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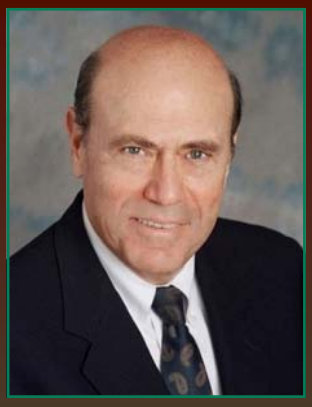
Bruce W. Carter Department of Veterans Affairs Medical Center



Michael D. Norenberg, M.D.

INSIDE THIS ISSUE:

PATHOLOGIST WINS ANNUAL VA RESEARCH AWARD

Michael D. Norenberg, M.D., Staff Neuropathologist at the Miami VA Medical Center and Professor of Pathology and Director of Neuropathology at the University of Miami Miller School of Medicine, has received the highest research recognition given by the Department of Veterans Affairs, the William S. Middleton Award.

Established 50 years ago, the Middleton Award is given in recognition of outstanding scientific contributions in biomedical and biobehavioral research related to the health care of veterans and non-veteran patients. Dr. Norenberg is the first investigator at the Miami VA Medical Center ever to have received this recognition. The Award carries with it $50,000 per year of additional research support for three years.

Dr. Norenberg has worked in the VA health care system for almost 40 years and joined the Miami VAMC and the University of Miami School of Medicine 28 years ago. In the VA, Dr. Norenberg has received almost continuous support for his research and has held various research career development awards, including the most senior of these, appointment to the position of VA Medical Investigator. He has also served the VA in various local and national positions of research leadership, oversight and administration. At the Miller School, in addition to his senior position in the Department of Pathology, Dr. Norenberg also holds appointments in the Departments of Biochemistry/Molecular Biology, Neurology and Neurological Surgery, as well as being a Faculty Affiliate in the Miami Project to Cure Paralysis.

In the laboratory, Dr. Norenberg has focused much of his work on the study of metabolic changes in nerve cells and their contribution to abnormal neurologic function.

Early on in his career, he identified for the first time the cause of central pontine myelinolysis (CPM), a debilitating, usually untreatable disorder of the central nervous system (CNS) that occurred suddenly in patients with recent severe metabolic abnormalities, as well as in patients with various chronic illnesses. He demonstrated that the development of CPM was associated with a rapid increase toward normal of the blood level of sodium in patients with very low sodium levels (hyponatremia) who were being treated aggressively to correct this abnormality, an accepted clinical approach up to that time. Dr. Norenberg's work clarified the mechanisms whereby rapid correction of hyponatremia brought about demyelination in the CNS. As a result of this work, the clinical guidelines

Dr. Norenberg with Robert A. Petzel, MD, Under Secretary for Health, Veterans Health Administration, Department of Veterans Affairs (left) Joel Kupersmith, MD, Chief Research and Development Officer, Office of Research and Development, Department of Veterans Affairs

Pathologist Wins Annual VA Research Award

Michael D. Norenberg, M.D.

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for correcting hyponatremia have been changed and CPM has become a rare condition today.

Dr. Norenberg has been extensively involved in studies of the biology of astrocytes, the main supporting cells in the CNS that are critical to nerve cell function and integrity and have important interactions with other associated CNS cells, including neurons, microglia and oligodendrocytes. Early on he demonstrated that the enzyme glutamine synthetase (GS) is exclusively localized to astrocytes, where it plays a critical role in the metabolism of the key excitatory and inhibitory neurotransmitters glutamate and GABA. The identification of GS in astrocytes also implicated these cells as the site of ammonia detoxification in the brain. Ammonia is a neurotoxin whose blood levels are greatly increased in patients with severe liver dysfunction, as commonly seen in hepatic cirrhosis, viral hepatitis and exposure to various hepatotoxins, often resulting in neurological condition known as hepatic encephalopathy (HE). Dr. Norenberg's work supported the concept that the clinical manifestations of HE are the result of ammonia-induced impairment of critical astrocytic functions, thereby leading to neuronal dysfunction. One important consequence of ammonia toxicity is the development of astrocyte swelling and cerebral edema, often resulting in potentially life-threatening increases in intracranial pressure and brain herniation. The characterization by Dr. Norenberg and his associates of some of the critical pathways involved in CNS swelling carry great potential for therapeutic translation in a host of disorders, including spinal cord injuries, traumatic brain injuries and stroke, as well as severe liver disease. Promising work in these areas is ongoing in his laboratory.

Dr. Norenberg graduated from Trinity College (Hartford) and obtained his medical degree from the University of Rochester School of Medicine and Dentistry, Rochester, NY. He completed his Anatomic Pathology Residency and Neuropathology Fellowship at the University of Rochester School of Medicine and Dentistry. He also trained as a resident in Internal Medicine at Rochester General Hospital. Dr. Norenberg served in the Armed Forces as a General Medical Officer, U.S. Air Force, and was stationed at Lackland AFB, San Antonio (Wilford Hall Medical Center).

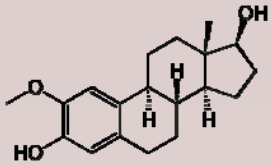
Dr. Norenberg has held several Career Development Awards from the Veterans Administration, including Research Associate, Clinical Investigator and Medical Investigator. He has published 180 peer reviewed journal articles, 37 book chapters and one book.

