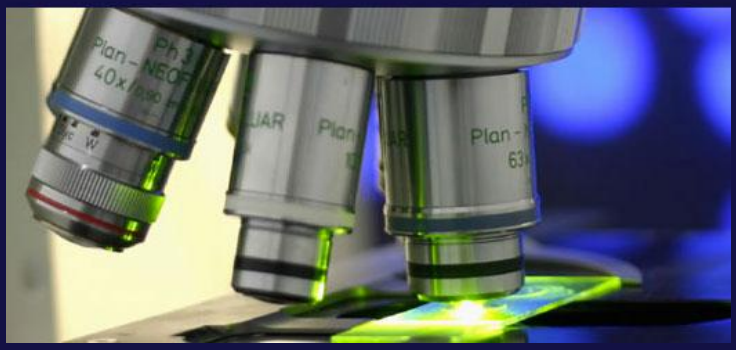
Miami VA R&D eNewsletter
Bruce W. Carter Department of Veterans Affairs Medical Center
Issue 16 August 1, 2013

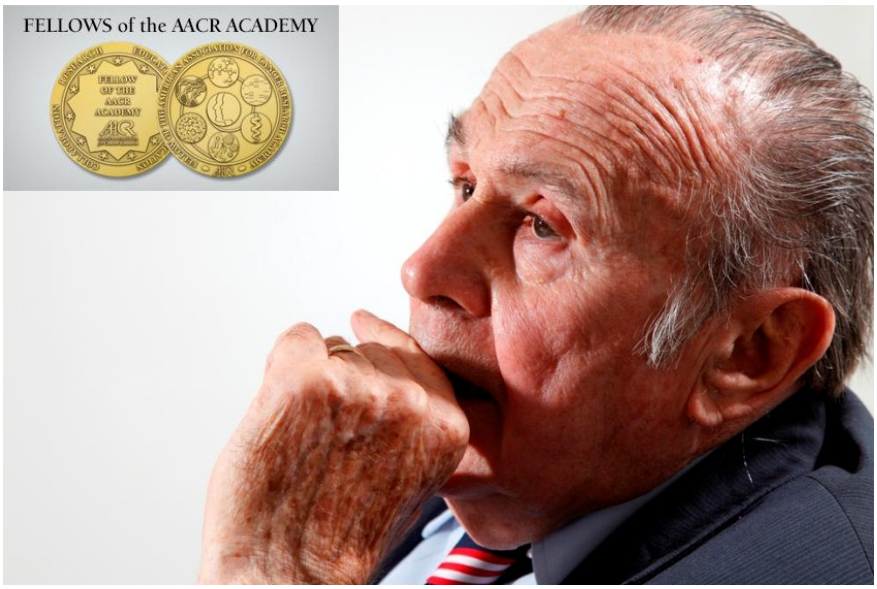


In this issue

Latest News

American Association of Cancer Research Honors Schally

Andrew V. Schally, Ph.D., MDhc (Multi),D.Sc.hc was elected as a Fellow of the inaugural class of the American Association of Cancer Research (AACR) Academy. This accolade was presented at the induction ceremony on April 5, 2013 at the AACR Annual Meeting.



The AACR Academy serves to recognize and honor distinguished scientists whose major contributions have propelled significant innovation and progress against cancer. Fellows are selected through a rigorous peer review process that evaluates individuals on the basis of their stellar scientific achievements in cancer research or cancer-related biomedical science.

Dr. Schally, a pioneer in the understanding of endocrine signaling in the nervous system and a 1977 Nobel Laureate, characterized various secretory, hypothalamic signaling hormones that affect downstream pituitary gland function. Such studies began with the co-discovery of corticotropin releasing factor (CRF) and continued with the isolation and synthesis of

various additional hypothalamic hormones including thyrotropin-releasing hormone (TRH), luteinizing hormone-releasing hormone (LH-RH; also known as gonadotropin-releasing hormone, GnRH), and somatostatin.

These trailblazing studies established the foundation for many research areas including neuroendocrinology and reproductive endocrinology and illuminated the previously unknown relationship between the hypothalamus, pituitary gland, and endocrine system. More recently, these fundamental discoveries have been utilized to further the understanding and treatment of endocrine-related diseases such as breast and prostate cancer. Dr. Schally also pioneered the development and use of synthetic analogs of hypothalamic hormones for therapy of various cancers.

As a member of the inaugural class of Fellows, Dr. Schally is among an elite group of individuals who have been vital to the progress made in the understanding, diagnosis, treatment, and prevention of cancer.

VA Selected as Site for Study of Diabetes Drug Effectiveness

Miami VA Healthcare System and Miller School of Medicine have been selected as a clinical study site for the NIH-funded project Glycemia Reduction Approaches in Diabetes (GRADE): A Comparative Effectiveness Study.

The study is led by Jennifer B. Marks, M.D., professor of medicine and Section Chief of Endocrinology at the VA, and Hermes Florez, M.D., Ph.D., MPH, associate professor of medicine and public health sciences and Interim Director of the Geriatric Research, Education and Clinical Center (GRECC) at the VA. The study will compare the long-term benefits and risks of four widely used diabetes drugs in combination with metformin, the most common medication for

treating type 2 diabetes. According to Dr. Marks, the long-term study will answer the questions of how to intensify treatment in type 2 diabetes after the use of metformin which is considered first-line treatment. According to Dr. Florez there is a significant need for high-quality comparative effectiveness research, particularly regarding costs and outcomes that matter most to patients and quality of life and avoidance of morbid and life-limiting complications.

The GRADE study aims to enroll up to 5,000 patients to study drug effects on glucose levels, side effects, diabetes complications and quality of life over an average of 5 years.

The Miami VA is currently enrolling patients diagnosed with type 2 diabetes within the last five years, who may be on metformin, but not on any other diabetes medication. During the study, all participants will take metformin along with a second medication randomly assigned from among four classes of FDA-approved medications.

