Florez Promotes New Care Guidelines for Diabetes in Long-term Care Facilities

Senior faculty member and diabetes researcher, Hermes J. Florez, MD, PhD, MPH, collaborating with colleagues from several other institutions, all of whom are affiliated with the American Diabetes Association (ADA), recently developed guidelines to improve the management of diabetes in patients living in long-term care facilities.

“There is a growing concern over how to care for older patients with diabetes who have experienced significant functional decline and consequently need admission to assisted living, skilled nursing and nursing facilities,” said Dr. Florez, Director of the Geriatrics, Research, Education and Clinical Center at the Miami Veterans Affairs Healthcare System, who is co-author of the position statement, which appears in the February issue of *Diabetes Care*.

The ADA statement seeks to help diabetes clinicians reduce hypoglycemia in older adults, which can have catastrophic consequences leading to hospitalizations. Glycemic goals, say the authors, should balance the prevention of hypoglycemia while avoiding extreme hyperglycemia. In addition, the use of sliding-scale insulin should be limited, since it may lead to wide variations in blood glucose, producing great burden on patients, and requiring more nursing time and resources. *(Read more)*
Peptide Developed by Schally May Help Control High Levels of Lipids in Type 1 Diabetes

In a recent collaborative study, Nobel Laureate Andrew V. Schally, PhD, MD.hc (Multi), DSc, renowned for his work in cancer research and a member of Sylvester Comprehensive Cancer Center, and vascular biology researchers at the Medical College of Georgia at Augusta University found that the peptide MIA-602 blocked a key cellular receptor for growth hormone-releasing hormone (GHRH), which is elevated in many patients with diabetes. The peptide, a chain of amino acids, also reduced two indicators of diabetes: protein in the urine, a sign of kidney damage, and the inability of blood vessels to relax, an indicator of blood vessel damage.

“These laboratory findings expand the therapeutic potential of antagonists of GHRH to diabetes, which affects a significant percentage of the world’s population,” said Schally, the Distinguished Leonard M. Miller Professor of Pathology and Professor of Hematology/Oncology, and International Medicine Institute Research Scientist at the Miller School of Medicine, and Distinguished Medical Research Scientist and Head of The Endocrine, Polypeptide and Cancer Institute at the Veterans Affairs Medical Center in Miami. (Read More)

Anat Galor, MD, MPH and her clinical laboratory aim to study the relationship between dry eye and somatosensory function. The multidisciplinary team found that many dry eye patients describe features of neuropathic pain, including spontaneous eye pain, dyesthesias (unpleasant, abnormal sensation), hyperalgesia (exaggerated pain response to suprathreshold noxious stimuli), and allodynia (pain response to normally non-noxious stimuli).

Her team found that dry eye symptoms correlate more closely to non-ocular pain, depression, and post-traumatic stress disorder, than to traditionally measured signs of dry eye (tear production, evaporation, corneal damage). The finding reinforces the hypothesis that dry eye is one of several overlapping pain conditions and that some patients with dry eye need treatment that extends beyond the ocular surface. An open research trial to study somatosensory function in individuals with and without dry eye is currently recruiting veterans to a 1-day study and offers $50 compensation for their time. Please contact Mireya Hernandez (mireya.hernandez@va.gov; 305 342 1483) for more information. Any interested patient can contact Mireya directly.
Geriatric Research, Education, and Clinical Center- GRECC

Kevin Curtis, PhD, GRECC affiliate investigator, served as a reviewer for the Conrad Foundation and the South African Medical Research Council earlier in 2016. Dr. Curtis also was a judge for the ESRF in March 2016.

Silvina Levis, MD, GRECC investigator is serving as a permanent member of the NIH Aging Systems and Geriatrics (AGS) Study section.

Priyamvada Rai, PhD, GRECC investigator, served as a reviewer for the NIH Tumor Cell Biology study section, February, 2016. Dr. Rai served as a reviewer for the European Research Council review panel this year.

Herman Cheung, PhD, GRECC investigator, served as a member of the Department of Defense (DoD) Rehabilitation and Orthopedic study section in February, 2016.

