EASTERN-ATLANTIC
2014
STUDENT RESEARCH FORUM

40th Annual Meeting
February 26 - March 1, 2014
Miami, Florida
Program and Abstracts
February 26 – March 1, 2014

Hosted by the University of Miami
Leonard M. Miller School of Medicine

Frank Kuo, Editor
Paul Yang, Editor
Jeanna Harvey, Editor

Eastern-Atlantic Student Research Forum (M-18)
University of Miami Miller School of Medicine—P.O. Box 016960—Miami, FL 33101
http://uresearch.miami.edu/esrf
# TABLE OF CONTENTS

Welcome from the Directors ................................................................. 1
Welcome from the Dean ...................................................................... 2
University of Miami Leonard M. Miller School of Medicine ..................... 3
2014 Program Schedule ...................................................................... 5
Welcome Address – Pascal J. Goldschmidt, MD ....................................... 6
Keynote Address – Josephine P. Briggs, MD ......................................... 7
Banquet Address – Alessia Fornoni, MD, PhD ....................................... 8
Career Development Workshop- Jaime S. Rubin, PhD ............................. 10
Plenary Session .................................................................................. 11
Faculty Judges ................................................................................... 13
ESRF Sponsors .................................................................................. 14
The Alving Award ................................................................................ 15
2014 ESRF Executive Committee .......................................................... 16
About the Directors ............................................................................ 17
Previous ESRF Directors .................................................................... 18
Participating Institutions .................................................................... 19
Acknowledgments .............................................................................. 21
Oral Presentations I ........................................................................... 22
Oral Presentations II .......................................................................... 27
Oral Presentations III .......................................................................... 33
Poster Presentations ........................................................................... 39
Index of Authors ............................................................................... 65
WELCOME FROM THE DIRECTORS

To All Participants:

It is our distinguished pleasure to welcome you to the 40th annual Eastern-Atlantic Student Research Forum. This is a very special anniversary for the forum which allows us to look back and reflect upon 40 years of providing an opportunity for medical students, graduate students and residents to present their research before a group of peers. We hope that the ESRF has and continues to promote the development of our future physician-scientists and researchers.

We are very lucky to have gathered a wonderful group of distinguished investigators and students to present at this year’s forum. We are pleased to announce that Pascal J. Goldschmidt, MD, Senior Vice President for Medical Affairs and Dean of the University of Miami Leonard M. Miller School of Medicine will provide the welcome address.

We are honored to have award winning physician Josephine P. Briggs, MD, a very accomplished director from the NIH, deliver our keynote address. Since training as a nephrologist, she has become a prolific researcher who has held director positions for multiple departments of the NIH, as well as serving on the editorial board of several publications. We thank her very much for much for enhancing the forum.

In addition to our student presentations throughout the forum, we will also have wonderful educational opportunities for our participants. We have a plenary session entitled "How will technological advancements shape the future of medicine and the role of physicians/scientists in it?" Our enthusiastic faculty facilitating the session are sure to deliver a memorable afternoon. Also, for the first time in ESRF history, we have included a career development workshop taught by Jamie S. Rubin, PhD, the Director for Research Development in the Department of Medicine at Columbia University Medical Center. We are grateful for Dr. Rubin’s willingness to impart her wisdom in obtaining funding.

Alessia Formoni, MD, will conclude this year’s forum at our annual Awards Banquet. She is an Associate Professor of Medicine at the University of Miami Miller School of Medicine, as well as Director of the Diabetic Nephropathy Clinic, Director and Chair of the Peggy and Harold Katz Drug Discovery Institute, Assistant Professor of Molecular and Cellular Pharmacology and Candidate Global Head of Discovery in Cardiovascular and Metabolism at Hoffman-La Roche in Basel. Her pioneer work in diabetic kidney disease truly embodies the attributes of the physician-scientist, and we are very pleased she will be speaking about her experiences in that role.

It is truly amazing that the ESRF has reached its ruby anniversary, but it would not be possible without all of the wonderful presenters, committee chairs, faculty advisors, and support staff who contribute so much time to ensure a successful conference. We give special thanks to Isabel Perez, who works year round to make this conference perfect, and is a great advocate of student research. Without her there would be no ESRF. It has been a wonderful 40 years, and hopefully, 40 years from now, new ESRF directors will be able to reflect upon the continued success of the forum.