Dr. Norenberg declares that he is "very honored and humbled to receive this award" and expresses his gratitude for the unwavering support he has received from numerous colleagues and associates at the Miami VA Research Service. Among these, include Dr. Robert Jackson, currently Associate Chief of Staff for Research and Professor of Medicine; Dr. Lawrence Fishman, formerly, Associate Chief of Staff for Research and now Professor Emeritus of Medicine, who recruited Dr. Norenberg to the Miami VA; and Gustavo Godoy, M.B.A., who for much of Dr. Norenberg's stay in Miami, was Administrative Officer for Research at the VA and is currently Director of Research for the International Medicine Institute at the Miller School of Medicine.

Research Welcomes

Philip D. Harvey, Ph.D.

Dr. Philip Harvey, professor of Psychiatry, recently transferred from Emory University School of Medicine. He was formerly professor of Psychiatry at Mt. Sinai School of Medicine and Chief Psychologist at Mt. Sinai Hospital. Dr. Harvey received his PhD in Clinical Psychology from SUNY at Stony Brook in 1982. He is a member of the American Psychological Association, the American College of Neuropsychopharmacology (Fellow), the Collegium Internationale Neuropharmacologium (Fellow) , the Society for Research in Psychopathology (Founding Member), the Society for Biological Psychiatry, International Neuropsychological Society, the Schizophrenia International Research



RESEARCH HIGHLIGHTS

John W. Brown, Ph.D.

Dr. John W. Brown (VA/UM Research Professor of Medicine) presented a paper at the 49th Annual Meeting of The American Society of Cell Biology as well as three papers at the 2010 Endocrine Society Meeting in San Diego. The ASCB presentation showed differential expression of neuromedin-B, gastrin releasing peptide, and bombesin S-3 neuropeptide receptors in the SW-13 and H-295r adrenal carcinoma cell-lines while the three presentations at the Endocrine Society Meeting showed strong cell growth-inhibitory effects of two experimental chemotherapeutic estrogen derivatives (2-methoxy-estradiol and ENMD-1198), as well as similar effects of a cytotoxic somatostatin analog (AN-162) in SW-13 cultures. These studies also demonstrated that the estrogen derivatives strongly decreased the expression of anti-apoptotic genes while they increased the expression of apoptosis-inducing factors. The net result was significantly increased rates of programmed cell death (apoptosis) in tumor cells relative to control or doxorubicin-treated cultures. Additionally, Dr. Brown is a co-author on a paper to be presented by Dr. Sabina Casula VA/UM Endocrinology Fellow) and Dr. Antonio Blanco (UM Chief of Endocrinology & Professor of Medicine) in September at the 2010 Meeting of the International Thyroid Congress in Paris. This presentation will demonstrate similar effects of 2 methoxyestradiol and ENMD-1198 in the ACT-1 anaplastic thyroid cancer cell line. Dr. Carlos Perez-Stable (VA-GRECC/UM Research Associate Professor of Medicine) and Mr. Ricardo Parrondo (VA-GRECC) were important collaborators and co-authors on four of these presentations while Dr. Sabina Casula and Dr. Monica Moreno (VA/UM Endocrinology and VA/UM Geriatrics Fellows) were primary authors on two of the papers. Dr. Lawrence M. Fishman (former Miami VA Associate Chief of Staff for Research, Chief of Endocrinology and current UM Emeritus Professor of Medicine) and Dr. Andrew Schally (VA Distinguished Scientist and Director of the Endocrine, Polypeptide and Cancer Institute, as well as UM Distinguished Professor of Medicine and Pathology and 1977 Nobel Laureate in Medicine) were co-authors on three of these presentations while Dr. Andrea Treszl (VA Endocrine, Polypeptide and Cancer Institute) was a key participant in the neuropeptide receptor studies and was a co-author on the ASCB paper Colleagues at the Technical University of Dresden (Drs. Christian Ziegler, Stefan Bornstein and others) were important collaborators and coauthors on an additional presentation involving neuropeptide analog studies in adrenal carcinoma which was presented at the 2010 Endocrine Society Meeting and published in the Proceedings of the National Academy of Sciences. Dr. Ziegler was primary author of this work.

Philip D. Harvey, Ph.D.

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Society (Founding Director), and the International Society for Clinical Trials and Methodology (Founding Member). His research has focused for years on cognition and he has written extensively on aging in schizophrenia, functional impairments in the illness, the cognitive effects of typical and atypical antipsychotics, as well as studying the effects of cognitive enhancing agents in various conditions, including schizophrenia, dementia, and traumatic brain injury. He directs a large and successful biennial conference on cognition that is an official satellite of the International Congress on Schizophrenia Research. The last two meetings of this conference were attended by more than 450 scientists from around the world and this meeting was also an official satellite of the Schizophrenia Winter Workshop. He is also active in clinical work and teaching, performing over 1,000 psychological assessments and teaching and supervising undergraduate, predoctoral, and postdoctoral psychology students and medical students, residents, and fellows for the past 25 years.

Dr. Harvey will have a dual appointment at the Miami VAMC and the University of Miami Miller School of Medicine, Department of Behavioral Medicine. We are very lucky to have him at the Miami VAMC Research to continue his research here.

Awards and Honors

Arumugam Jayakumar, Ph.D.

Dr. Jayakumar, VA Scientist, Neuropathology and UMMSM Assistant Professor of Neuropathology was awarded the Stanley J. Glaser Research Award for the proposal entitled “STAT3 inactivation in the mechanisms of astrocyte swelling by ammonia”. The award of $40,000 with a one year term from June 1, 2010 to May 31, 2011 will be presented at the second annual Stanley J. Glaser Symposia on September 15, 2010.

