



# Miami VA Research & Development

MIAMI VA HEALTHCARE SYSTEM

AUGUST 1, 2008  
VOLUME 1, ISSUE 1

## CRADA Special points of interest:

- Protect background inventions
- Access to VA research resources
- Establish IP ownership
- Leverage federal expertise
- Supported fully by FTTA
- Government-wide collaborative relationships
- Consistency w/federal statutes
- Single CRADA for multi-center studies & execution of Master CRADA w/major sponsors

## Inside this issue:

Research Highlights	2
SFVAFRE Corner	2
Research Week (con't)	3
Upcoming Events	3
Important News &	3
Renewed Funding	5
Research Highlights (con't)	4
Recent Publications	4-5

## From the Editor

Welcome to the first issue of the Miami VA Research & Development Newsletter. The goal of the newsletter is to increase communication among the research faculty and staff and to increase our awareness of the considerable accomplishments of members of our service. Contributions of news, events, publications, workshops, and career information to the newsletter are always welcome. Since it is the first issue, there is scope to improve its content after receiving comments and suggestions from you the readers. I look forward to your feedback.

## Research Week 2008



As part of the 2008 National VA Research Week, the Miami VA Research Service hosted the Miami VA Research Awareness Day Poster Presentation. The organization process for this year's program was challenging and began with a general invitation to the event and a call for abstracts to all VA research investigators. The feedback was very positive. Over 50 abstracts were submitted. The evaluation form was created using a 1 to 5 grading scale. Each abstract was anonymously sent to three appropriate judges who graded the abstracts. The judging forms were returned electronically and the results were calculated. Four top winners were selected and 13 awards for honorable mention were given.

The program took place on May 13, 2008 from 1:30 pm to 3:30 pm in the TC Doherty Auditorium. The abstracts were compiled in Abstract Books,

which were printed and distributed to all presenters and attendees. Several research coordinators publicized their current clinical studies and provided brochures and other educational material. As a special keepsake for the Miami VA Research Awareness Day, a pewter lapel pin in the shape of a microscope was given to everyone who attended the event.

The program commenced with opening remarks from Dr. Robert M. Jackson, ACOS for Research. Dr. P. Gwendolyn Findley, Assistant Director, summarized historical accomplishments made by the Office of Research and Development.



Continued on Page 3

## In the News



Honored for cancer research with VA's Meritorious Service Award by Chief Research and Development Office, Officer Joel Kupersmith, MD (left) and Under Secretary for Health Michael Kussman, MD, during the Research Forum event at VA headquarters on May 23.

**Andrew V. Schally, PhD** of the Miami VA Healthcare System and Miller School of Medicine, received a Meritorious Service Award from VA for his work on innovative cancer treatments. Winner of the Nobel Prize in Physiology or Medicine in 1977, Dr. Schally discovered and synthesized three hormones-all peptides, or chains of amino acids-produced in the hypothalamus region of the brain. The discoveries had a significant impact on reproductive medicine, among other areas, leading to the development of fertility and contraceptive compounds. More recently, his research has focused on the development of "smart" chemotherapy that targets tumors but leaves surrounding tissues unharmed. The approach involves combining cancer drugs with synthetic versions of hormones and then targeting tumors that have receptors for those hormones.

## Research Highlights

**Carlton S. Gass, PhD** is the Director of the Neuropsychology Clinic at the Miami VAHCS. He is engaged in applied clinical research aimed at improving the clinical assessment of veterans with known or suspected brain injury, as well as veterans with emotional difficulties such as PTSD. Dr. Gass is the Principle Investigators on the following current VA projects:

A Component Analysis of the Trail Making Test (co-author: Dr. Esther Misdraji) and Impact of Depression on Auditory Memory Storage and Retrieval (co-author: Alison Dowd, M.S.)