Sincerely,

Jeremy Dennis
UMMSM, Class of 2014
ESRF Co-Director

Zachary Most
UMMSM, Class of 2015
ESRF Co-Director

Holly Stradecki
UMMSM MD-PhD, GS1
ESRF Co-Director
WELCOME FROM THE DEAN

Dear Participant:

The University of Miami Miller School of Medicine is proud and pleased to welcome you to the 2014 Eastern-Atlantic Student Research Forum. This four-day international meeting is a unique opportunity to bring together some of the brightest young minds beginning their biomedical research careers. The investigations you will review at this 40th annual conference, and your future research, will lead to important discoveries for fighting and preventing diseases that take a terrible toll on our fellow humans.

It is my hope that this forum’s distinguished presenters -- medical, graduate, M.D./Ph.D. students and resident physicians from the United States and dozens of other countries around the world -- will challenge you to fully engage in basic science and clinical research.

Thank you for joining us in the vital pursuit of a deeper understanding of medical science. There is no more important mission than finding answers for the patients who depend on us for our knowledge and our compassion, both now and in the future.

With warmest regards,

Pascal J. Goldschmidt, M.D.
Senior Vice President for Medical Affairs and Dean,
University of Miami Leonard M. Miller School of Medicine
CEO, University of Miami Health System
Serving more than five million people as the only academic medical center in South Florida, UHealth – University of Miami Health System/ Miller School of Medicine has earned international acclaim for research, clinical care, and biomedical innovations. Founded in 1952 as Florida’s first accredited medical school, the University of Miami Leonard M. Miller School of Medicine provides medical staff for the nationally renowned University of Miami/Jackson Memorial Medical Center and University of Miami Hospital. University of Miami Hospital is the flagship facility of UHealth, which also includes two additional University-owned hospitals: Sylvester Comprehensive Cancer Center and Anne Bates Leach Eye Hospital, home to the top-ranked Bascom Palmer Eye Institute. Our affiliated hospitals on the medical campus include Jackson Memorial Hospital, Holtz Children’s Hospital, and the Miami VA Medical Center.

Each year the medical school’s more than 1,200 faculty physicians have more than a million patient encounters in primary care and more than 100 medical specialties and sub-specialties. UHealth also has more than 8,000 employees. In 2013, U.S. News & World Report listed Bascom Palmer Eye Institute as the number one hospital in the country for ophthalmology for the tenth year in a row. Three other UM Miller School of Medicine specialties were also listed among the nation’s best: ear, nose and throat, Neurology/Neurosurgery and geriatrics.

Research is a top priority, with more than 1,500 ongoing projects funded by more than $200 million in external grants and contracts to UM faculty. The medical campus consists of nearly 68 acres within the 153-acre complex of the University of Miami/Jackson Memorial Medical Center, including more than 500,000 square feet of research space not including the UM Life Science Park, which has two million square feet of space adjacent to the medical campus. The UM Life Science Park brings together academia and industry for collaboration in bioscience research innovation. The medical campus is also home to the following acclaimed medical facilities:

- **Bascom Palmer Eye Institute** has been named the country’s number one eye hospital ten years in a row by *U.S. News & World Report* for its ongoing excellence in ophthalmic clinical care and research. The Anne Bates Leach Eye Hospital annually serves 160,000 outpatients of ophthalmology and other specialties, largely for microsurgery procedures.
- **The Diabetes Research Institute** is a recognized world leader in cure-focused research. The DRI has pioneered many of the techniques used worldwide in islet cell transplantation, including advances in cell biology, immunology and harnessing the power of stem cells as a reliable source of insulin-producing cells for transplantation.
- **The Sylvester Comprehensive Cancer Center** treats nearly 4,000 newly-diagnosed cancer patients each year, and treats thousands more in ongoing treatment from throughout the United States and Latin America. Approximately 200 clinical trials are underway, supported by more than $33 million in research grants.

Dedicated to finding a cure for paralysis resulting from spinal cord injury, researchers at the Miami Project to Cure Paralysis found the first direct evidence of successful regeneration of adult human central nervous system tissue. The Miami Project, the
world’s largest comprehensive spinal cord injury research center, conducts basic and clinical research trials, as well as a program that permits spinal cord injured men to father children. The center is currently awaiting FDA approval for human trials on schwann cell transplantation.

- The University of Miami Ear Institute houses the nation’s second most active cochlear implant program, restoring hearing to adults and children with profound deafness. Over the years the ear, nose and throat program has steadily climbed up the *U.S. News & World Report* rankings.

- The nationally renowned research efforts of the Department of Pediatrics are housed in the magnificent Batchelor Children’s Research Institute. The Miller School’s Mailman Center for Child Development has a number of model programs that help children with developmental disabilities.