MVAHS Named Top Recruiter in Traumatic Brain Injury trial


Based on enrollment data, Miami VAMC site, under the leadership of Dr. Mercedes Rodriguez-Suarez and research coordinator, Melyssa Sueiro, was officially the #1 recruiter for this trial.

The Chairs offices in Hines and Albuquerque extended their appreciation for the dedication, hard work and effort devoted to help complete recruitment for the project.

The information gained by the study will be of particular relevance, as rivastigmine patch (Exelon Patch) recently became available in a generic form. If found effective, it will provide valuable information to help guide the treatment of Veterans with TBI.
**PRESENTATIONS**

**Spencer Eth, MD.**
Associate Chief of Psychiatry for Mental Health, and Dr. Daniella David, Chief of Psychiatry Service, Medical Director, PTSD, recorded a Psychiatry Board Review CME lecture for Audio Digest Foundation on *Diagnosing and Treating PTSD in a Military Environment.*

**Geriatric Research, Education, and Clinical Center - GRECC**

**Gaetan Delcroix, PhD**
presented the project *Viscoelastic Behavior of ACL Grafts With and Without Pretensioning* at the Orthopaedic Research Society annual meeting March 5-8, 2016 in Orlando, FL. Co-investigators included Cerminara A, Alhandi A, Barton M, Qureshi A, Cooper S, Kaimrajh D, Lesniak BP, Temple HT, Latta LL.

Dr. Delcroix also presented the project *Role of Mechanical Stimulation in the Pharmacologically Active Microparticles-induced Hyaline Cartilage Differentiation of MIAMI Cells* at this meeting. Co-investigators included D'Ippolito G, Reiner T, Malinin T, Temple HT, Huang C-Y, Montero-Menei CN and Schiller PC.

**Kristina Aenlle, PhD.**
Curtis KM, Austin E, Howard GA presented the project entitled *Hepatocyte Growth Factor Splice Variant NK1 but Not NK2,*

*Promotes Osteogenic Differentiation of Human Mesenchymal Stem Cells* at the Endocrine Society annual meeting, April 1-4, 2016, Boston, MA.

**Priyamvada Rai, PhD.**
was invited to present a research seminar to the Department of Biochemistry, Tulane University, New Orleans, LA on December 7,
The presentation was entitled *Reactive Oxygen Species – A Double Edged Sword for Aggressive Cancers.*

**Kevin Curtis, PhD** presented the following studies at the Endocrine Society National Meeting on April 2016 in Boston, MA:

- **Characteristics and Patterns of Metastatic Disease from Chordoma** (Poster presentation: SUN078) and
- **Hepatocyte Growth Factor Splice Variant NK1 but not NK2, Promotes Osteogenic Differentiation of Human Mesenchymal Stem Cells** (Poster presentation: SUN359)

**Christopher Aguila,** Delcroix GJ-R, Kaimrajh D, Milne E, Temple HT, Latta LL, presented the *Effects of Gamma Irradiation on the Biomechanical Properties of Peroneus Tendons* at the Orthopaedic Research Society annual meeting on March 5-8, 2016 in Orlando, FL.

### VA Researcher Elected to National Academy of Inventors

**Andrew V. Schally, PhD, M.D.h.c. (Multi), D.Sc,** whose groundbreaking research into the endocrine system was recognized with a 1977 Nobel Prize, was recently elected a Fellow in the National Academy of Inventors.

“While this is a great honor, it is even more gratifying to note that my 40-plus patents have provided millions of dollars in royalties to public and academic institutions committed to medical research,” said Schally, who is the Distinguished Leonard M. Miller Professor of Pathology and Professor of Hematology/Oncology, and International Medicine Institute Research Scientist at the University of Miami Miller School of Medicine, and Distinguished Medical Research Scientist and Head of The Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center in Miami.