Dr. Gass is also a consulting editor for the Archives of Clinical Neuropsychology, (the official journal of the National Academy of Neuropsychology) and a frequent reviewer for the journal Psychological Assessment

The **Functional Outcomes Research and Evaluation (FORE)** center is dedicated toward amputee rehabilitation and minimizing the risk of secondary complications associated with an amputation. FORE developed an innovative tool called Symmetry in External mechanical Work (SEW), that would help physical therapists, physicians and prosthetists determine the “quality” of everyday activities, such as walking, going up and down stairs and ramps, turning, sitting down and standing up from a chair. One of the investigators, Vibhor Agrawal, was awarded the first prize in recognition of this new measure. The other researchers involved with the development of the SEW tool include Robert Gaily, Ignacio Gaunaard and Christopher O’Toole. The FORE center has received external funding to advance knowledge about this new measure as well as to evaluate the cutting edge bionic prosthetic technology. Ron Tolchin, chief of physical medicine and rehabilitation, has been named as the principal investigator for this research project.

The adrenal research group of **Dr. Lawrence M. Fishman** and **Dr. John W. Brown** within the Miami VAHCS (including former UM/VA Endocrinology fellows Drs. Maribel Montoya and Luz Prieto) recently published three journal articles in *Hormone & Metabolic Research* describing their findings on the comparative effects of established and experimental cancer chemotherapy agents, steroid hormones and derivatives on cell-cycle alterations, as well as on growth and apoptosis in the SW-13 human adrenal cortical carcinoma cell-line. Dr. Carlos Perez-Stable (Miami VA/GRECC) was an important contributor and co-author in these studies. Among other findings, their work showed that low dose 2-methoxy-estradiol ( $10^{-7}$  M) and high dose progesterone ( $10^{-5}$  M) treatment both have strong growth-inhibitory effects which involve a G2/M blockade, as well as the induction of apoptosis. They have also demonstrated high dose  $17\beta$ -estradiol induced apoptosis. The results of estrogen analog studies indicate that this effect is probably mediated by the  $\alpha$  receptor.

This group is now pursuing collaborative studies with Dr. Andrew V. Schally, Director of the VA Endocrine, Polypeptide & Cancer Research Institute and Dr. Lisa Young (UM/VA Endocrinology fellow) investigating hypothalamic neuropeptide analog effects on the growth and survival of human adrenal carcinoma cell-lines in culture. Dr. Andrea Treszl from Dr. Schally’s laboratory was a key participant in experiments demonstrating receptor and/or receptor variant expression of neuropeptide analogs for somatostatin, LHRH, GHRH and Bombesin/GRP in these cells. Dr. Brown was invited to present the adrenal carcinoma data at the INTERNATIONAL SYMPOSIUM ON ENDOCRINE-RELATED TUMORS at the University of Dresden (GERMANY). Dr. Schally gave the keynote lecture on neuropeptide analog effects in other cancers at the same conference. Preliminary findings of their collaborative research in adrenal cortical carcinoma was also presented and published in three posters at the 2008 Endocrine Society Meeting in San Francisco, CA.

### SFVAFRE Corner

#### Status of Master CRADA’s

<u>Completed Master Phase III/IV</u>	<u>In Negotiations</u>
Genentech	Abbott
Lilly	Bristol-Myer Squibb
Novartis	Forest Lab
Roche	Johnson & Johnson
	Merck
<u>Almost Completed</u>	Sanofi-Aventis
Amgen	Schering-Plough
Astra-Zeneca	Wyeth
Pfizer	

**WWW.SFVAFRE.org is getting an extreme make-over. Please stay tuned.**

Effective March 26, 2008, the VA switched to CRADA’s for industry-sponsored research. The use of CRADA’s will create consistency throughout the VA system, making it easier for VA investigators to participate in multi-site clinical trials which occur in later stages of research and involve a number of locations and a large number of participants.

The SFVAFRE has established a relationship with Novartis. Current areas of specialties include cardiology, endo/diabetes,

hypertension and COPD. We are working with our contact to reach out to investigators who practice in these areas.

If you are interested in pursuing research studies with a company not currently on the master CRADA list, the SFVAFRE has the ability to negotiate and execute a locally generated CRADA.

Currently the SFVAFRE is negotiating local CRADAs with Forest Research Institute and IDEALLIFE.

If you have any questions or would like copies of the CRADA models, please contact our office at (305) 575-7000 ext. 3722.

## Research Week 2008 from Page 1

Dr. Jackson highlighted the work of several leading Miami VA investigators. He concluded with the announcement of the winners and distribution of awards.