The Glaser Awards are a time-honored annual tradition which reward up-and-coming research stars among Miller School of Medicine faculty.

Andrew V. Schally, Ph.D., M.D.h.c., D.Sc.h.c.

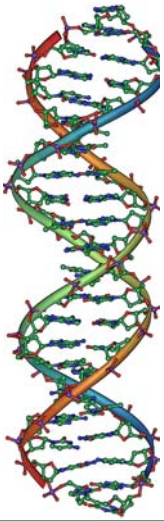
Dr. Schally, the 1977 Nobel Prize winner for physiology or medicine, Distinguished Medical Research Scientist of the Department of Veterans Affairs, and professor of pathology and medicine at the Miller School of Medicine, was bestowed with yet another Doctor Honoris Causa. Dr. Schally was recognized for his contribution of peptide science and modern endocrinology by the Department of Pharmacy, University of Patras in Greece at a special ceremony in May.

ΣΥΝΕΔΡΙΟ
ΙΑΤΡΙΚΗΣ
ΧΗΜΕΙΑΣ

University of Patras

Kevin Curtis, Ph.D.

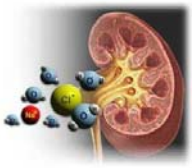
Kevin Curtis, a graduate student with Dr. Paul Schiller, received his PhD in May from the University of Miami Miller School of Medicine, Department of Biochemistry & Molecular Biology. His dissertation was entitled: “Rac1b Regulates the Neurotrophin-3 Mediated Neuronal Commitment of Bone Marrow Derived MIAMI Cells”.



Carmen Rios, Ph.D.

Carmen Rios, a graduate student with Dr. Paul Schiller, received her PhD in May from the University of Miami Miller School of Medicine, Department of Biochemistry & Molecular Biology. Her dissertation was entitled: “Molecular Mechanisms of Self-Renewal in Marrow Stromal Stem Cells”.

Awards and Honors



Ivonne Schulman, M.D.

Dr. Ivonne Schulman, Staff Physician, Miami VA Healthcare System and Assistant Professor of Clinical Medicine, University of Miami Miller School of Medicine was awarded the Instructor of the Year Award by the UMMSM nephrology fellows. This annual award recognizes excellence in teaching in clinical, academic and research aspects of nephrology fellow training. We congratulate Dr. Schulman for her outstanding efforts.

Leonard M. Miller School of Medicine

University of Miami

Miami, Florida

Division of Nephrology and Hypertension

Be it known that

Ivonne Schulman, M.D.

Has been recognized by the nephrology fellows as

Instructor of the Year

For excellence in teaching in clinical, academic and research aspects of our training

For the academic year 2009-2010

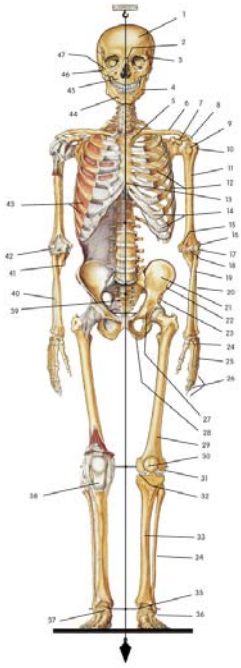
In witness we have affixed our hands and the seal of the University on this 19th day of June 2010

GRECC Members

Dr. Bruce Troen was Chair of the Program Committee for the 2010 Annual Meeting of the American Geriatrics Society, which took place in Orlando, FL, May 2010.

Dr. Herman Cheung returns to the Miami VAMC at the end of July from a two-month Visiting Professorship at Hong Kong University, where he has been expanding his collaborations and work on stem cells.

Research Highlights GRECC



Dr. Guy Howard, GRECC Research Director recently chaired the VA non-Clinician PhD Eligibility Committee that meets to review applications from non-clinician PhD scientists for eligibility to submit a VA Merit Review application. This meeting was held in Washington, DC in mid-July.

Dr. Howard is a member of the NIH Skeletal Biology Development and Disease (SBDD) Study Section, Center for Scientific Review. He recently participated in reviewing applications for NIH funding at a meeting held this round in late June in Washington, DC

Dr Howard also chaired the VA Research Career Scientist and Promotion Evaluation Committee in early July held in Washington, DC.

Dr. Paul Schiller, GRECC Investigator, a member of the VA ENDO-B Merit Review Board took part in their recent review session. This review panel reviews applications involving research on skeletal formation and repair, including stem cell mechanisms

Dr. Carlos Perez-Stable served as a Scientific Reviewer for the DOD Prostate Cancer Research Program (PCRP) online review in the Endocrinology Section, a position that he has held for some time.

2010 Miami VA Research Week

Best Overall Poster Presentations

Basic Science

1st Place

Gianluca D'Ippolito, Ph.D.

Roy C. Levitt, M.D.

2nd Place

Lourdes Gomez, M.D.

Clinical Science/Health Service

1st Place

Andrea Melo Sosa, M.D.

2nd Place

Greta Bujaker, B.S.

Young Research Investigator

1st Place

Lisett Oropesa, M.D.

2nd Place

Kevin Curtis, M.S.

Rosemeire Kanashiro-Takeuchi, DVM, Ph.D.