Study coordinators at the VA and UM are Lisset Oropesa, M.D., senior research associate in the Department of Public Health Sciences and Miriam Gutt, Ph.D., research assistant professor of medicine

DAV Selects Schally as Outstanding Employee for 2013

The DAV (Disabled American Veterans) has selected Dr. Andrew Schally as the Outstanding Department of Veterans Affairs Veterans Health Administration Employee for 2013. The National Commander's Award will be presented to him at the National Convention to be held in Orlando, Florida on August 11, 2013.

Nobel laureate Dr. Andrew Schally, a medical research scientist and head of the endocrine, polypeptide and cancer institute at the Miami VA medical center, will receive the National Commander's Outstanding Veterans Health Administration Employee Award for his remarkable 50-year career of research and treatment of veteran cancer patients at VA medical centers.

"I am very proud to serve in the VA health care system," Dr. Schally said. "Veterans have been treated for prostate cancer with methods I've discovered for over 30 years. I am very proud to receive this award for saving thousands of lives."

"We have proven methods of treatment for many cancers, and now we can treat women veterans for ovarian cancer," Schally said. His discoveries are also pointing to possible

new treatments for diabetes and heart disease. "I'm hopeful that my discoveries can be implemented for the healing of many other illnesses that veterans suffer," he said.

"I deeply respect veterans because I never served in the military," Schally said. "My father was a member of the Free Polish forces serving at Allied Headquarters under General Eisenhower in London during World War II. My work is a small compensation for not serving. I always greatly admired and respected American veterans."

With more than 33 awards and 22 honorary degrees to his credit, Schally has authored or co-authored 2,400 publications, and holds the position of Distinguished Medical Research Scientist at VA. He continues to work at the Miami VA medical center, averaging 10 hour days, five days a week.

"I wanted to work for VA," he said. "It was a lot of hard work to discover the brain's control of endocrine glands. I am very proud to have been here for 50 years and working on these discoveries, especially the applications for women veterans."

"I am proud and honored to accept this award, and I will continue to help veterans in the VA system," Schally said. "I'm hopeful my discoveries can be implemented to heal many other conditions afflicting veterans."

Miami Celebrates 6th Annual VA Research Week

As part of the 2013 National VA Research Week, the Research Service organized a two-day program. The sixth annual Miami VA Research Day Poster Session took place on May 16. Posters representing the work of numerous investigators were displayed from noon to 4:00 pm in the T.C Doherty Auditorium. Investigators, presenters, judges and other attendees were available to discuss their work and its significance to veterans. The poster session was an ideal time for collaboration with academic partners and an opportunity for researchers to exhibit their findings and share ideas. Thirty-two abstracts were submitted in the categories of Basic Science, Clinical Science/Health Services and Young Research Investigator. The winners were:

Basic Science	Clinical/Health	Young Investigator Basic Science	Young Investigator Clinical Science
First Place **Paul Schiller, PhD** *Combinatorial Strategies to Tissue Compartment Repair in the CNS*	**First Place** **Allison McClellan, OD** *The Epidemiology of Ocular Surface Squamous Neoplasia in a Veterans Affairs Population*	**First Place** **Gaetan Delcroix, PhD** *Enhancement of Hyaline Cartilage Formation by MIAMI Cells Through Attachment onto TGF-β3-Releasing Pharmacologically Active Microcarriers and Human Cartilage Microparticles* **Laurin Pacheco, BS** *Progerin Expression Interferes with Stem Cell Functions that Contribute to Vascular Repair*	**First Place** **Chandana Karanam, MBBS** *Examining Veterans' Attitudes about and Abilities to Use the VA's MyhealtheVet System*
Honorable Mentions **Micheline McCarthy, PhD, MD** *Apolipoprotein E-dependent Differences in Innate Immune Responses of Maturing Human Neuroepithelial Progenitor Cells Exposed to HIV-1* **Carlos Perez-Stable, PhD** *Targeting the Mcl-1 Anti-Apoptotic Protein to Improve Prostate Cancer Chemotherapy*	**Honorable Mentions** **Douglas Wallace, MD** *Race-ethnicity Interacts with CPAP Adherence and Sleep-related Quality of Life* **William Wohlgemuth, PhD** *Measuring Insomnia in Sleep Apnea: A Confirmatory Factor Analysis of the Insomnia Severity Index* **Sandra Winkler, PhD, OTR/L** *Non-Veteran Level Factors Related to the Prescription of Assistive Technology Devices and Services to Veterans Post-stroke*	**Medhi Wangpaichitr, PhD** *Selectively Kill Cisplatin Resistant Lung Cancer Cells by Exploiting ROS and Metabolic Differences* **Honorable Mentions** **Roberto Ruiz-Cordero, MD** *Cryoglobulin and Cryofibrinogen: A Solution to the Specimen Thermal Stability Challenge With a Blood Cryo-Kit* **Nicole Salazar, MS** *Interaction of CXC-Chemokine Receptor CXCR7 with EGF-Receptor in Breast Cancer* **Melvys Valledor, MS** *Human Cells Recombineering*	**Honorable Mentions** **Deborah Clarke, PhD, RN** *Selected Predictors of Empowerment among Nurse Managers* **Kenneth Seldeen, PhD** *Physical Performance in an Animal Model of Vitamin D Insufficiency*

The second part of the program included a special Grand Rounds that highlighted VA research and how it directly and indirectly benefits veterans. **Dana Ascherman, M.D**., an internationally renowned expert in autoimmune muscle disease, presented the talk entitled *Serum Biomarkers of RA-associated Interstitial Lung Disease: How will they help us?* His current research is observational and does not involve therapeutics or direct assessment of various treatments. As a result, veterans who enroll in the study do not derive any direct benefits and will not undergo any change in treatment approach based on study results. Dr. Ascherman's work has centered on defining novel biomarkers of connective tissue disease-associated interstitial lung disease. These biomarkers of early lung disease will help clarify pathogenesis an set the stage for future trials and/or non-invasive screening strategies.