- The Transplant Institute at the University of Miami/Jackson is one of the nation’s best and busiest, responsible for half of the pediatric multi-visceral transplants in the world. University of Miami/Jackson has an active transplant program for bone marrow, heart, lungs, kidneys, liver, pancreas and intestines.

- Significant federal funding supports research at the Comprehensive AIDS Program, including HIV studies in pregnant women, pediatric AIDS clinical trials, various drug protocol studies, heterosexual transmission of AIDS, transfusion safety studies, and the national cooperative drug discovery group. The Miller School’s Developmental Center for AIDS Research (DCFAR), is one of the first of its kind in the state of Florida.

- The John P. Hussman Institute for Human Genomics is designed to discover the genetic influences on human health and apply the knowledge to the practice of medicine through improved diagnostics, treatments and medications. Under the stewardship of two of the most highly-acclaimed geneticists in the world, Margaret Pericak-Vance, Ph.D., and her husband Jeffery Vance, M.D., Ph.D., their work has uncovered critical clues to the origins of diseases such as Parkinson’s, Alzheimer’s and macular degeneration, and now they will work to integrate all of the School’s existing genetics research strengths into a single powerhouse program. The researchers and their collaborators at other medical centers have identified the first common genetic risk factor for autism spectrum disorder, nine genes that may increase susceptibility for Alzheimer’s disease and confirmed a region on chromosome 12q long believed to harbor an Alzheimer’s risk gene.

- The Interdisciplinary Stem Cell Institute is leading the way in the use of adult stem cells to repair malfunctioning human organs. Joshua M. Hare, M.D., director of the Interdisciplinary Stem Cell Institute, led the Transendocardial Autologous Cells in Ischemic Heart Failure Trial (TAC-HFT) study, using a novel catheter and is at the forefront of stem cell therapy research. The Institute’s goal is to find new treatments for heart disease, neurological disorders and other chronic and incurable diseases.

- The new Biomedical Research Building, a 182,000-square-foot facility houses the Interdisciplinary Stem Cell Institute, the John P. Hussman Institute for Human Genomics and will serve as a wet lab facility with office space for researchers. The facility is also LEED (Leadership in Energy and Environmental Design) certified, reducing the negative environmental impact of the building and improving occupant health and well-being.
# 2014 ESRF Program Schedule

## Wednesday, February 26, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
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</thead>
<tbody>
<tr>
<td>Noon-1:30 PM</td>
<td>Registration for UM Students</td>
<td>RMSB 2nd Floor Student Lounge</td>
</tr>
<tr>
<td>6:00 PM - 8:00 PM</td>
<td>Welcome Reception/Registration (Non-UM)</td>
<td>SpringHill Suites at Marriott</td>
</tr>
<tr>
<td>8:00 PM – 11:00 PM</td>
<td>Hospitality Suite Open</td>
<td>SpringHill Suites at Marriott</td>
</tr>
</tbody>
</table>