As part of the 2010 National VA Research Week, the Miami VA Research Service Office hosted the third Miami VA Research Awareness Day Poster Presentation. The theme was "85 Years of Discovery, Innovation and Advancement for Veterans". The event was kicked off with special lectures presented by Drs. Leonardo Tamariz *("Introduction to VA Research Grants")* and Robert Gailey *("Advances in Prosthetic Care: Lesson Learned from Around the World")* held on April 26.

The second part of the program included the Poster Session which took place on April 27 from 1:30 pm to 3:30 pm in the TC Doherty Auditorium. The response was once again very positive. Forty abstracts were submitted and approved in the following categories: Basic Science (19), Clinical Science/Health Services (8) and Young Research Investigators (13). Four first and second place awards were presented. Informational materials was provided by the Research Service Office and ORD. There were over 100 attendees including distinguished Veterans.

The program began with an introduction from Dr. Robert M. Jackson, ACOS for Research, followed with remarks by Ms. Mary D. Berrocal, MBA, the Medical Center Director. Special guest, Ms. Gisselle G. Reynolds, representing the Office of Congressman Mario Diaz-Balart was present. Also in attendance were other hospital staff and Veterans currently participating in relevant clinical studies and interested faculty and researchers from the University of Miami Miller School of Medicine.

The Miami VA Research Week was yet another successful event that highlighted the achievements of VA researchers and the role they play in providing high quality care for Veterans and advancing medical science. We would again like to extend our appreciation to all those that participated in the program for their continued support.

Presentations

Dr. Bruce Troen

Geriatric Medicine Grand Rounds, Albert Einstein College of Medicine, Bronx, NY, June 2010, ***"Vitamin D: Skeletal Health and Beyond (a Stealthy Epidemic)"***

(Dr. Bruce Troen)
Department of Medicine Research Conference, University of Texas Health Science Center, San Antonio, TX, March 2010, ***"Prolongevity Compounds and Aging Bone"***

(Dr. Bruce Troen)
Osteoporosis Symposium, American Geriatrics Society Annual Meeting, Orlando, FL, May 2010, ***"Osteoporosis: State of the Art Clinical Update."***

Dr. Stuti Dang

Technology-Assisted Care Coordination for Chronic Disease Management conference, Little Rock, AR, April, 2010, ***"Best Practices in the Continuum of Care: Innovative Models of Care for Older Adults"***

Dr. Niramol Savaraj

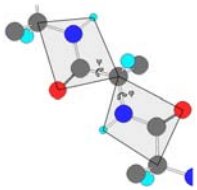
VISN7&8 Joint Research Symposium, Orlando, FL, July 21,2010, ***"Arginine Deprivation: A Targeted Therapy for Melanoma".***

Dr. Andrew Schally

Medicinal Chemistry : Drug Discovery and Design Conference, University of Patras, Patras, Greece, April 27, 2010, ***"Discovery of LHRH, the Peptide of Life: Reproduction, Cancer, Therapies"***

(Dr. Andrew Schally)
Wallace H Coulter Center for Translational Research 2010 Project Presentation, University of Miami Miller School of Medicine, Miami, FL May 19, 2010, ***"Agonists of Growth Hormone Releasing Hormone (GH-RH) for Cardiac applications, including stimulation of cardiac myocytes and regeneration of the heart after myocardial infarction"***

PUBLICATIONS



VA Endocrine, Polypeptide and Cancer

Peer Review Journals

Hohla F, Buchholz S, **Schally AV**, Krishan A, Rick FG, Szalontay L, Papadia A, G Halmos, Koester F, Aigner E, Datz C, Seitz S. *Targeted cytotoxic somatostatin analogue AN-162 inhibits growth of human colon carcinomas and increases sensitivity of doxorubicinresistant murine leukemia cells.* Cancer Letters 2010; 294:35-42.

Hohla F, **Schally AV**. *"Targeting gastrin releasing peptide receptors: new options for the therapy and diagonis of cancer"* Cell Cycle Vol. 9 (9) May 1, 2010. (EPub ahead of Print)

Abstracts

Kanashiro-Takeuchi RM, Takeuchi LM, Dulce R, Treuer AV, Hu Q, Block NL, Schally AV, Hare JM. "*Growth hormone releasing hormone (GHRH) agonist improves cardiac performance in the chronic model of myocardial infarction (MI) in rats".* AHA Basic Cardiovascular Sciences 2010 Scientific Sessions, July 19-22, 2010 – Rancho Mirage, CA

Kovacs M, Schally AV, Hohla F, Rick F, Pozsgai E, Szalontay L, Varga J, Zarandi M, *A correlation of endocrine and anticancer effects of some antagonists of GHRH*. ENDO 2010 Annual Meeting, San Diego, CA June 19-22, 2010. Endocrine Reviews, Supplement 1, June 2010, 31(3):S1293

Bellyei S, **Schally AV**, Zarandi M, Varga JL, Vidaurre I, and Pozsgai E, *GHRH antagonists, reduce the invasive and metastatic potential of human cancer cell lines in vitro.* CANCER LETTERS 2010; 293(6):31-40

Wu HM, Cheng JC, **Schally AV**, Zarandi M, Varga JL, and Leung PCK. *Growth hormone-releasing hormone (GHRH) antagonist induces apoptosis through PKCδ-mediated activation of p53/*

Books & Book Chapters

Schally AV, Block NL. Book Chapter: *Luteinizing hormone -releasing hormone (LH-RH) and its agonistic, antagonistic and targeted cytotoxic analogs in prostate cancer*. In: Drug management of Prostate Cancer. Edited by William Figg, Eric Small and Cindi H. Chau. Humana Press, New York, NY. 1st Edition 2010, Chapter 2, 698 pages .

