veterans who have not had improved PTSD symptoms when treated with antidepressants.

5) Stroke rehabilitation (CSP #558) —chaired by Dr. Albert Lo, West Haven. This trial, a jointly funded effort with the Rehabilitation Research & Development Service, will investigate the safety and efficacy of a robotic arm device in rehabilitating chronic stroke patients with upper extremity impairment.

6) Chronic Obstructive Pulmonary Disease (CSP #560) —chaired by Drs. Vincent Fan, Seattle, and Dennis Niewoehner, Minneapolis. This study will determine if self-management and case-management can be feasibly implemented and decrease the risk for hospitalizations in COPD patients.

Each study is unique in its approach to investigating treatments, but all represent collaborative efforts involving many dedicated VA clinician investigators, statisticians, research pharmacists, health economists, and administrative personnel committed to the VA research mission. Two of these studies (CSP #553 and CSP#555) also include industry collaborators with whom VA has negotiated Cooperative Research and Development Agreements (CRADAs).

For more information about these studies, visit the CSP website at www.csp.research.va.gov. ■

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