The program was well attended by hospital staff and patients currently participating in relevant clinical studies. Interested faculty and researchers from the University of Miami Miller School of Medicine also attended. Dr. Audrey Kalehua, Scientific Program Manager, Rehabilitation Research and Development, Washington D.C. was an invited guest.

The interaction between the presenters and attendees was a key factor in achieving our goal of promoting collegiality.

We received positive feedback from investigators who stated they were not aware of the superb quality of research being conducted in other areas within the Miami VA Healthcare System. The poster presentation sparked new research interest for future collaborations among Miami VA investigators.



*Dr. Hermes Florez receives his award.*

## Poster Presentation Winners

**Best Overall Clinical Science Presentation**  
Joseph Signorile, Ph.D.

*Honorable Mention*  
Eva Widerstrom-Noga, DDS, PhD

**Best Overall Basic Science Presentation**  
Carlos Perez-Stable, Ph.D.

*Honorable Mention*  
K.S. Panickar, Ph.D., Guy Howard, Ph.D.,  
Manhui Pang, M.D.

**Best Overall Health Services Presentation**  
Gary Lees, M.S.N., A.R.N.P.

*Honorable Mention*  
Jason Dahn, Ph.D., Daisy Galindo-Ciocon, PhD, ARNP,  
Stuti Dang, M.D., Sara Mow, B.S.

**Best Overall Young Research Investigator Presentation**  
Hermes Florez, M.D., Ph.D.

*Honorable Mention*  
Maria Carpintero, M.D., Ivonne Schulman, M.D.,  
Kevin Curtis, B.S., Irving Vidaurre, B.S., Stephen Seitz, M.D.

## Upcoming Events

**August 7-8, 2008**  
**AARHPP Site Visit**

*Association for the  
Accreditation of  
Human  
Research  
Protection  
Programs*

Preparations for the AARHPP site visit have been underway for several months. This is a time and person intensive process, involving detailed assessment, evaluation, and fine-tuning of our entire research program. The results of our application for accreditation and site visit will be determined in early December.

## Informational Workshop

**Friday, October 17, 2008**

8:30 am to 4:30 pm



## Institutional Review Board 250

Speakers for IRB 250  
**Drs. Jeffrey Cohen**  
**Ernest Prentice.**

**PRIMOR** AT YOUR DOORSTEP

**IRB 250** is a topic-specific educational program that has been customized to the interests and needs of the Miami VA Healthcare System. The program begins with a discussion on the Criteria for the Review of Research followed by four modules that include:

*HIPAA as it Pertains to Research*  
*Informed Consent*  
*Conflicts of Interest*  
*IDE/IND*

## IMPORTANT Training Required

**DEADLINE FOR COMPLETION: 8-31-08**

### DIRECTIONS:

1. Log onto LMS at [www.lms.va.gov/plateau/user/login.do](http://www.lms.va.gov/plateau/user/login.do)
2. In the Search box type: [Information Security 201 for Research & Development Personnel](#)
3. Complete in the following order:
  - a. Course "[Information Security 201 for Research & Development Personnel](#)"
  - b. Post test.
4. Print certificate and give a copy to the main research office.

You must be able to view all graphics to complete the course. If you have trouble viewing the graphics on your VA Computer, call IRMS help desk at x 3201.

For more guidance on course completion, please contact Katrina Washburn, PhD in the Main Research Office at extension 3431.

A new course has been developed for Information Security Training entitled "Information Security 201 for Research & Development Personnel." There is a one time requirement to complete this course for existing personnel in the capacity listed below; new hires must complete upon employment.

**Information Security 201 for Research & Development Personnel:** All VA Research Office personnel, investigators, study coordinators, research assistants, trainees involved in human subjects research projects, administrative support staff (including secretaries and clerks), and members of the IRB and Research & Development Committee. Personnel includes compensated and without compensation (WOC) employees, and IPAs.

If a non-employee VA staff member (WOC or IPA) is required to take this training, he/she currently must access it through VA LMS. The local VA LMS Administrator will need to manually create a VA LMS account for the individual. If you fall in this category, please contact Mr. Luis Gonzalez, AO for Research, at 305-575-3179.