Anat Galor, M.D., a cornea and uveitis specialist presented the talk entitled *Dry Eye Syndrome in Veterans.* Her research focuses on understanding the scope of dry eye syndrome in veterans. Dry eye syndrome (DES) is a prevalent condition that affects between 5-30% of older adults in the United States (US) and world-wide. While historically believed to be a disease predominately affecting females, Dr. Galor's research found that 19% of male veterans carried a diagnosis of DES. Her talk focused on the epidemiology of dry eye syndrome in the veteran population and she discussed several ongoing research projects including the role of bacteria and corneal nerve dysfunction in DES. She was paired with a Veteran patient who explained how Galor's research directly benefited him.

2nd Annual 5K Run/Walk for SFVAFRE Promotes Fitness

The traditional 5K Mercedes-Benz Corporate Run/Walk for employees took place on April 25, 2013. The Corporate Run promotes lifelong fitness at all levels and encourages camaraderie in the workplace through healthy and happy employees. Once again SFVAFRE teamed up with the Miami VA Healthcare System. The SFVAFRE participation increased from 6 to 11 employees. Kumar Anam, Evelyn Bolanos, Carlos Canales, Jennifer Denizard, Rolando Garcia Rojas, Zsuzanna Nemeth, Ferenc Rick, Maria Rodriguez, Luis Salgueiro, Zunner Soliz, and Andrew Sorial of SFVAFRE participated. The SFVAFRE hopes to continue this tradition

Research Service Highlights

Dry Eye Syndrome (DES) Research Update

Anat Galor's team is currently recruiting patients for a tear film study entitled *Characterization of organisms on the surface of the eye in patients with ocular surface disorders*. In addition to providing information to patients on the function of their tears, the study aims to evaluate

Allison McClellan, OD

the relationship between bacteria that live on the ocular surface and DES. The team is looking for individuals with normal eye anatomy who are not using antibiotics or eye medications (artificial tears are acceptable). The study is a 1 day study and takes about 30 minutes to complete. Please contact Mireya Hernandez (mireya.hernandez@va.gov) or page Dr. Galor at 305-288-2000 if interested in participating.

Current study findings were presented at the Miami VA Research Day. A poster evaluating the epidemiology of ocular surface squamous neoplasia (OSSN) in the veteran population received a first place price in the young investigator category. The team found that the period prevalence of OSSN was 0.1% (n=28/24,179) in our population. Sun exposure (as reflected by the surrogate markers basal and squamous cell cutaneous carcinoma) was the most significant risk factor for the eye cancer. Another presentation included work regarding dry eye associated quality of life in veterans. It was found that dry eye symptoms resulting from the use of glaucoma medications impacted the physical and emotional functioning of veterans. Emotional health was significantly more affected in black veterans using drops compared to white veterans. Finally, Dr. Galor's team presented research evaluating the role of environment on dry eye syndrome. Combining information from the national VA database and from the National Climatic Data Center (NCDC) and National Aeronautics and Space Administration, (NASA) they found that several environmental factors influenced the risk of DES including increased air pollution and decreased relative humidity.

Galor's team continues to evaluate the scope of dry eye syndrome in veterans. One recent paper assessed whether systemic inflammation (as measured by C reactive protein levels) affected tear film parameters in 233 prospectively evaluated veteran men. In this study, they were not able to demonstrate a relationship between systemic inflammation and dry eye syndrome. However, they plan to continue studying this important research question by looking at more specific parameters of ocular inflammation such as the presence of cytokines in tears. *(Crane et al, Ophthalmology. 2013 May;120(5):1099.e1)*

Sarah Wellik, MD

Another recent study evaluated the effect of a PTSD and depression diagnosis on DES. Interestingly, the presence of either diagnosis affected the presence of symptoms; those with PTSD and depression reported higher DES symptoms compared to a control population without these disorders. However, no differences in tear film parameters were found between the groups. This paper stressed the importance of evaluating the mechanisms behind ocular pain in DES. *(Fernandez et al. Invest Ophthalmol Vis Sci. 2013 May 1;54(5):3666-72.)* Finally, a recent review paper provided an update on the clinical and experimental literature for the ocular surface effects of glaucoma therapy. Specifically, the effects of preservatives found in these medications, such as benzalkonium chloride (BAK), were reviewed. These agents continue to contribute to ocular surface disease and demonstrate a variety of toxic ocular effects on the epithelium both in vitro, and in animal/human studies. (*Anwar et al. CurrOpinOphthalmol. 2013. Mar;24(2):136-43.*

Study Evaluates Disinfection Techniques for Reusable Lens

Ninel Gregori, M.D., Chief of the Miami VA Eye Care section, and Dr. Ashkan Abbey, Bascom Palmer Eye Institute ophthalmology resident, recently conducted a study evaluating disinfection techniques utilized for ophthalmic reusable medical equipment. This study is being submitted to the American Journal of Ophthalmology. In their clinical practice eye providers use various lenses which are placed on the eye for diagnostic and therapeutic purposes. These lenses come into direct contact with the eye and are considered semi critical items which must be cleaned and disinfected properly between patients. No scientific references confirming efficacy of disinfection methods recommended by the manufacturers of ophthalmic lenses are available. Ocular and Volk Optical Inc., major lens manufacturers, recommend cleaning lenses with mild detergent solution and a clean cotton swab, then

disinfecting with an approved disinfectant solution. Volk Optical Inc. gives several options depending on the lens style, including 1:10 sodium hypochlorite (bleach) solution, cidex OPA, glutaraldehyde, bode mikorbac tissues, and CaviWipes for all lens types. The bleach method is a commonly used disinfection technique. The wear and tear on the lenses due to multiple rounds of bleaching is significant, as are the extra costs and personnel required for lens processing. The purpose of the study was to evaluate efficacy of manufacturers' protocols, and to compare efficacy of detergent and water versus bleach for elimination of common ocular bacterial and viral pathogens from ophthalmic lenses. Dr. Gregori and her team demonstrated that washing with detergent and water effectively eliminates bacteria and viruses from the surface of gonioscopy and direct contact laser lenses heavily contaminated in the laboratory. Disinfection with bleach did not add any additional benefit.