Engel JB, **Schally AV**. *Agonists and antagonists of luteinizing hormone-releasing hormone (LHRH) in the treatment of endometriosis* in "Endometriosis: Current management and future trends" Eds. Juan A. Garcia-Velazco and Botroz Rizk. Jaypee Medical Publishers. 2010. Chap. 25, p204-209

BCVS 2010

Barabutis N, Siejka A, and **Schally AV**. *Effects of growth hormone releasing hormone and its agonistic and antagonistic analogs in cancer and non-cancerous cell lines*. International Journal of Oncology 2010; 36:1285-1289

Siejka A, **Schally AV**, Block NL, Barabutis N, *Antagonists of growth hormone-releasing hormone inhibit the proliferation of human benign prostatic h yperplasia cells*. The Prostate: 2010; 70:1087-1093.

In Press

Pozgai E, **Schally AV**, Varga J, Halmos G, Rick F, Bellyei S, *The inhibitory effect of a novel cytotoxic somatostatin analog, A-162 on experimental glioblastoma.* Hormone and Metabolic Research: In Press

Schally AV, Engel JB, Emons G, Block NL, Pinski J, *Use of analogs of peptide hormones conjugated to cytotoxic radicals for chemotherapy targeted to receptors on tumors.* Current Drug Delivery: In Press

Barabutis N, Siejka A, **Schally AV**. *"Growth hormone releasing hormone induces the expression of nitric oxide synthase".* Journal of Cellular and Molecular Medicine: In Press

Ludwig B, Ziegler CG, **Schally AV**, Richter C, Steffen A, Jabs N, Funk RH, Brendel MD, Block NL, Ehrhart-Bornstein M, Bornstein SR. *"Agonist of growth hormone releasing hormone as a potential effector for survival and proliferation of pancreatic islets"* PNAS: In Press

Siejka A, **Schally AV**, Block NL, Barabutis N, *Mechanisms of Inhibition of Human Benign Prostatic H yperplasia in vitro by LHRH antagonist Cetrorelix*. BJU International (EPub ahead of Print Feb. 11, 2010)

Guo J, **Schally AV**, Zarandi M, Varga J and Leung PCK. *Antiproliferative effect of growth hormone-releasing hormone (GHRH) antagonists on ovarian cancer cells through the EGFR-Akt pathway*. Reproductive Biology and Endocrinology 2010; 8:54

Submitted for Publication

Emons G, Kaufmann M, Gorchev G, Tsekova V, Grundker C, Sindermann H, Engel J, and **Schally AV**. *Dose escalation and pharmacokinetic study of AEZS-108 (AN-152) an LHRH agonist linked to doxorubicin, in women with LHRH receptor positive tumors*. Journal of Clinical Oncology: Submitted

Wen J, Feng Y, Ahs ZZ, Zu Y, **Schally AV**, Chang CC. *Luteinizing hormone-releasing hormone (LHRH) antagonist Cetrorelix inhibits myeloma cell growth in vitro and in vivo.* Clinical Cancer Research: Submitted

Liu SV, **Schally AV**, Hawes D, Xiong S, Fazli L, Gleave M, Cai J, Groshen S, Brands F, Engel J, and Pinski J. "*Expression of receptors for luteinizing hormone-releasing hormone (LH-RH) in prostate cancers following therapy with LH-RH agonists*". Clinical Cancer Research: Submitted

PUBLICATIONS

Geriatrics Research Education & Clinical Centers

Recent Publications

Calvo A, Perez-Stable C, Segura V, Catena R, Guruceaga D, Nguewa P, Blanco D, Parada L, Reiner T, Green JE. Molecular Characterization of the Ggama-globin-Tag Transgenic Mouse Model of Hormone Refractory Prostate Cancer: Comparison to Human Prostate Cancer. Prostate. 70:630-645, 2010

Yamazaki Y, Kamei Y, Sugita S, Akaike F, Kanai S, Miura S, Hirata Y, Troen BR, et al. The Cathepsin L Gene is a Direct Target of FXO1 in the Skeletal Muscle. Biochem J. 427:171-178, 2010

Golden AG, van Zuilen MH, Mintzer MJ, Issenberg SB, Silverman MA, Roos BA. A Fourth-year Medical School Clerkship that Addressed Negative Attitudes Toward Geriatric Medicine. J Am Geriatr Soc. 58:746-750, 2010

Golden AG, Roos BA, Silverman MA, Beers MH. Home and Community-based Medicaid Options for Dependent Older Floridians. Am Geriatr Soc. 58:371-376

Tan ZS, Mulhausen PL, Smith SR, Ruiz JG. Virtual Patients in Geriatric Education. Gerontol Geriatr Educ 31:163-173, 2010

Cherniack EP, Cherniack NS. Obstructive Sleep Apnea, Metabolic Syndrome, and Age: Will Geriatricians be Caught Asleep on the Job? Aging Clin Exp Res 22:1-7, 2010

Cherniack EP. Would the Elderly be Better off if They were Given more Placebos? Geriatr Gerontol Int 10:131-137, 2010

Hebert K, Lopez B, Horswell R, Tamariz L, et al. The Impact of a Standardized Disease Management Program on Race/Ethnicity and Gender