Schally was one of 168 new Fellows named to the National Academy of Inventors (NAI), whose 582 members represent more than 190 prestigious research universities and governmental and non-profit research institutions. He will be inducted on April 15, 2016, at NAI’s fifth annual conference at the U.S. Patent and Trademark Office in Alexandria, Va. Fellows will be presented with a special trophy, medal and rosette pin in honor of their outstanding accomplishments. (Read more)
Schally elected to the Florida Inventors Hall of Fame

The 2016 Florida Inventors Hall of Fame Selection Committee elected Andrew V. Schally, PhD, M.D.h.c. (Multi), D.Sc., to the Florida Inventors Hall of Fame for his discovery of hypothalamic hormones and subsequently pioneering application of analogues of hypothalamic hormones to cancer treatment, including the therapy of prostate cancer with agonists of LHRH used worldwide.

Dr. Schally will receive the honor at the 3rd Annual Florida Inventors Hall of Fame Induction Ceremony & Gala, to be held at the Hilton Tampa Downtown on September 16, 2016.

Dr. Schally, Nobel Laureate and Distinguished Medical Research Scientist at the Department of Veterans Affairs, Distinguished Professor of Pathology at the University of Miami, and Chief of the Miami Veterans Affairs Medical Center received the 1977 Nobel Prize in Physiology or Medicine and was elected to the National Academy of Sciences in 1978 for his discovery of hypothalamic hormones. Subsequently he pioneered the application of analogues of hypothalamic hormones to cancer treatment, including the therapy of prostate cancer with agonists of LHRH used worldwide.

Schally holds 32 U.S. patents licensed to 5 companies and is author or co-author of more than 2,400 publications.

Herman S. Cheung, PhD, GRECC investigator was invited to conduct a workshop entitled Update and Evaluation of Stem Cell Therapy for Eye Diseases to ophthalmologists, visual scientists and research students at the Chinese University of Hong Kong Eye Centre, March 21-22, 2016. He was also invited to participate in the Asia Pacific Academy of Ophthalmology (APAO) Annual Congress 2016, where he chaired the symposium on Ocular Stem Cells in the Scientific Program and delivered a symposium presentation in Taipei, Taiwan on March 24-26.

PUBLICATIONS

Objective: Impairments in cognition and everyday functioning are common in schizophrenia and bipolar disorder (BPD). The article presents factor analyses of cognitive and functional capacity (FC) measures based on 2 studies of schizophrenia (SCZ) and bipolar I disorder (BPI) using similar methods. The overall goal of these analyses was to determine whether performance-based assessments should be examined individually, or aggregated on the basis of the correlational structure of the tests, as well as to evaluate the similarity of factor structures of SCZ and BPI.

Method: Veterans Affairs Cooperative Studies Program Study #572 (Harvey et al., 2014) evaluated cognitive and FC measures among 5,414 BPI and 3,942 SCZ patients. A 2nd study evaluated similar neuropsychological (NP) and FC measures among 368 BPI and 436 SCZ patients. Principal components analysis, as well as exploratory and CFAs, were used to examine the data.

Results: Analyses in both datasets suggested that NP and FC measures were explained by a single underlying factor in BPI and SCZ patients, both when analyzed separately or as in a combined sample. The factor structure in both studies was similar, with or without inclusion of FC measures; homogeneous loadings were observed for that single factor across cognitive and FC domains across the samples.

Conclusion: The empirically derived factor model suggests that NP performance and FC are best explained as a single latent trait applicable to people with SCZ and BPD. This single measure may enhance the robustness of the analyses relating genomic data to performance-based phenotypes.

Eva Widerström-Noga, DDS, PhD
Professor, Health Scientist
Miami Veterans Affairs
The Miami Project to Cure Paralysis, Departments of Neurological Surgery, Physical Medicine & Rehabilitation Neuroscience program
University of Miami Miller School of Medicine


Subacute Pain after Traumatic Brain Injury is Associated with Lower Insular N-Acetylaspartate


Anat Galor, MD
Assistant Professor of Clinical Ophthalmology, University of Miami Miller School of Medicine
Staff Physician, Miami VA Healthcare System


Objective: The purpose of this study was to examine the severity and quality of ocular pain complaints in patients with dry eye symptoms.