Rothenberg's Research Tests Benefits of Cupron's Copper Socks

Cupron, creator of a copper-based antimicrobial and skin enhancement technology, recently announced that its pioneering technology has received the U.S. Environmental Protection Agency's (EPA) approval to make a first-of-its-kind Public Health Claim. This is the third EPA Public Health Claim awarded to Cupron and the first highlighting the unique anti-fungal capability of Cupron's copper-based technology.

In awarding the Public Health Claim, the EPA found that Cupron's copper-enhanced textile material can kill *Trichophytonmentagrophyte,* the active fungus in athlete's foot, by more than 99.9% after 12 hours of contact with the fiber. The unique Public Health Claim covers the use of Cupron anti-fungal fibers in a variety of settings, including socks, shoe inserts and bathmats.

Gary Rothenberg, M.D. and his research team at the Miami VA have recently completed a randomized, double-blind placebo controlled trial in partnership with Cupron studying the effects of copper socks in people with diabetes. Tineapedis and other dermatologic complications of the feet can often lead to ulcerations and even amputations in the "at risk" patient with diabetes and peripheral neuropathy/ peripheral vascular

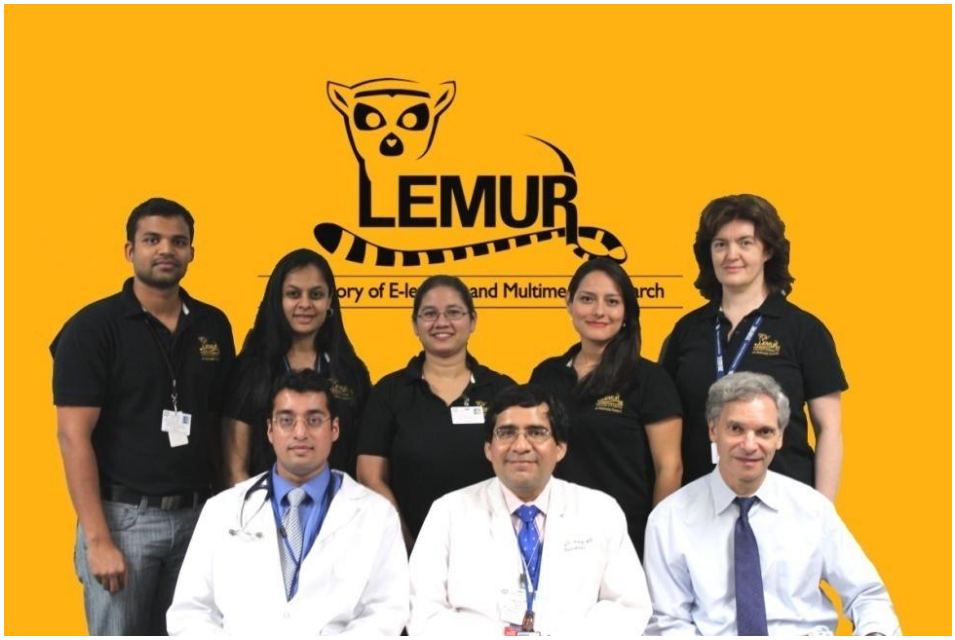
disease. The primary outcome point of the trial was incidence of ulcerations within a six month follow-up period. Secondary and tertiary outcomes included time to onset of ulceration and overall cosmesis through utilization of the copper socks. All patients enrolled were considered "high risk" for developing diabetic foot complications. Enrollment for the Miami VA trial closed in November, 2012 with 86 patients. The final follow-up visits were completed in May, 2013 and the data has been submitted to an independent agency for analysis. Dr. Rothenberg and his team look forward to the results of the trial.

Example of Cupron Copper Socks

Information Prescription Service serves 200 Veterans in 2 months

The Information Prescription Service team of the GRECC Laboratory of E-learning and Multimedia Research led by Dr. Jorge G. Ruiz, MD, FACP, met its projected yearly goal within two months and served the 200th Veteran on July 9th, 2013.

The service was initiated on May 1, 2013 at the Miami VA Health System in response to the National VA Strategic Plan Refresh to enhance the Veteran experience and access to health care using the MyHealth*e*Vet personal health record to provide world class communication between patients, providers, and care coordinators. The Information Prescription Service, a T21 project grant awarded to the Bruce W. Carter VA GRECC, provides individualized patient education and self-management training to veterans. Using the Information Prescription Service, Veterans receive patient-centered and evidence-based health information tailored to



Front row: Allen D. Andrade, MD, MRCP(UK), Jorge G. Ruiz, MD, FACP, Joseph Sharit, PhD; Back row: Ramana Kumar Anam MD, MS(AGER), Chandana Karanam, MBBS, Dhurga Krishnamoorthy, MBBS, Lorena Nino-Castro, MD, Zsuzsanna Nemeth, MLIS.

their individual need through regular mail, the MyHealth*e*Vet Secure Messaging system, or by visiting the MyHealth*e*Vet Clinic in person. In addition, veterans may also sign-up for basic computer training classes.

Focusing on health behavior change to further improve the health of veterans, health care providers prescribe specific information to Veterans on their particular health problems. The staff of the service responds to these requests by delivering health information using a variety of evidence-based consumer health information resources as well as the Veterans Health Library. In addition, Veterans are often referred to local events and theVHA National Center for Health Promotion and Disease Prevention activities and peer support groups.

Presentations

VA Endocrine, Polypeptide and Cancer Institute

Andrew V. Schally, PhD, MDhc, DSchc

Yasir S, Umar SA, Fernandez-Castro G, Nadji M, Block N, Schally A, Cote R, Jorda M. *Immunohistochemical expression of LHRH in muscle-invasive carcinoma of urinary bladder: a potential predictive marker for targeted cytotoxic hybrid analog of LHRH (AEZS-108)* USCAP Abstract

Fernandez GL, Schally AV, Koru-Sengul T, Jorda M, Merchan JR, Flores AM, Block N, Manoharan M, Engel J. *Long term response in a patient with urothelial cancer (UC) treated with AEZS-108.* ASCO 2013, Chicago, IL, May 31-June 4, 2013.