Fletcher MA, Zeng XR, Maher K, Levis S, Hurwitz B, Antoni M, Broderick G, Klimas NG. Biomarkers in Chronic Fatigue Syndrome: Evaluation of Natural Killer Cell Function and Dipeptidyl Peptidase IV/CD26. PLoS One 5(5):e10817

Levis S, Strickman-Stein N, Doerge DR, Krischer J. Design and Baseline Characteristics of the Soy Phytoestrogens as Replacement Estrogen (SPARE) Study--A Clinical Trial of the Effects of SoyIsoflavones in Menopausal Women. Contemp Clin Trials 31:293-302

Schwartz AV, Bauer DC, Cummings SR Cauley JA,...FLEX Research Group, incl. Levis S, et al. Efficacy of Continued Alendronate for Fractures in Women with and without Prevalent Vertebral Fracture: the FLEX Trial. J Bone Miner Res 25:976-982, 2010

Hebert K, Lopez B, Michael C, Franco E, Dias A, Trahan P, Huang S, Tamariz L, Arcement L. The Prevalence of Peripheral Arterial Disease in Patients with Heart Failure by Race and Ethnicity. Congest Heart Fail 16:118-121, 2010

Contreras G, Mattiazzi A, Buerra G, Ortega LM, Tozman EC, Li H, Tamariz L, et al. Recurrence of Lupus Nephritis after Kidney Transplantation. J Am Soc Nephrol 21:1200-1207, 2010

Florez H, Luo J, Castillo-Florez S, Mitsi G, Hanna J, Tamariz L, Palacio A, et al. Impact of Metformin-Induced Gastrointestinal Symptoms on Quality of Life and Adherence in Patients with Type 2 Diabetes. Postgrad Med 122:112-120, 2010

Tamariz L, Hare JM. Inflammatory Cytokines in Heart Failure: Roles in Aetiology and Utility as Biomarkers. Eur Heart J 31:768-770, 2010

Manuscripts accepted for publication

Subbaravan PR, Sarkar M, Impellizzeri S, Raymo F, Lokeshwar BL, et al. Anti-Proliferative and Anti-Cancer Properties of Achyranthes aspera: Specific Inhibitory Activity Against Pancreatic Cancer Cells. J Ethnopharmacol. 2010 Jun 9 [Epub ahead of print] PMID: 20541002

Davila EP, Florez H, Fleming LE, et al. Prevalence of the Metabolic Syndrome among US Workers. Diabetes Care. 2010 Jun 28 [Epub ahead of print] PMID: 20585004

Golden AG, Ma, Q, Nair V, Florez HG, Roos BA. Risk for Fractures with Centrally Acting Muscle Relaxants: An Analysis of a National Medicare Advantage Claims Database (September). Ann Pharmacother. 2010 Jul 6 [Epub ahead of print] PMID: 20606016

Hebert K, Dias A. Delgado MC, Franco E, Tamariz L, et al. Epidemiology and Survival of the Five Stages of Chronic Kidney Disease in a Systolic Heart Failure Population. Eur J Heart Fail. 2010 May 19 [Epub ahead of print] PMID: 20484366

Parrondo R, de Las Pozas A, Reiner T, Rai P, Perez-Stable C. NF-kappa B Activation Enhances Cell Death by ANtimitotic Drugs in Human Prostate Cancer Cells. Mol Cancer. 2010 Jul 9 [Epub ahead of print] PMID: 20618955

Diaz R, Nquewa PA, Parrondo R, Perez-Stable C, et al. Antitumor and Antiangiogenic Effect of the Dual CGFR and HER-2 Tyrosine Kinase Inhibitor Lapatinib in a Lung Cancer Model. BMC Cancer. 2010 May 11 [Epub ahead of print] PMID: 20459769

Golden AG, Tewary S, Dang S, Roos BA. Care Management's Challenges and Opportunities to Reduce the Rapid Rehospitalization of Frail Community-Dwelling Older Adults. Gerontologist. 2010 Feb 25 [Epub ahead of print] PMID: 20185522

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John W. Brown, Ph.D.

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Brown, J.W., Schally, A., Treszl, A., Young, L. and Fishman, L.M. (2009). Differential Expression of Neuromedin-B, Gastrin Releasing Peptide and Bombesin S-3 Receptor in SW-13 and H-295r Human Adrenal Cortical Carcinoma Cultures. Proceedings of the 49th Annual Meeting of The American Society for Cell Biology, Cancer II Session, Program 891, Abstract B49.

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Ivonne Schulman, M.D.

Manuscript entitled ***"Altered Renal Expression of Angiotensin II Receptors, Renin Receptor, and ACE-2 Precede the Development of Renal Fibrosis in Aging Rats"*** was recently accepted for publication in the American Journal of Nephrology.