Methods: Subjects with clinically relevant dry eye symptoms (dryness, discomfort, tearing) of unknown origin seen in the Miami Veterans Affairs eye clinic were administered questionnaires for dry eye symptoms and ocular pain and underwent a standardized ocular examination. Qualities and severity ratings of ocular pain in subjects with idiopathic dry eye were compared with similar measures from published data in other chronic pain populations.

Results: The study sample consisted of 154 subjects, of which 91% were men and ranged in age from 27 to 89 (mean age=61). Fifty-three percent of participants reported an average ocular pain of at least moderate intensity (numerical rating scale≥4), with specific characteristics (i.e., "burning" spontaneous pain) reported at frequencies comparable to prevalent chronic neuropathic pain syndromes as reported in the literature. Significant correlations were found between ocular pain metrics and dry eye symptom severity scores (r=0.57-0.66). Dry eye signs, however, did not generally correlate with ocular pain severity.

Conclusions: A significant proportion of subjects with idiopathic dry eye symptoms reported moderate or greater ocular pain intensity, with most endorsing descriptors commonly used by patients with nonocular neuropathic pain conditions. Identifying subgroups of dry eye patients based on the presence and characteristics of ocular pain complaints may improve dry eye subclassification and better individualize treatment strategies.

Purpose: To examine associations between corneal mechanical thresholds and metrics of dry eye.

Methods: This was a cross-sectional study of individuals seen in the Miami Veterans Affairs eye clinic. The evaluation consisted of questionnaires regarding dry eye symptoms and ocular pain, corneal mechanical detection and pain thresholds, and a comprehensive ocular surface examination. The main outcome measures were correlations between corneal thresholds and signs and symptoms of dry eye and ocular pain.

Results: A total of 129 subjects participated in the study (mean age 64 ± 10 years). Mechanical detection and pain thresholds on the cornea correlated with age (Spearman's ρ = 0.26, 0.23, respectively; both P < 0.05), implying decreased corneal sensitivity with age. Dry eye symptom severity scores and Neuropathic Pain Symptom Inventory (modified for the eye) scores negatively correlated with corneal detection and pain thresholds (range, r = -0.13 to -0.27, P < 0.05 for values between -0.18 and -0.27), suggesting increased corneal sensitivity in those with more severe ocular complaints. Ocular signs, on the other hand, correlated poorly and non-significantly with mechanical detection and pain thresholds on the cornea. A multivariable linear regression model found that both posttraumatic stress disorder (PTSD) score (β = 0.21, SE = 0.03) and corneal pain threshold (β = -0.03, SE = 0.01) were significantly associated with self-reported evoked eye pain (pain to wind, light, temperature) and explained approximately 32% of measurement variability (R = 0.57).

Conclusions: Mechanical detection and pain thresholds measured on the cornea are correlated with dry eye symptoms and ocular pain. This suggests hypersensitivity within the corneal somatosensory pathways in patients with greater dry eye and ocular pain complaints.


Recent data show that dry eye (DE) susceptibility and other chronic pain syndromes (CPS) such as chronic widespread pain, irritable bowel syndrome, and pelvic pain, might share common heritable factors. It was previously shown that DE patients described more severe symptoms and tended to report features of neuropathic ocular pain (NOP). It was hypothesized that patients with a greater number of CPS would have a different DE phenotype compared with those with fewer CPS. A cohort was recruited of 154 DE patients from the Miami Veterans Affairs Hospital and defined high and low CPS groups using cluster analysis. In addition to worse nonocular pain complaints and higher post-traumatic stress disorder and depression scores (P < .01), it was found that the high CPS group reported more severe neuropathic type DE symptoms compared with the low CPS group, including worse ocular pain assessed via 3 different pain scales (P < .05), with similar objective corneal DE signs. This was the first study to show that DE patients who manifest a greater number of comorbid CPS reported more severe DE symptoms and features of NOP. These findings provided further evidence that NOP might represent a central pain disorder and that shared mechanistic factors might underlie vulnerability to some forms of DE and other comorbid CPS.