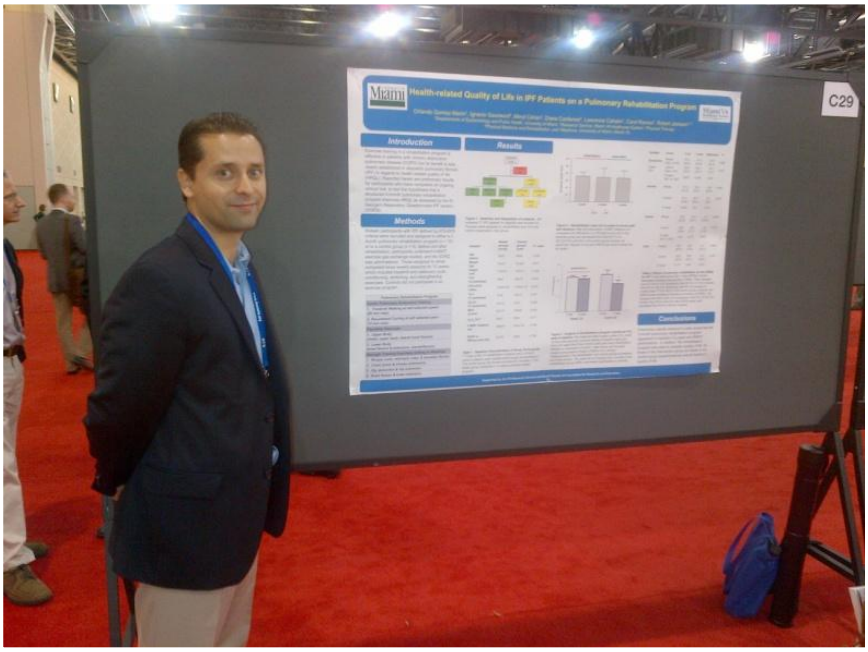
Pinski JK, Schally AV, Tsao-Wei DD, Dorff TB, Groshen SG, Xiong S, Quinn DI, Tai YC, Engel J, Liu SV. *A phase I dose escalation trial of AEZS-108 in taxane- and castration-resistant prostate cancer (CRPC).* ASCO Annual Meeting, Chicago, IL, May 31 – June 4, 2013.

Rick FG, Abi-Chaker A, Szalontay L, Perez R, Halmos G, Block NL, Schally AV. *Combination of bombesin/gastrin-releasing peptide antagonist with growth-hormone-releasing hormone antagonist augments shrinkage of benign prostatic hyperplasia in rats*. AUA Annual Meeting 2013, May 4-8, 2013, San Diego, CA. Accepted abstract - Moderated Poster - MP58. Accepted abstract.

Rick FG, Abi-Chaker A, Szalontay L, Block NL, Halmos G, Schally AV. *Targeted cytotoxic analog of somatostatin AN-162 [AEZS-124] inhibits proliferation of PC-3 and DU-145 human androgen-independent prostate cancers in vitro and in vivo*. AUA Annual Meeting 2013, May 4-8, 2013, San Diego, CA. Accepted abstract - Moderated Poster - MP13.

Kanashiro-Takeuchi R, Takeuchi LM, Cai RZ, Zarandi M, Block NL, Schally AV, Hare JM. *Targeting growth hormone-releasing hormone receptor as a new therapeutic approach to improve cardiac repair after myocardial injury*. American Heart Association.

Robert Jackson, M.D. and **Ignacio Gaunaurd, PT, Ph.D., MSPT** recently attended and presented their Rehabilitation Research & Development supported research findings at the American Thoracic Society International Conference on May 17-22, 2013. They presented two posters: *Effects of Pulmonary Rehabilitation Program on Exercise Capacity and Functional Mobility for Patients with IPF* and *Health-related Quality of Life in IPF Patients in a Pulmonary Rehabilitation Program*. The posters addressed the successful implementation of a standardized pulmonary rehabilitation program for veterans with Idiopathic Pulmonary Fibrosis (IPF) and its significant impact on their exercise capacity, mobility, and reduction of symptoms related to IPF. It was very well received and manuscripts for both of these posters will be submitted for publication this fall 2013.



Awards, Appointments and Honors

VA Research Foundation Hires New Executive Director

On July 15th, 2013 the South Florida Veterans Affairs Foundation for Research and Education, Inc. (SFVAFRE, Inc) welcomed its new Executive Director, **Ms. Frances Fernandez, MHSA.**

Fernandez began her career as staffing supervisor at Mount Sinai Medical Center managing coordinators, improving staffing and overtime controlling. After completing her graduate studies, she joined Mercy Hospital as Administrator of the Home Health Department. While there, she managed operations including finance, budgeting, business development and strategic planning. Subsequently, Frances became director of special immunology services at Mercy Hospital, where she

oversaw grants and development and management with awards over $7.1 million.

Her leadership and experience complements the South Florida VA Foundation for Research and Education's mission as an innovative leader in research and education programs that promote veterans health and education. Frances aims to help raise the foundation's profile of the Miami VA Healthcare System. Her goals include enhancing principal investigators' involvement in the foundation as well as reviving its partnership with affiliated universities, as a way of building links on and off campus to scholars whose research fits in the areas of Veterans Affairs.
"I am very fortunate in having come to a foundation with a range of very strong projects and partnerships, as well as people who are strongly committed to our mission of research and education that improves the lives of veterans and their caregivers" stated Frances. "I look forward to continuing to build and grow the foundation over the years to come."

Founded in 1990, the foundation addresses veterans' research and education needs and provides technical assistance to physicians and scientists. For more information on the foundation visit: www.sfvafre.com.