## Thursday, February 27, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:30 AM - 9:30 AM</td>
<td>Breakfast/Late Registration</td>
<td>Café 20/20</td>
</tr>
<tr>
<td>9:30 AM – 9:45 AM</td>
<td>Welcome Address</td>
<td>Bascom Palmer Eye Institute (BPEI)</td>
</tr>
<tr>
<td>10:00 AM – 12:00 PM</td>
<td>Oral Presentations I (Session 1)</td>
<td>BPEI Jose Berrocal Auditorium</td>
</tr>
<tr>
<td>12:00 PM - 1:00 PM</td>
<td>Keynote Address (Session 2)</td>
<td>BPEI Jose Berrocal Auditorium</td>
</tr>
<tr>
<td>1:00 PM - 2:00 PM</td>
<td>Keynote Luncheon</td>
<td>Café 20/20</td>
</tr>
<tr>
<td>2:15 PM – 4:45 PM</td>
<td>Oral Presentations II (Session 3)</td>
<td>BPEI Jose Berrocal Auditorium</td>
</tr>
<tr>
<td>8:00 PM- 11:00 PM</td>
<td>Hospitality Suite Open</td>
<td>SpringHill Suites at Marriott</td>
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## Friday, February 28, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
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</thead>
<tbody>
<tr>
<td>7:00 AM- 8:00 AM</td>
<td>Poster set up</td>
<td>Lois Pope Life Center (Walkway)</td>
</tr>
<tr>
<td>7:00 AM- 8:00 AM</td>
<td>Breakfast</td>
<td>Café 20/20</td>
</tr>
<tr>
<td>8:15 AM- 10:45 AM</td>
<td>Oral Presentations III (Session 4)</td>
<td>BPEI Jose Berrocal Auditorium</td>
</tr>
<tr>
<td>11:00 AM- 12:00 PM</td>
<td>Career Development Workshop (Session 5)</td>
<td>BPEI Jose Berrocal Auditorium</td>
</tr>
<tr>
<td></td>
<td>Jaime S. Rubin, PhD</td>
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<td></td>
<td>Director for Research Development</td>
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<td></td>
<td>Columbia University, NY</td>
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<tr>
<td>12:00 PM- 1:00 PM</td>
<td>Lunch</td>
<td>Café 20/20</td>
</tr>
<tr>
<td>1:00 PM – 2:00 PM</td>
<td>Plenary Session (Session 6)</td>
<td>BPEI Jose Berrocal Auditorium</td>
</tr>
<tr>
<td>2:15 PM – 4:30 PM</td>
<td>Poster Presentations (Session 7)</td>
<td>Lois Pope Life Center (Walkway)</td>
</tr>
<tr>
<td>3:00 PM – 4:30 PM</td>
<td>Wine &amp; Cheese Reception</td>
<td>Lois Pope Life Center (Walkway)</td>
</tr>
<tr>
<td>8:00 PM – 11:00 PM</td>
<td>Hospitality Suite</td>
<td>SpringHill Suites at Marriott</td>
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## Saturday, March 1, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
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<tbody>
<tr>
<td>6:00 PM– 9:30 PM</td>
<td>Awards Banquet Address</td>
<td>University of Miami Hospital</td>
</tr>
<tr>
<td></td>
<td>Alessia Fornoni, MD PhD</td>
<td>1400 NW 12 Ave. (Seminar A,B &amp; C)</td>
</tr>
<tr>
<td></td>
<td>Katz Family Associate Professor of Medicine &amp; Pharmacology</td>
<td>Miami, FL 33136</td>
</tr>
<tr>
<td></td>
<td>Director, Peggy and Harold Katz Drug Discovery Center</td>
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<td></td>
<td>University of Miami Miller School of Medicine</td>
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WELCOME ADDRESS

Pascal J. Goldschmidt, M.D.

Pascal J. Goldschmidt, M.D., an internationally renowned cardiologist and cardiovascular researcher, is Senior Vice President for Medical Affairs and Dean of the University of Miami Leonard M. Miller School of Medicine. He also serves as Chief Executive Officer of the University of Miami Health System (UHealth), which includes six hospitals and more than two dozen outpatient facilities in Miami-Dade, Broward, Palm Beach, Monroe and Collier counties, with more than 1,200 physicians and 8,000 staff.

Since his arrival in April 2006, Dean Goldschmidt has overseen tremendous growth on the medical campus in Miami, with the November 2007 purchase of Cedars Medical Center, which is now University of Miami Hospital, the flagship hospital of UHealth. He also established the first allopathic internal medicine residency training program in Palm Beach County.

New global health clinical and research initiatives include the Global Institute for Community Health and Development and the International Medicine Institute. It was through the Global Institute for Community Health and Development that Dean Goldschmidt was able to launch and oversee the medical relief effort in Haiti after the January 2010 earthquake. A team of Miller School physicians, nurses and staff was the first to arrive in Port-au-Prince, and within nine days of the earthquake the University of Miami Hospital in Haiti was open and treating patients.

The research enterprise has also grown significantly since 2006 with the creation of the John P. Hussman Institute for Human Genomics and the Interdisciplinary Stem Cell Institute. Both institutes are headed by world-renowned researchers.

In October 2008, Dr. Goldschmidt received the inaugural Jay and Jeanie Schottenstein Prize in Cardiovascular Sciences from the Ohio State University Heart and Vascular Center. The prize is awarded biennially to an international leader in the clinical sciences of cardiovascular medicine, cardiothoracic surgery, or the basic sciences of molecular or cellular cardiology.

Dr. Goldschmidt, whose research applies genomics and cell therapy to the prevention, diagnosis and treatment of coronary artery disease, was previously chairman of the Department of Medicine at Duke University Medical Center. Before taking the chairman’s role, he served as chief of Duke’s Division of Cardiology.

Before joining the Duke faculty in 2000, he was director of cardiology at The Ohio State University College of Medicine and Public Health, where he built the Heart and Lung Research Institute and a heart hospital.