Schulman IH, Zhou MS, Treuer AV, Chadipiralla K, Hare JM, Raij L. Altered Renal Expression of Angiotensin II Receptors, Renin Receptor, and ACE-2 Precede the Development of Renal Fibrosis in Aging Rats. American Journal of Nephrology, 2010 (in press)

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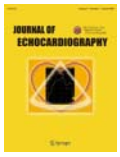

Esther L. Misdraji
Carlton S. Gass

The Trail Making Test and its neurobehavioral components
This study investigates the neurobehavioral components involved in Trail Making Test (TMT; Parts A and B) performance and their relation to MMPI–2 measures of anxiety and depression. Consecutive patients (N = 192) referred for a comprehensive neuropsychological evaluation at a U.S. Department of Veterans Affairs (VA) Medical Center comprised the sample. Results: graphomotor speed and mental shifting were significantly associated with Wechsler Adult Intelligence Scale–Third Edition (WAIS–III) indexes, whereas visual scanning efficiency was not. Graphomotor speed accounted for a substantially greater portion of the variance in TMT performance within impaired than within normal groups. Levels of anxiety and depressive symptoms were unrelated to TMT performance. Implications and directions for future research are discussed.
Journal of Clinical and Experimental Neuropsychology 2010, 32 (2), 159–163

Gass, CS, Williams, CL, Cumella, E., Butcher, JN, Kally, Z. ***"Ambiguous Measures of Unknown Constructs: The MMPI-2 Fake Bad Scale (aka Symptom Validity Scale, FBS, FBS-r)"***
Psychol. Inj. and Law. Received: 11 November 2009 / Accepted: 15 December 2009

From Cancer to Cardiology, Nobel-winning Scientist is Closing in on Cures

Andrew V. Schally, Ph.D., M.D.h.c., D.Sc.h.c.

At age 80-plus, Dr. Andrew Schally, winner of the 1977 Nobel Prize in Physiology or Medicine is hot on the trail of compounds he believes will revolutionize cancer treatment. But over his decades-long career, Dr. Schally has been credited with weighty advances in a wide range of additional specialties, among them, gynecology, gastroenterology, endocrinology, and now, cardiology. He has published more than 2,200 papers, more than 1,200 of them after winning the Nobel Prize.

Joining VA in 1962, Dr. Schally set up a lab devoted to research on the hypothalamus. His early work established the fact that the pituitary gland and certain other glands of the endocrine system are regulated by the region in the brain called the hypothalamus. This work, which has been called the foundation of modern endocrinology, earned him his Nobel in 1977. The prize was shared with Rosalyn Yalow, a friend and VA colleague who pioneered the field of radioimmunoassay, and hormone researcher Roger Guillemin.

In those early years, Schally's focus was in the field of human reproduction, leading to the development of both fertility and contraceptive compounds. His work since then has pyramided on these initial scientific breakthroughs. Dr. Schally's scientific curiosity has fueled his long line of achievements in medical science. "This is a trait I still have," says the scientist. "I want to know how nature controls these mechanisms." It was this curiosity, along with a strong sense of ethical responsibility as a scientist, that in the 1970s caused Schally to shift the focus of his earliest hormone research from reproductive health to oncology.

One example of Dr. Schally's revolutionary discoveries in the fight against cancer, the current treatment for testosterone-dependent prostate cancer used successfully in hundreds of thousands of men around the world, is derived from a brain chemical called luteinizing hormone-releasing hormone (LHRH), which he discovered. Schally calls LHRH the "biggest prize" of his long career. More recently, a Schally-led research team found that a synthetic compound called JMR-132 stops the spread of human prostate cancer cells and also acts as a strong antioxidant. Like some other compounds that Schally has explored, the compound works as an antagonist to a tumor-nourishing natural body chemical called growth hormone-releasing hormone. Schally has studied thousands of potential therapies, including analogs, modified compounds that can pack 100 times the punch of natural hormones, and out of this far-reaching investigation has created several auspicious cancer therapies. Schally is now exploring hormone-based treatments for breast, ovarian, pancreatic, lung and other tumors, and his team is involved in several clinical trials of hormone based therapies. "I believe we are very, very close to new methods for cancer treatment," says Schally, who recently received a Meritorious Service award from VA for his work on innovative cancer therapies. Schally is now set on developing "smart" chemotherapies to zap cancer cells while leaving surrounding tissue unscathed. While Schally is careful to distinguish between effective treatments and "cures," he brims with excitement when describing this latest work. "The beauty of these methods is that they are targeted to tumors," says Schally of his approach, which combines cancer drugs with synthetic versions of hormones and then hunts down tumors that have receptors for those hormones. "They go to the tumor and they can destroy malignant cells. If you repeat it two, three times, you can perhaps totally destroy the tumor. In such a case, you have a treatment that comes very close to being a cure."

Heart-protective compound identified

In a potentially important advance in the study of congestive heart failure, a leading cause of disability, Dr. Schally and his University of Miami colleagues have found a compound that sparked major recovery in rats after heart attack, which often leads to heart failure. The compound is a derivative of growth hormone-releasing hormone (GHRH), and the research team's findings were published earlier this year in the *Proceedings of the National Academy of Sciences.* Schally has studied GHRH extensively for its cancer-fighting potential, and his laboratory synthesized the compound used in this study. He and his colleagues plan to study the mechanisms further so they can move the compound into human testing, and Schally predicts that GHRH will prove able to repair the heart in humans, too.

SFVAFRE Celebrates its 20th Anniversary

The South Florida VA Foundation for Research and Education, Inc. (SFVAFRE) celebrates its 20th year of improving Veterans' Health and Education. The SFVAFRE was incorporated on May 21, 1990 under the leadership of Dr. Lawrence Fishman, ACOS for Research and Mr. Gustavo Godoy, Administrative Officer for Research. The SFVAFRE was created with only one mission in mind: to facilitate and provide flexible funding for research and education activities conducted at the Miami VA Healthcare System.

During the first year of inception, the SFVAFRE managed 18 projects conducted by 12 investigators. One of those investigators was Dr. Nancy Klimas who produced 58% of total revenue on that year. This year we proudly announce that Dr. Klimas is the first principal investigator to receive an NIH-R01 grant through the SFVAFRE.