Lokeshwar Accepts NIH Membership

Bal Lokeshwar, PhD, accepted the invitation from the Department of Health and Human Services National Institute of Health (NIH) to serve as a member of the Chemo/Dietary Prevention Study Section, Center for Scientific Review, for the term beginning July 01, 2013 and ending June 30, 2019. Members are selected on the basis of their demonstrated competence and achievement in their scientific discipline as evidenced by the quality of research accomplishments, publications in scientific journals, and other significant scientific activities, achievements and honors. Service on a study section also

requires mature judgment and objectivity as well as the ability to work effectively in a group. According to Dr. Richard Nakamura, Director, Center for Scientific Review, Dr. Lokeshwar was selected to this important task based on his qualities. His functions will include reviewing grant applications submitted to the NIH, making recommendations on these applications to the appropriate NIH national advisory council or board, and surveying the status of research in his field of science.

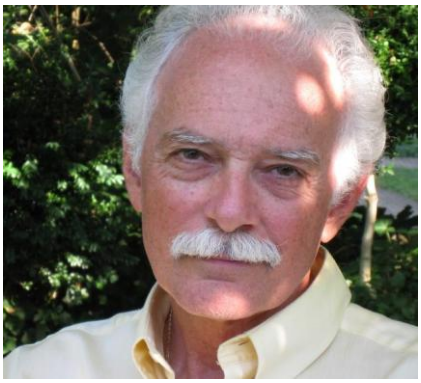
Dr. Lokeshwar's membership on the study section represents a major commitment of professional time and energy as well as a unique opportunity to contribute to the national biomedical research effort. His functions are of great value to medical and allied research.

GRECC *Geriatric Research, Education, and Clinical Center*

Bal Lokeshwar, Ph.D. served as a reviewer on three study sections, including the NIH ZRG1 BMCT-C: Molecular Targets and Cancer Therapeutics, NIH ZRG1 OBT-M Cancer Health Disparities/Diversity in Basic Cancer Research, and on NIH SEP: Cell biology IRG.

Hermes Florez, **M.D., Ph.D. MPH**, Acting GRECC Director served as a member of the VA Geriatrics Research Education and Clinical Center (GRECC) Study Section.

Guy Howard, Ph.D.,GRECC Research Director, served on his last review panel as a full member of the NIH Skeletal Biology Development and Disease (SBDD) Study Section, Center for Scientific Review.



He also served as an *ad hoc* reviewer for the VA Endo-B Merit Review Panel.

Agency for Healthcare Research & Quality Awards Winkler

Sandra Winkler, Ph.D., OTR/L, Research Health Scientist in the Miami VA Research Service, received a three-year R24 award from the Agency for Healthcare Research & Quality (AHRQ) for a project titled *Dissemination of Amputation and Prosthetic Evidenced-based Medicine (DAP-EM).* The project compared two strategies for dissemination of evidence-based and health self-management information to amputees: a CDRom and a virtual world environment.

The objective of the *DAP-EM* project was to provide amputees with evidence-based information to improve their health and quality of life while decreasing the burden of this chronic condition on society. The project was based on the assumption that a virtual world environment will be appealing to the next generation of healthcare consumers, the millennials.

The first year of the project was a development phase. Drs. Winkler, PI, and **Ignacio Gaunaurd**, **MSTP, Ph.D.**, Co-Investigator, are developing the self-management intervention. Based on Bandura's theory of learning, the modules will address five learning objectives: Historical Perspectives of Amputation, Etiology, Incidence, and Prevalence of Amputation, Phases of Rehabilitation, Pain and Comorbidity, Current Prosthetic Technology. Two amputee actors have been hired to capture spontaneous video that will be used in the modules. Both actors, one a bilateral lower limb amputee and the other an upper limb amputee, were injured in the Operation Iraqi Freedom (OIF) conflict. After the modules have been beta-tested by occupational and physical therapists and amputees, the experimental phase will begin (years 2 and 3). Amputee subjects will be randomized to an experimental group that will view the self-management intervention in a virtual world environment and a control group where the intervention will be viewed on a CDRom. Mixed methods will be used for analysis of data. The quantitative outcomes will be measures pre and post intervention and at six-months follow up. The quantities outcomes are: use of prosthetic devices, self-efficacy, psychosocial status, pain interference, and physical function.

Qualitative analyses will be based on phenomenology theory that explores the subjects' experience of living with an amputation and experience with the virtual world. Triangulation will be used to combine quantitative and qualitative data. The project was awarded to Dr. Winkler at NOVA Southeastern University and partners via sub awards with Virtual Ability, Inc., SFVAFRE, and the University of Florida.

Publications

P. Resniera, S. David, N. Lautrama, **Gaëtan J.-R. Delcroix**, A. Clavreula, J-P. Benoita, C. Passirani. *EGFR siRNA lipid nanocapsules efficiently transfect glioma cells in vitro,* Int J Pharm. 2013 Apr 10. pii: S0378-5173(13)00285-8. doi: 10.1016/j.ijpharm.2013.04.001. [Epub ahead of print]

Gaëtan J.-R. Delcroix, D. N. Kaimrajh, D. Baria, S. Cooper, T. Reiner, L. Latta,G. D'Ippolito, P.Schiller, and H. T. Temple. *Histologic, Biomechanical, and Biological Evaluation of Fan-Folded Iliotibial Band Allografts for Anterior Cruciate Ligament Reconstruction*. Arthroscopy: The Journal of Arthroscopic and Related Surgery, Volume 29, Issue 4 , Pages 756-765, April 2013.