A native of Belgium, Dr. Goldschmidt received his medical degree from the Universite Libre de Bruxelles and completed residency and fellowship training in Brussels at Erasme Academic Hospital and in the United States at The Johns Hopkins University. Following his training at Hopkins, he served as an associate professor in the university’s Department of Cell Biology and Anatomy, Department of Pathology, and Division of Cardiology in the Department of Medicine until 1997.
KEYNOTE ADDRESS

Josephine P. Briggs, M.D.

Research on Motivating Behavior Change—The Patient is in Charge

Dr. Josephine P. Briggs, M.D., is the Director, National Center for Complementary and Alternative Medicine. An accomplished researcher and physician, Dr. Briggs received her A.B. in biology from Harvard-Radcliffe College and her M.D. from Harvard Medical School. She completed her residency training in internal medicine and nephrology at the Mount Sinai School of Medicine, followed by a fellowship at Yale, then work as a research scientist at the Physiology Institute at the University of Munich.

In 1985, Dr. Briggs moved to the University of Michigan where she held several academic positions, including associate chair for research in the Department of Internal Medicine and professorships in the Division of Nephrology, Department of Internal Medicine, and the Department of Physiology. She joined the National Institutes of Health (NIH) in 1997 as director of the Division of Kidney, Urologic, and Hematologic Diseases at the National Institute of Diabetes and Digestive and Kidney Diseases. In 2006, Dr. Briggs accepted a position as senior scientific officer at the Howard Hughes Medical Institute. In January 2008, she returned to NIH as the Director of the National Center for Complementary and Alternative Medicine.

Dr. Briggs has published more than 175 research articles, book chapter, and scholarly publications and has served on the editorial boards of several journals, and was deputy editor for the Journal of Clinical Investigation. Dr. Briggs is an elected member of the American Association of Physicians and the American Society of Clinical Investigation and a fellow of the American Association for the Advancement of Science. She is a recipient of many awards and prizes, including the Volhard Prize of the German Nephrological Society, the Alexander von Humboldt Scientific Exchange Award, and NIH Director’s Awards for her role in the development of the Trans-NIH Type I Diabetes Strategic Plan and her leadership of the Trans-NIH Zebrafish committee. Dr. Briggs is also a member of the NIH Steering Committee, the senior most governing board at the NIH.
BANQUET ADDRESS

Alessia Fornoni, M.D., Ph.D.

Cyclodextrin: an old drug for a new indication

Dr. Alessia Fornoni is an Associate Professor of Medicine at the University of Miami Miller School of Medicine. She is Director of the Diabetic Nephropathy Clinic, Director and Chair of the Peggy and Harold Katz Drug Discovery Institute, Assistant Professor of Molecular and Cellular Pharmacology and Candidate Global Head of Discovery in Cardiovascular and Metabolism at Hoffman-La Roche in Basel.

Dr. Fornoni received her medical degree from School of Medicine, University of Pavia, Italy. She completed sub-internship at University Hospital I.R.C.C.S, Policlinico San Matteo, Pavia, in Obstetrics, Surgery, Pediatrics, Internal Medicine and Emergency Medicine and her internship on Nephrology and Dialysis Unit at University Hospital Policlinico San Matteo. Dr. Fornoni obtained a Ph.D. Degree in Medical Pharmacology at the University of Pavia, Italy.

Dr. Fornoni is a physician-scientist who has maintained a resolutely focused research program that has provided novel and seminal contributions to our understanding of the pathogenesis of kidney disease. Her work was the first to uncover how chronic inflammation in diabetes may negatively affect pro-survival insulin signaling pathways in podocytes. (Kidney International, 2008; NEJM, 2010). She was the first to describe that insulin resistance occurs in podocytes prior to the onset of microalbuminuria in diabetic nephropathy (Kidney International, 2008). In an attempt to elucidate the mechanisms of insulin resistance in podocytes and pancreatic beta cells, she reported a key role of the stress-activated-protein-kinase JNK (Kidney International, 2009, Diabetologia, 2008). More recently, she uncovered that impaired reverse cholesterol transport strongly contributes to podocyte insulin resistance and apoptosis in diabetes (Diabetes 2013). Dr. Fornoni also uncovered how nephrin regulates pancreatic beta cell function (Diabetes, 2010, JBC, 2012).