The SFVAFRE has worked on broad spectrum of research, including clinical trials, basic science and educational activities. Currently there are 31 projects conducted by 26 investigators. In the past 20 years SFVAFRE budget has increased from $756,654 to $3,371,963 in net assets. During this time many scientific discoveries and contributions have taken place. A major contribution has been the recruitment of VA's only remaining Nobel Laurent Dr. Andrew Schally whose contribution to VA Research initiatives in the field of Cancer research continues to expand with newly developed therapies and treatments.

We look forward to new endeavors and breakthroughs as we serve the Veterans that fight to protect our country. We would like to extend our deepest appreciation to all of our investigators and staff for their continued support and dedication.

S F V A F R E CORNER

CRADA Update:

- Currently there are over 600 active VA CRADAs with more than 220 different companies.
- Master CRADAs negotiated by TTP Technology Transfer Specialist Jeffrey Moore, PhD, and OGC Professional Staff Group (PSG) III continue to be the most expeditious path to an executed CRADA. Over 50 CRADAs have been executed using the Novartis master alone.
- The CRADA Registry is regularly reviewed to identify companies that have executed 3 or more CRADAs and contacts them to assess interest in negotiating a master.

Master CRADAs

Amgen
Astellas
Astrazeneca
Avigen
Bristol-Myers Squibb
Celgen
Genentech
GSK
Lilly & Lilly
Merck
Novartis
OncoGenex
Pfizer
Regenesis Biomedical
Roche
Sanofi-Aventis
Sucampo
Takeda
Watson Pharma

Miami VA CRADAs

Executed

Karmacharya Endologix– *CT Device*
Jeffers Eisai– *CT Phase II*
Jackson Novartis– *CT Phase II*

Under negotiation

Savaraj Novartis– *PI Initiated*
Rothenberg Cupron– *CT Device*

If you have a project you would like to pursue, please stop by. We are happy to help.

Other Funding

Awarded

Klimas: *"Chronic Fatigue Syndrome: Pathophsiology and Treatment"* (NIH R01)

Wangpaichiter: Florida Bio-Medical James and Esther King Grant

Nash & Martinez-Arizala: *Obesity/ Overweight in Persons with Early and Chronic SCI: a Randomized Multicenter, Controlled Lifestyle Intervention"* (DOD)

Submitted

Yu: NIH R-21 *"Neutrophil Homing and its Contribution to Angiogenesis"*
Klimas: DOD *"Gulf War Illness Research Program"*

GRANTS FUNDED

Dr. Stuti Dang is a Partnering PI together with Dr. Kris Siddharthan from the Tampa VAMC on a Department of Defense award entitled *"Comparative Effectiveness of Telerehabilitation for OIF/OEF Returnees with Combat-Related Traumatic Brain Injury/ Post-Traumatic Stress Disorders"* that is funded 06/1/2011 – 05/31/2014 with a total direct cost of $1.73M. This 3-year project will provide specially formatted computers to Veterans with mild Traumatic Brain injury, and coordinate their care. The investigators will measure if this support improves the outcomes of depression, anxiety, PTSD, job procurement, and drug use with this veteran population.

Dr. Stuti Dang is the PI of a State of Florida Biomedical Research Foundation Grant entitled *"A Novel Fully Integrated Mobile Management Solution Using Cellular Phone Technology for Heart Failure"* funded 03/01/10-02/28/11 for $99,999 total direct costs. This is a Technology Transfer Commercial Partnership (TTCP grant). The goal of this project is to refine a mobile phone technology for comprehensive heart failure management and to examine impact on self-care and cost.

Dr. Stuti Dang is also the PI of a $50,000 award from Ideal Life (a private corporation) for a project entitled *"Home Telehealth in Heart Failure",* for the period 01/01/10 – 12/30/10. This study will evaluate the impact of daily automated transmission of weights using Bluetooth technology on patient health care utilization, self care efficacy, and quality of life.

Dr. Hermes Florez received Comparative Effectiveness Research award from the Department of Health and Human Services entitled "*Telemedicine Intervention to Increase CER Adoption for Diabetes Prevention in Obese Older Veterans"* for the period 06/01/10-05/31/13. The three-year study is funded for $500,000 direct costs. This project is designed to enhance the focus on developing and implementing evidence-informed, innovative interventions to increase adoption of this comparative effectiveness research (Enhance Fitness and Diabetes Prevention Program) by obese older adults and their providers, translating this evidence into practice by the effective use of telehealth technology and effectively addressing the health and economic challenges of our aging society. Dr. Stuti Dang is a co-PI on this project.

Dr. Priya Rai received a Stanley J. Glaser Award for her project entitled *"Oxidative Stress-Protective Proteins as Novel Molecular Targets for Improving Efficacy of Androgen Ablation Therapy in Androgen-Responsive Prostate Cancer"* for $40,000, with a term from 6/1/2010 to 5/31/ 2011.

Dr. Leo Tamariz received a Comparative Effectiveness Research award from the Department of Health and Human Services entitled *"Innovative Strategies for Disseminating and Increasing Adoption of the AHRQ Comparative Effectiveness Summary Guides in Elderly Patients and Their Physicians"* for $1.0M for the period 06/01/10-05/31/13.

FEEDBACK

Faculty and staff submissions can be e-mailed to the Office of Research Communications at
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