The purpose of this study was to thoroughly characterize the fan-folded iliotibial band (FITB) allograft and compare it with anterior tibialis tendons (ATs) and native anterior cruciate ligaments (ACLs) to determine whether it measures up to those tissues. The histologic structure, tensile strength to failure, creep, and stress-relaxation properties of FITBs with those of ATs and ACLs were compared. In vitro cytotoxicity and biocompatibility of FITBs were also compared with ATs. No structural difference was observed between the tissues studied. FITB ultimate tensile strength (3,459 ± 939 N) was not significantly different (P > .9999) from ultimate tensile strength of ATs (3,357 ± 111 N) and was significantly greater (P = .0005) than that of ACLs (886 ± 254 N). No significant difference (P > .9999) was observed in the increase in length resulting from creep testing between FITBs (9.5 ± 3.0 mm) and ATs (9.7 ± 4.0 mm). During stress-relaxation testing, FITBs reached 181 ± 46 N, which was not significantly different (P > .9999) from ATs (166 ± 40 N). Cytotoxicity of FITBs and ATs was shown to be negligible. In vitro biocompatibility of FITBs and ATs was very good, whereas FITBs had a higher propensity to favor the attachment and infiltration of cells that proliferated for at least 4 weeks on their contact. It was found that FITBs, ACLs, and ATs shared a similar structure made of aligned collagen fibers. No significant difference was observed between FITB and AT ultimate tensile strength, creep, and stress-relaxation viscoelastic

properties. Ultimate tensile strength to failure of ACLs was lower than that of FITBs and ATs, whereas ACLs were superior to both FITBs and ATs during creep and stress-relaxation testing. FITBs and ATs showed low cytotoxicity and excellent biocompatibility in vitro, with a somewhat higher propensity of FITBs to favor cell attachment and infiltration over time. Clinical Relevance: This study suggests that FITBs have the potential to perform as well as ATs for ACL reconstruction.

Rebeca Geffin & Ricardo Martinez & Roberto Perez & Biju Issac & **Micheline McCarthy**. *Apolipoprotein E-Dependent Differences in Innate Immune Responses of Maturing Human Neuroepithelial Progenitor Cells Exposed to HIV-1*. J Neuroimmune Pharmacol. 2013 Jun 7

HIV enters the brain early during infection and induces a chronic inflammatory state that can result in neurological abnormalities in a subset of infected individuals. To investigate the effects of HIV exposure on neurogenesis and neuronal survival in the brain, Dr. McCarthy's lab used a model system consisting of human neuroepithelial progenitor (NEP) cells that undergo directed differentiation into astrocytes and neurons in vitro. Changes in gene expression in NEP cultures as a result of HIV exposure were investigated using gene expression microarrays with the Illumina HT-12 V4_0_R1 platform array. Through this approach, they identified a group of genes specifically upregulated by exposure to virus that are strongly related to interferon induced responses and antigen presentation. When the data were stratified by their apolipoprotein genotype, this innate immune response was more robust in the apolipoprotein E3/E3 genotype cultures than in the apolipoprotein E3/E4 counterparts. Biological processes as defined by the gene ontology (GO) program were also differently affected upon virus exposure in cultures of the two genotypes, particularly those related to antigen presentation and the actions of interferons. Differences occurred in both in numbers of genes affected and their significance in the GO processes in which they

participate, with apoE3/E3> apoE3/E4. These data suggest that maturing NEP cultures recognize HIV and respond to it by mounting an innate immune response with a vigor that is influenced by the apolipoprotein E genotype of the cells.

GRECC

Geriatric Research, Education, and Clinical Center

Resnier P, David S, Lautram N, Delcroix GJ, Clavreul A, Benoit JP, Passirani. *EGFR siRNA lipid nanocapsules efficiently transfect glioma cells in vitro*. Int J Pharm. 2013 April 10. [Epub ahead of print]

Chamaladevi N, Lyn DA, Shaaban KA, Zhang L, Rohr VS, Lokeshwar BL. *Ericifolin: A novel antitumor compound from Allspice that silences androgen receptor in prostate cancer*. Carcinogenesis. 2013 May 9. [Epub ahead of print]

Lagari V, Gomez-Marin O, Levis S. *The role of vitamin D in improving physical performance in the elderly* J Bone Miner Res. 2013 Apr 2 [Epub ahead of print]

Zhang L and Lokeshwar BL. *Medicinal properties of the Jamaican Pepper plant Pimenta dioica and Allspice*. Curr Drug Targets 13:1900-6, 2012.

Burton DG, Giribaldi MG, Munoz A, Halvorsen K, Patel A, Jorda M, Perez-Stable C, Rai P. *Androgen deprivation-induced senescence promotes outgrowth of androgen-refractory prostate cancer cells*. PLoS One 8:e68003, 2012.

Andrade AD, Anam R, Sun H, Mintzer JG, Ruiz JG. *Effects on performance of individual versus dyadic practice during an avatar-based three-dimensional virtual home safety simulation*. Stud Health Technol Inform 184:13-19, 2013.

Delcroix GJ, Kaimrajh DN, Baria D, Cooper S, Reiner T, Latta L, D'Ippolito G, Schiller PC, Temple HT. *Histological, biomechanical and biological evaluation of fan-folded iliotibial band allografts for anterior cruciate ligament reconstruction*. Arthroscopy 29:756-65, 2013.

Roche S, D'Ippolito G, Gomez LA, Bouckenooghe T, Lehmann S, Montero-Menei CH, Schiller PC. *Comparative analysis of protein expression of three stem cell populations: models of cytokine delivery system in vivo*. Int J Pharm 440:72-82, 2013.

Lagari VS, Levis S *Phytoestrogens for menopausal bone loss and climacteric symptoms.* J Steroid Biochem Mol Biol. 2012 Dec 14. [Epub ahead of print]

VA Endocrine, Polypeptide and Cancer Institute

Andrew V. Schally, PhD, MDhc, DSchc

Jaszberenyi M, Rick FG, Szalontay L, Block NL, Zarandi M, Cai RZ, Schally AV. *Beneficial effects of novel antagonists of GHRH in different models of Alzheimer's disease.* Aging 4(11):755-767, 2012.

Jaszberenyi M, Schally AV, Block NL, Nadji M, Vidaurre I, Szalontay L, Rick F. *Inhibition of U-87 MG, human glioblastoma by AN-152 (AEZS-108), a targeted cytotoxic LHRH analog*. Oncotarget 4(3);422-432, 2013.