While maintaining a primary focus on diabetes, she has expanded her research interests to another glomerular disorder that shares several aspects with diabetic nephropathy, focal segmental glomerulosclerosis (FSGS). Her seminal work in this area was the first report that rituximab protected from recurrent FSGS after transplantation. Her studies demonstrated that rituximab has beneficial off-target effects in cells other than B-lymphocytes, such as podocytes, through modulation of sphingomyelin...
related enzymes (Science TM, 2011). She was the first to recognize the de novo appearance of B7-1 in transplanted kidneys of patients with FSGS and to contribute to a new study describing the utilization and mechanism of action of abatacept in B7-1 positive proteinuric kidney diseases (NEJM, 2013). She has developed and patented new assays to predict proteinuria in patients with glomerular diseases (Science TM, 2011; Diabetes, 2013). Finally, she has also substantially contributed to several collaborative studies that have resulted in high-impact publications (Nature Medicine and Journal of Clinical Investigation, 2011) attesting to her abilities as an integral member of “team science”.

Dr. Fornoni’s research has been supported by grants from National Institutes of Health and private foundations. She has received prestigious awards, invited to write reviews for prestigious journals (e.g. NEJM), was nominated to the editorial board of Diabetes, presented at national and international meetings, served as grant reviewer for NIH, ADA and AHA and is the PI on two NIH-sponsored clinical trials. She has 69 peer review publications, 15 as first author, 14 as senior author, and 19 as corresponding author. Her contributions have been published in high impact journals: Journal of Clinical Investigation, NEJM, Science Translational Medicine, Journal of Biological Chemistry, Diabetes, Kidney International and the Journal of the American Society of Nephrology. She has also contributed to two textbook chapters related to diabetic nephropathy. She has been able to combine a successful career with an active family life (with 2 children) and serves as an outstanding role model for many trainees. This further supports her accomplishments, dedication and perseverance, and more importantly her unstinted commitment as a physician-scientist.
Career Development Workshop

Jaime S. Rubin, Ph.D.

Funding and Grantsmanship for Junior Investigators

Dr. Rubin received a B.S. in physics *sigma pi sigma* in 1977 from The Cooper Union for the Advancement of Science and Art (New York, NY). She then received M.Sc. and Ph.D. degrees from the Ontario Cancer Institute/University of Toronto in 1980 and 1984, respectively. Her Ph.D. thesis, published in the journal, *Nature*, described the first molecular identification and characterization of a human DNA repair gene. Since 1985, she has held a number of senior level positions at Columbia University's Medical Center, including Acting Associate Dean for Graduate Affairs, having served as the founding Director of the Office of Graduate Affairs, and Acting Associate Vice President/Acting Associate Dean for Research Administration, having served as one of the founders of the Office of Research Administration. She is currently the Director for Research Development in the Department of Medicine. All of these positions have allowed for the teaching and mentoring of junior investigators, including medical and graduate students, postdoctoral fellows, and assistant professors. She founded the graduate-level course "Funding for Research Activities: Basic Issues in Obtaining Support" in 1996 and served as an Associate Program Director for the Doris Duke Clinical Research Fellowship Program, having helped initiate the program at Columbia in 2000. She started and continues to co-direct the Medical Center's course on "Responsible Conduct of Research." Other roles include serving as Associate Director for Career Development on a number of NIH-funded pre-doctoral and postdoctoral training grants as well as an advisory board member of Columbia’s Patient-Oriented Research (POR) Master of Science Program and CTSA (Education).
PLENARY SESSION

"How will technological advancements shape the future of medicine and the role of physicians/scientists in it?"

Gary H. Danton, M.D., Ph.D.

Gary Danton is the current Director of the Radiology Residency Training Program at University of Miami and an assistant professor of Clinical Radiology. Dr. Danton completed all his training at the University of Miami, beginning with a Bachelors of Science, followed by the physician scientist program with a PhD in Neuroscience and finally his residency training in Radiology. He is also current director of Residency Research in the Department of Radiology. He has published book chapters, as well as many journal articles in both radiology and neuroscience. He is an active teacher in the University of Miami community, lecturing at various specialties grand rounds about the ins and outs of radiology. Dr. Danton has won many research awards at various conferences throughout his training, of note our own “Best UM Presentation” at ESRF in 2002. He is also a past director of ESRF.

Ricardo J. Komotar, M.D.

Dr. Komotar is an Assistant Professor of Neurological Surgery at the University of Miami School of Medicine. After earning his B.S. in neuroscience from Duke University, he received his medical degree from The Johns Hopkins University School of Medicine. Dr. Komotar completed his internship and neurosurgical residency at Columbia University Medical Center/The Neurological Institute of New York, followed by a surgical neurooncology fellowship at Memorial Sloan-Kettering Cancer Center.