## Renewed Funding

The following principal investigators have received funding for their meritorious research projects:

<b>Eric Greidinger, MD</b> (Renewed)	<i>Apoptosis and Innate Immunity in Autoimmunity</i>
<b>Micheline McCarthy, MD., PhD.</b> (Renewed)	<i>Neurogenesis and Neuronal Survival in HIV-1 Infection</i>
<b>Carlos Perez-Stable, PhD</b> (Renewed)	<i>2-Methoxyestradiol and Induction of Apoptosis in Prostate Cancer</i>
<b>Herman Cheung, PhD</b> (New Funding)	<i>Aging Diminishes Compression-Induced Chondrogenesis in Stem Cells</i>

We would like to welcome the following new principle investigator who also received funding for his research project:

<b>Balakrishna Lokeshwar, PhD</b>	<i>Transregulation of Chemokine Receptors in Prostate Cancer Progression</i>
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*Congratulations from the faculty and staff at the Research Office*

## Research Highlights

(continued)

### Carlos Abaira, MD

*Co-Chair, VA Diabetes Trial (VADT, CSP # 465)*

*Professor of Medicine-VAMC, U. of Miami Miller School of Medicine*

The VA Diabetes Trial (VADT) has recently concluded, and there were several important findings that will affect the care of diabetes in veterans. This trial lasted altogether 7 years, with a mean follow-up of 6 years, involving 1,800 patients in 20 VA medical centers nationwide. One of the 2 co-chairs, Dr. Carlos Abaira, is at the Miami VAMC, and the Miami team, headed by Dr. Jennifer Marks, Chief of Endocrine Section, also participated in this trial.

The main purpose of the VADT was to see if a strict blood sugar control was better than standard control at preventing new cardiovascular disease. As it turns out, there was no difference between the intensive treatment group and the patients who continued regular treatment. The same results were also found in two other studies recently completed, the ACCORD trial (sponsored by the U.S. National Institute of Health) and the ADVANCE study, which was done in Europe, Asia, Australia and Canada. However, the total number of new cardiovascular problems seen in the people who participated in the VADT overall was 25% less than expected, probably because of the excellent blood pressure control, reduced blood lipids and changes in lifestyle that were part of the research program.

### Andrew Schally, PhD, ScD, MDHC

*Head of the Endocrine, Polypeptide and Cancer Institute* was one of eight great scientists who were invited to attend the BIT's Annual World Cancer Congress held in Shanghai, China on June 12-17, 2008. Dr. Schally's Keynote Address was entitled "Antagonists of Growth Hormone Releasing Hormone (GHRH) in Cancer Therapy". Dr. Schally gave 3 other lectures in Shanghai on anticancer compounds and received an honorary professorship of Tonji University.

## Recent Publications



### Michael M. Cohen, DPM, FACFAS

*Chief Podiatry Section, Surgical Service*

Safety and Efficacy of Intra-articular Sodium Hyaluronate (Hyalgan) in a Randomized, Double-Blind Study for Osteoarthritis of the Ankle; Foot and Ankle International, July 2008 / Volume 29 / Number 7. 657-663

Michael M. Cohen DPM, Roy D Altman MD, Richard Hollstrom DPM, Craig Sun DPM, Bradley Gipson DPM

### Endocrine, Polypeptide and Cancer Institute

#### Schally AV

*New approaches to therapy of various tumors based on peptide analogs.*

Hormone and Metabolic Research (HMR)2008; 40:315-322.

#### Schally AV, Varga JL, Engel JB

*Drug Insight: Clinical use of antagonistic analogs of growth hormone-releasing hormone: an emerging new therapy for cancer.*

Nat Clin Pract Endocrinol Metab 4(1): 33-43, 2008.

#### Szepeshazi K, Schally AV, Halmos G.

Therapy of experimental hepatic cancers with cytotoxic peptide analogs targeted to receptors for luteinizing hormone-releasing hormone, somatostatin or bombesin.

Anti-cancer Drugs 2008, 19:349-358.