Perspective: Patients reported more frequent CPS (high CPS group) and reported worse DE symptoms and ocular and nonocular pain scores. The high CPS group reported symptoms of NOP that share causal genetic factors with comorbid CPS. These results imply that an NOP evaluation
and treatment should be considered for DE patients. Dr. Galor’s team has found that patients with more severe dry eye symptoms have higher sensitivity to a mechanical stimulus (wind) applied to their central cornea.

Dr. Galor testing corneal sensitivity with a modified Belmonte aesthesiometer.

Seemant Chaturvedi, MD
Professor of Clinical Neurology
Vice Chair for VA Programs, Miami VA Healthcare System
Department of Neurology, University of Miami Miller School of Medicine

Dr. Chaturvedi was co-investigator of two national studies published in the New England Journal of Medicine which compared the effectiveness of inserting a stent versus opening the artery through a surgical procedure called endarterectomy.

The study analyzed the outcomes for 2,502 patients at 117 centers that participated in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). A prior study had found no significant differences in respect to the risk of periprocedural stroke, myocardial infarction, or death up to four years after the procedures, and the study extended those results to 10 years. The study was funded by the National Institutes of Health and Abbott Vascular Solutions.


The study compared carotid-artery stenting with embolic protection and carotid endarterectomy in patients age 79 or younger. It focused on the results of the Asymptomatic Carotid Trial (ACT), which involved 1,453 patients with carotid-artery stenosis of greater than 60 percent of the diameter of the artery. The trial was funded by Abbott Vascular Solutions.

Kevin Curtis, PhD


Chordoma is a rare, slow-growing malignant tumor arising from notochordal remnants. A retrospective review of patient records at two major referral centers was undertaken to assess the incidence, location, and prognostic factors of metastatic disease from chordoma. 219 patients with chordoma (1962-2009) were identified. 39 patients (17.8%) developed metastatic disease, most frequently to lung (>50%). Median survival from the time of initial diagnosis was 130.4 months for patients who developed metastatic disease and 159.3 months for those who did not (P = 0.05). Metastatic disease was most common in the youngest patients (P = 0.07), and it was 2.5 times more frequent among patients with local recurrence (26.3%) than in those without (10.8%) (P = 0.003). Patient survival with metastatic disease was highly variable, and it was dependent on both the location of the tumor primary and the site of metastasis. Metastasis to distal bone was the most rapid to develop and had the worst prognosis.


Bone marrow-derived mesenchymal stem cells (MSCs) can differentiate into multiple cell types, including osteoblasts, chondrocytes, and adipocytes. These pluripotent cells secrete hepatocyte growth factor (HGF), which regulates cell growth, survival, motility, migration, mitogenesis and is important for tissue development/regeneration. HGF has four splice variants, NK1, NK2, NK3, and NK4 which have varying functions and affinities for the HGF receptor, cMET. HGF promotes osteoblastic differentiation of MSCs into bone forming cells, playing a role in bone development, health and repair.
Geriatric Research, Education, and Clinical Center- GRECC


Endocrine, Polypeptide and Cancer Institute


Cui T, Jimenez JJ, Block NL, Badiavas EV, Rodriguez-Menocal L, Granda AV, Cai...

Munoz-Moreno L, Arenas MI, Carmena MJ, Schally AV, Prieto JC, and Bajo AM. Anti-proliferative and Pro-apoptotic Effects of GHRH Antagonists in Prostate Cancer. ONCOTARGET. Accepted for publication

EVENTS

Miami VA Research Week Call for Abstracts Poster Session on May 10, 2016

In conjunction with National VA Research Week May 16-20, the Miami VA Healthcare System will host a Poster Session on May 10. The theme this year is “VA Research: The Path of Progress”

VA Research Week annually celebrates the achievements of VA researchers and the role they play in providing high quality care for Veterans and advancing medical science. It also serves to educate Veterans, the public, and the media about the research being conducted at our medical center and its impact on treating and preventing disease and disability. The program will begin at noon on May 10 with the Annual Miami VA Research Week Poster Session featuring a display of research posters investigators. If you are interested in submitting an abstract, please contact Isabel Perez at iperez4@med.miami.edu or Isabel.Perez1@va.gov before April 15.