As Director of the University of Miami Brain Tumor Initiative, Director of Neurooncology at the University of Miami Hospital, and Co-Director of Neurooncology at the Sylvester Comprehensive Cancer Center/University of Miami Health Clinics, Dr. Komotar’s main clinical interests are surgical and radiosurgical treatment of primary and metastatic brain tumors, as well as meningiomas and pituitary lesions. His research interests include clinical trial development and translational neurooncologic investigations designed to pioneer new therapies for brain tumors. He is the Founder and Director of the Annual Neurosurgery Charity Softball Tournament to benefit brain tumor research, as well as an Emmy ® nominated physician for his work on the series “Breakthrough Medicine”.
Mustafa Tekin, M.D.

Dr. Tekin is an Associate Professor in the Dr. John T. Macdonald Foundation Department of Human Genetics and John P. Hussman Institute for Human Genomics at the University of Miami Miller School of Medicine. As a clinical and molecular geneticist, Dr. Tekin’s research focuses on the identification of genetic factors in human disorders, with a special emphasis on hearing loss and unique and rare phenotypes. His studies have identified causative genetic variants in more than 10 human disorders shedding light on the pathogenesis of these conditions.

Robin N. Fiore, Ph.D.

Dr. Robin N. Fiore joined the University of Miami Ethics Programs in 2010, where she is Associate Professor of Medicine and Director of Special Ethics Initiatives. She serves as Co-Director of UM’s Research Ethics Consultation Service and Chairs the UHealth/University of Miami Hospital Ethics Committee. Currently, as part of the Miami Clinical and Translational Science Initiative (CTSI), Dr. Fiore is working to create ethically sound practices around the development of research involving biobanks and electronic health data.

Prior to joining the University of Miami Miller School Of Medicine, Dr. Fiore she was Adelaide R. Snyder Professor of Ethics and Associate Professor of Philosophy at Florida Atlantic University in Boca Raton FL.

Dr. Fiore earned her Doctorate in Philosophy from Georgetown University in Washington, DC, after studying religion and ethics at Drew University Graduate and Theological School, Madison, New Jersey. Her undergraduate degree in History from Upsala College was earned Summa cum Laude.
FACULTY JUDGES

The directors and staff of the 2014 ESRF would like to express their gratitude to the following individuals for contributing their time and expertise in the evaluation of this year’s Forum presentations:

Dragana Ajdic, Ph.D.  Julia Escandon, M.D.  Kathryn McCollister
Brandon Allport, M.D.  Anat Galor, M.D.  Mark O’Connell, M.D.
Verma Ashok  Enrique Ginzb erg, M.D.  Clifton Page, M.D.
Morad Askari, M.D.  Lisa Gwynn, D.O.  Joseph Panoff, M.D.
Livia Bajenaru, Ph.D.  Abigail Hackam, Ph.D.  Anthony Panos, M.D.
Sanjoy Bhattacharya, Ph.D.  Guy Howard, Ph.D.  Irena Pastar, Ph.D.
Ross Bullock, M.D., Ph.D.  Barry Hudson, Ph.D.  Carlos Perez-Stable, Ph.D.
Margaret Byrne, Ph.D.  Joaquin Jimenez, M.D.  David Pitcher, M.D.
Kara Cavuoto, M.D.  Warren Kupin, M.D.  Vittorio Porciatti, D.Sc.
Richard Cote, M.D.  David Landy, M.D.  Suhrud Rajguru, Ph.D.
Kevin Curtis, Ph.D.  Sandra Lemmon, Ph.D.  Lina Shehadeh, Ph.D.
Pirouz Daftarian, Ph.D.  Vance Lemmon, Ph.D.  Robert Warren, Ph.D.
Kunjan Dave, Ph.D.  Robert Levy, Ph.D.  Donald Weed, M.D.
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We thank the following individuals for contributing their time and expertise in the evaluation of presentations by students eligible to receive the prestigious Alving Award:

Alessia, Fornoni, M.D., Ph.D.  Maureen Lowery, M.D.  Micheline McCarthy, M.D., Ph.D.
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The Alvings made a $100,000 gift to the Miller School of Medicine to endow the Dr. Carl and Barbara Alving Endowed Award. The award will be presented to the medical student who has had the most outstanding research achievement for the year. An award committee at the medical school will select the winning candidate based on a set of criteria established by the committee. The student would win a medal and also a substantial unrestricted personal monetary award to encourage the student to pursue medical research. The award is open to any medical student and not limited to one win during the course of the student’s medical school career.