#### Kidd M, Schally AV, Pfragner R, Malfertheiner MV, Modlin IM

*Inhibition of proliferation of small intestinal and bronchopulmonary neuroendocrine cell lines: Peptide analogs targeting the receptors*

Cancer 112:1404-14, 2008.

#### Kovács M, Schally AV, Varga JL, Zarandi M

*Endocrine and antineoplastic actions of growth hormone-releasing hormone antagonists.*

Curr Med Chem 2008;15(4):314-321.

#### Barabutis N, Schally AV

*Knocking down gene expression for Growth Hormone Releasing Hormone inhibits proliferation of human breast, prostate and lung cancer cell lines*

British Journal of Cancer 2008; 98:1790-1796.

#### Papadia A, Schally AV, Seitz S, Treszl A, Engel J, Block NL, Lucci JA. *Experimental therapy of ES-2 human platinum resistant ovarian cancer with targeted cytotoxic analogue of somatostatin AN-162 [AEZS-124]*

Abstract: AACR Annual Meeting, April 12-16, 2008, San Diego, CA

Joint Meeting of The Western Association of Gynecologic Oncologists and The Felix Rutledge Society, June 11-14, 2008, Sonoma, CA.

#### Seitz S, Schally AV, Treszl A, Papadia A, Engel JK, Block NL. *Experimental therapy of MDA-MB-231 human breast cancers with targeted cytotoxic analogue of somatostatin AN-162 (AEZS-124)*

Abstract: AACR Annual Meeting, April 12-16, 2008, San Diego, CA

#### Kovács M, Szepeshazi K, Schally AV.

*Endocrine and antineoplastic effects of antagonistic and cytotoxic LHRH analogs.*

Book Chapter: Peptides Review

In: Merchenthaler I and Kovacs M: Transworld Research Network

**Recent Publications***(Continued)***Endocrine, Polypeptide and Cancer Institute**

**Zhao L**, Yano T, Osuga Y, Nakagawa S, Ohshi H, Wada-Hiraike O, Tang X, Yano N, Kugu K, Schally AV, Taketani Y  
*Cellular mechanisms of growth inhibition of a (or HEC-1A) human endometrial cancer cell line by an antagonist of growth hormone- releasing hormone*  
Int J Oncol 2008 Mar;32(3):593-601.

**Hohla F**, Moder A, Mayhauser U, Kronberger-Hauser C, Schally AV, Varga JL, Zarandi M, Buchhlz, Rudolf H, Aigner E, Datz C  
*Differential expression of GHRH receptor and its splice variant 1 in Human normal and malignant mucosa of the esophagus and colon.*  
Int J Onc 2008 July; 33(1):137-43.

**Chatzistamou J**, Aspasia-Athina V, Schally AV, Kittas C, Kiaris H  
*Expression of growth hormone-releasing hormone receptor splice variant 1 in primary human melanomas.*  
Regulatory Peptides 2008, 147:33-36

**Young L**, Schally AV, Brown JW, , Treszl A, Fishman LM. *The LHRH antagonist Cetrorelix exerts cytotoxic effects on SW-13 human adrenal cortical carcinoma cells in culture.*  
Proceeding of the 90<sup>th</sup> Endocrine Society Annual Meeting, June 15-18, 2008, San Francisco, CA. Abstract P2-422.

**Brown JW**, Schally AV, Young L, Treszl A, Fishman LM. *The growth hormone releasing hormone (GHRH) antagonist MZ-4-71 inhibits the proliferation of SW-13 adrenal cortical carcinoma cells in culture.*  
Proceedings of the 90<sup>th</sup> Endocrine Society Annual Meeting, June 15-18, 2008, San Francisco, CA  
Abstract P2-423.

**Engel J**, Rozsa B, Schally AV, Dezso B, Toth G, Flasko T, Block NL, Nadji M and Halmos N.  
*Luteinizing Hormone-releasing hormone (LHRH) receptors 1 BPH as potential molecular targets for therapy with CETRORELIX.*  
Abstract: American Urological Association Annual Meeting, May 17-22, 2008, Atlanta, GA

**Bornstein SR**, Wirth M, Schally AV. *Update on Endocrine-Related Tumors.*  
Editorial: Hormone and Metabolic Research 2008;40:299-301.