Jaszberenyi M, Schally AV, Block NL, Zarandi M, Cai RZ, Vidaurre I, Szalontay L, Jayakumar AR, Rick FG. *Suppression of the proliferation of human U-87 MG glioblastoma cells by new antagonists of growth hormone-releasing hormone in vivo and in vitro.* Targeted Oncology [Epubahead of print Feb. 1, 2013)

Seitz S, Rick FG, Schally AV, Treszl A, Hohla F, Szalontay L, Zarandi M,

Ortmann O, Engel J, Buchholz S. *Combination of GHRH antagonists and Docetaxel shows experimental effectiveness in treatment of triple negative breast cancers.* Oncology Reports 30:413-418, 2013.

Ziegler CG, Eisenhofer G, Schally AV, Gebauer L, Gondek K, Ullrich M, Qin N, Ehrhart-Bornstein M, Bornstein SR. *Anti-tumor effects of peptide analogs targeting neuropeptide hormone receptors on mouse pheochromocytoma cells.* Molecular and Cellular Endocrinology 371:189-194, 2013.

Rick FG, Schaly AV, Block NLm Abi-Chaker A, Krishan A, Szalontay L. *Mechanisms of synergism between antagonists of growth hormone-releasing hormone and luteinizing hormone-releasing hormone in experimental benign prostatic hyperplasia*. Prostate 73:873-883, 2013.

Rick FG, Block NL, Schally AV. Reply to Kaplan SA: Re: *LHRH antagonist cetrorelix reduces prostate size and gene expressin of proinflammatory cytokines and growth factors n a rat model of beningn prostatic hyperplasia.* The Journal of Urology 189(4):1604-1605, 2013.

Rick FG, Block NL, Schally AV. *An update on the use of degarelix in the treatment of advanced hormone-dependent prostate cancer*. Review Onco Targets and Therapy 6:391-402, 2013.

Szepeshazi K, Schally AV, Block NL, Halmos G, Nadji M, Szalontay L, Vidaurre I, Abi-Chaker A, Rick FG. *Powerful inhibition of experimental human pancreatic cancers by receptor targeted cytotoxic LH-RH analog AEZS-108.* Oncotarget 4(5):751-760, 2013.

Siejka A, Schally Av, Barabutis N. *The effect of LHRH antagonist Cetrorelix in crossover conditioned media from Epithelial (BPH-1) and Stromal (WPMY-1) prostate cells.* HormMetab Res: Accepted for publication

Lucas R, Czikora I, Sridhar S, Zemskov E, Gorshkov B, Siddaramappa U, Oseghale A, Lawson J, Verin A, Rick FG, Block NL, Pillich H, Romero M, Leustik M, Schally AV, and Chakraborty T. *Mini-Review: Novel therapeutic strategies to blung actions of pneumolysin in the lungs*. Toxins: accepted for publication

Nair D, Ramesh V, Li RC, Schally AV, Gozal D. *GHRH activity modulates intermittent hypoxia-induced cognitive deficits in mouse.* Journal of Neurochemistry: Submitted

SFVAFRE Corner

Important Guidelines for Executing Confidential Disclosure Agreements (CDA)/Non-disclosure Agreements (NDA)

The Director of the VAMC executes the CDA/NDAs through signature. **VA Principal Investigators (PI) are not authorized agents of the Government, and by executing these documents, they would act outside their capacity, and could be making themselves personally liable.** The VA PI does not have any authority to disclose VA non-public information. Research data

and other fruits of VA labor belong to VA, and not to VA researchers. By signing the CDA, the VAMC Director is authorizing the VA PI to disclose non-public information.
The PI(s) should sign an acknowledgement at the end of a particular CDA such as the following statement:
"I have read and acknowledged the Confidential Disclosure Agreement made and entered into by ABC company and VAMC Miami, FL, and I agree to abide by the terms therein.

Additionally, the NPC Executive Director (ED) is not a VA employee and may not bind VA in these relationships. Having the ED sign CDAs is inappropriate and unauthorized. However, if circumstances require NPCs to receive confidential information, they should also be identified as a party to the document for the purpose of confidentiality. In these circumstances, a provision should be added to the CDA to the effect that-

"All Parties to this agreement are independent from one another. This agreement does not establish a contract between any VA entity and the NPC."

Furthermore, the Specialty Team Advising Research (STAR) of the Office of General Counsel needs to review these agreements before they are signed.

If you have any questions, please contact the SFVAFRE Executive Director.

House Appropriations Committee Provides VA Research Increase

In May, the U.S. House Appropriations Committee provided a $3.5 million increase in funding for the VA Medical and Prosthetic Research program for a total of $585.6 million, as part of the large Military Construction and Veterans Affairs Appropriations bill. The House action matches the funding level recommended by President Barack Obama.

While the early progress on the Military Construction/VA bill is encouraging, the fate of this and all other appropriations bills is uncertain. Members of Congress continue to negotiate the federal budget issues and, at this point, it is unclear if the Military Construction/VA bill will go to the full House or will await further action.

Grants Funded

Executed CRADAs

Sponsor:	**Biosphere Medical, Inc.** Device CRADA
Project:	*Prospective, randomized, controlled investigation of prostate artery embolization with Embosphere Microspheres compared to transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia*
PI:	**Shivank Bhatia, MD**
Sponsor:	**TEI Biosciences, Inc.** Device CRADA
Project:	*Evaluation of new tissue generation in a chronic diabetic wound post-implantation of Primatrix through use of biopsies and histological analysis*
PI:	**Gary M. Rothenberg, MD**

Other Funding

Sponsor:	**Pfizer, Inc.**
Project:	*Technology and collaborative care improve the use of hormone therapy (HT) in Postmenopausal women veterans*
PI:	**Silvina Levis-Dusseau, MD**

Miami VA R&D Newsletter

is a service of the Research Service Office at the
Miami VA Healthcare System.
To view past issues, visit http://sfvafre.org/newsletter.php

Submissions

Faculty and staff submissions can be e-mailed to the
Office of Research Communications at
iperez4@med.miami.edu or Isabel.Perez1@va.gov.

Editor

Isabel Perez

Published quarterly by the Miami VA Research Service Office.