FUNDING

Chaturvedi Receives Grant to Research Stroke Prevention in Atrial Fibrillation Patients

Seemant Chaturvedi, MD, professor of clinical neurology and Vice Chair of VA Programs in the Department of Neurology, received a $330,000 research grant from drug-maker Boehringer Ingelheim to study new methods for preventing stroke in patients with atrial fibrillation.

Atrial fibrillation (AF), which affects an estimated 5.1 million people in the U.S., is a type of irregular heartbeat often caused by the two upper chambers of the heart beating unpredictably and sometimes rapidly. These irregular heartbeats can cause blood to collect in the heart and potentially form a clot, which can travel to a person’s brain and cause an ischemic stroke. Anticoagulant medications are the most common treatment for the condition. (Read more)
Priyamvada Rai, PhD, GRECC investigator, was awarded a University of Miami, Sylvester Bridge Funding Award for her project Targeting Early Adaptations in Androgen-Refractory Prostate Cancer. The award was $50,000, with duration of December 1, 2015-November 30, 2016.

South Florida VA Foundation for Research & Education, Inc.

Executed Cooperative Research and Development Agreements

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<tr>
<th>Sponsor</th>
<th>Project</th>
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<tr>
<td>BioScale, Inc., CT CRADA</td>
<td>Evaluation of COPD biomarkers: Miami VA COPD cohort.</td>
<td>Michael Campos, MD</td>
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<tr>
<td>USAMRICD, Basic Science CRADA</td>
<td>Understanding Gulf War Illness: An Integrative Modeling Approach</td>
<td>Mary Ann Fletcher, PhD</td>
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<td>Intercept Pharmaceuticals, Inc.</td>
<td>A Phase 3, Double-Blind, Randomized, Long-Term, Placebo-Controlled, Multicenter Study Evaluating the Safety and Efficacy of Obeticholic Acid in Subjects with Nonalcoholic Steatohepatitis</td>
<td>Lennox Jeffers, MD</td>
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<td>Polaris Pharmaceuticals, Inc., Basic Science CRADA</td>
<td>Arginine Deiminase-Polyethylene Glycol-20 (“ADI-PEG20”)</td>
<td>Niramol Savaraj, MD</td>
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<td>Gilead Sciences, Inc., CT CRADA</td>
<td>A Phase 3b, Multicenter, Open-Label Study to Investigate the Efficacy and Safety of Ledipasvir/Sofosbuvir, With or Without Ribavirin, in HCV Infected Subjects Who Have Failed Prior Treatment With Sofosbuvir-based Therapies</td>
<td>Maria del Pilar Hernandez, MD</td>
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<tr>
<td>Shionogi Incorporated, CT CRADA</td>
<td>A Phase 3 Randomized, Double-blind, Placebo controlled Study to Assess the Safety and Efficacy of S-888711 (Lusutrombopag) for the Treatment of Thrombocytopenia in Patients with Chronic Liver Disease Undergoing Elective Invasive Procedures (L-PLUS 2)” (“Study”).</td>
<td>Lennox Jeffers, MD</td>
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CRADAs Under Negotiation

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<th>Sponsor</th>
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<td>United Therapeutics, Inc</td>
<td>Michael Campos, MD</td>
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<td>Conatus</td>
<td>Lennox Jeffers, MD</td>
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<td>AOTI, LTC</td>
<td>Jimmy Trang, MD</td>
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<td>BIPI</td>
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<td>SynteractHCR</td>
<td>Medhi Mirsaedi, MD</td>
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**RESEARCH SERVICE WELCOMES…..**


Linda has been with the Miami VA Healthcare System for thirty years and has an extensive knowledge in both the administrative and clinical areas of the Medical Center. She will be overseeing employees Human Resources needs, PIV cards, WOC appointments and much more.

Linda is located on the second floor, Room 2B110, extension 7238, for assistance.