**VAHCS Neuropsychology Clinic**

**Carlton Gass, PhD.** (Author) "Use of the MMPI-2 in Neuropsychological Evaluations" in J.N. Butcher (Editor) ,Oxford Handbook of Personality and Clinical Assessment (New York: Oxford University Press)

**Carlton Gass, PhD.** (Co-author) "Potential for Bias in MMPI-2 using the Fake Bad Scale" in Psychological Injury and the Law.  
Note: MMPI-2 ("Minnesota Multiphasic Personality Inventory") is the most widely used and re-searched psychological test in the world)

**Lung Biology Laboratory**

**Jackson, R.** and R. Garcia-Rojas. Kinase activity, Hsp27 phosphorylation and lung epithelial cell glutathione. *Exp Lung Research* 34(5):245-262,2008.

**Gomez-Marin, O.**, C.Ramos, M.Glassberg, R.Jackson. Serum and urine isoprostanes as markers of oxidant stree after standardized exercise in patients with IPF. *Am J. Resp Crit. Care Med.* 177: A43, 2008

**PAGE 5****Recent Publications***(Continued)***Miami VAHCS Adrenal Research**

**Montoya, M.**, Brown, J.W., and Fishman, L.M. (2008) Comparative Effects of Chemotherapeutic Agents on the Growth and Survival of Human Adrenal Carcinoma Cells in Culture.  
*Hormone & Metabolic Research* 40, 302-305.

**Brown, J.W.**, Prieto, L.M., Perez-Stable, C., Montoya, M., Cappell, S., and Fishman, L.M. (2008) Estrogen and Progesterone Lower Cyclin B1 and D1 Expression, Block Cell Cycle in G2/M and Trigger Apoptosis in Human Adrenal Carcinoma Cultures.  
*Hormone & Metabolic Research* 40, 306-310.

**Prieto, L.M.**, Brown, J.W., Perez-Stable, C., and Fishman, L.M. (2008) 17 $\beta$ -Estradiol and an ER $\alpha$  Agonist (PPT) Trigger Apoptosis in Human Adrenal Carcinoma Cells but and Er $\beta$  Agonist (DPN) Does Not.  
*Hormone & Metabolic Research* 40, 311-314.

**Treszl, A.**, Schally, A.V., Brown, J.W., Young, L., and Fishman, L.M. (2008). SW-13 Human Adrenal Carcinoma Cells Express Multiple Somatostatin Receptors and The Somatostatin Receptor Agonist RC-160 (Vapreotide) Inhibits their Growth and Survival in Culture.  
Proceedings of the 90<sup>th</sup> Endocrine Society Annual Meeting, Abstract P2-421, p502.

**Brown, J.W.**, Schally, A.V., Young, L., Treszl, A., and Fishman, L.M. (2008). The Growth Hormone Releasing Hormone (GHRH) Antagonist (MZ-4-71 Inhibits the Proliferation of SW-13 Human Adrenal Cortical Carcinoma Cells in Culture.  
Proceedings of the 90<sup>th</sup> Endocrine Society Annual Meeting, Abstract P2-423, p502-503.

**Young, L.**, Schally, A.V., Brown, J.W., Treszl, A., and Fishman, L.M. (2008). The LHRH Antagonist Cetrorelix Exerts Cytotoxic Effects on SW-13 Human Adrenal Cortical Cells in Culture.  
Proceedings of the 90<sup>th</sup> Endocrine Society Annual Meeting, Abstract P2-422, p502.

**VAHCS Nephrology-Hypertension Section  
UMMSM Vascular Biology Institute**

**Zhou MS**, Schulman IH, Jaimes EA, Raij L. (2008) Renoprotection by statins is linked to a decrease in renal oxidative stress, TGF- $\beta$ , and fibronectin with concomitant increase in nitric oxide bioavailability.  
*Am J Physiol Renal Physio.* 2008 Jul;295(1):F53-9. Epub 2008 May 7.

The importance of this paper is that we demonstrate that "statins" popular agents for treating high cholesterol may have beneficial effects on the kidney that are independent of their effect on cholesterol. In the paper, we demonstrate the mechanisms that may participate in the salutary effects of statins.

Editor

**Isabel Perez**

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