Dr. Alving says, “Although I trained in internal medicine, I have actually dedicated my career to doing fundamental research rather than direct patient care. It naturally makes sense that I would want to inspire students who have an interest in research. My wife also has had an illustrious research career and is very deeply involved in medical research. We believe the promotion of research will benefit people very greatly because it provides the fundamental underpinning of medicine. I would hope there might be a possibility that this would serve as inspiration for provision of additional research resources to the medical school by others and provide stimulation for medical students who are interested in engaging in a research career.”

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**Holly Stradecki** entered the MD-PhD Program at the University of Miami Miller School of Medicine in 2011. As a first year graduate student, she is currently working on her thesis project examining excitability in the hippocampus after global ischemia. For her future, she hopes to combine clinical work in neurology/neurointensive care with a basic science career finding better ways to augment recovery after cerebral ischemia. She has served on the registration and hospitality committees prior and became a co-director this year.

**Zach Most** is a third year M.D. student at University of Miami Miller School of Medicine. Originally from New York, he has been a Cane since his undergraduate years. He is active in the medical school's academic society program and has participated in research varying from neurosurgery to ethics. After serving on the ESRF publications committee last year, this is his first year as co-director.

**Jeremy Dennis**, a native of South Florida, is currently a fourth year student at the University of Miami Miller School Of Medicine. This is his third year being involved with ESRF and second year as co-director. He received his Bachelor’s degree in Information Systems from Yeshiva University in New York City. Prior to attending medical school, Jeremy worked for Microsoft and on Wall Street. Jeremy is planning a career in anesthesiology.
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ACKNOWLEDGMENTS

The directors and staff of the 2014 ESRF would like to express their gratitude to the following individuals for their part in making this year’s forum a success through the contribution of their time, resources, and advice:

Our faculty advisors: Jennifer McCafferty PhD, and Marilyn K. Glassberg MD, who attend our meetings, offer invaluable guidance, and have dedicated a great deal of time and effort ensuring a successful forum.

Dean Pascal Goldschmidt MD, Omaida Velazquez, MD, and Mark O’Connell MD for their generous support of the ESRF. With your help, we can ensure that the ESRF continues to have many more successful events in the future.

Our Faculty Judges, who donate their time and expertise to enhance our experience by providing valuable feedback for our presenters.

Isabel Perez, whose dedication throughout the years to ESRF is unwavering. You truly make the ESRF a success year after year.
Oral Presentations I
Dermatology

THE INDUCTION OF ANGIONGESIS BY BONE MARROW DERIVED MESENCHYMAL STEM CELL EXOSOMES. Audrey Cox, Arsalan Shabbir, and Evangelos Badiavas. Department of Dermatology and Cutaneous Surgery, University of Miami School of Medicine, Miami, FL 33101

The treatment of chronic wounds represents a major challenge in current medical practice. Bone marrow derived mesenchymal stem cells (BM-MSC) have been shown to accelerate the healing of chronic wounds by inducing fibroblast proliferation and angiogenesis, although the mechanism through which they act remains elusive. This study examined the role of BM-MSC exosomes in wound healing. Exosomes are of endosomal origin, contain RNA, DNA, and protein, and are thought to be involved in intercellular communication. Differential ultracentrifugation was used to isolate exosomes. Exosomes were characterized by electron microscopy and were shown to contain the exosome markers: CD-9, CD-81, CD-63, Alix, Flotillin-1, Tsg-101, and Hsp-70. To demonstrate the role of these particles in angiogenesis, a tube formation assay utilizing human umbilical vein endothelial cells (HUVEC) was used. BM-MSC derived exosomes were labeled by the cell-linker dye, PKH-26, and found to be up taken by HUVEC cells. Further, there was a significant increase in capillary tube formation correlated to the concentration of BM-MSC exosomes utilized. In summary, this study shows that BM-MSC derived exosomes may act as “communication vehicles” through which BM-MSC induce wound healing. Importantly, it represents a potential area for further study into additional roles of exosomes in wound healing.

EVALUATING MELANOMA METASTASIS USING ENGINEERED METASTATIC PLATFORMS. Yiannis Koullias1,2 and Rhoda M. Alani1. 1. Department of Dermatology, Boston University School of Medicine, Boston, MA 02118; 2. Department of Biomedical Engineering, Duke University School of Medicine, Durham, NC 27710

Metastasis is the critical event leading to over 90% of cancer deaths. Unfortunately, our understanding of the genetic and epigenetic pathways leading to metastasis is limited because of the absence of relevant in vitro and in vivo models. Two-dimensional in vitro systems do not allow for discernment of faithful cell interactions. In vivo systems do not allow for spatiotemporal control of cell environments. Microfluidic devices allow for precise control of microenvironments, and can model in vivo cell behavior in a manipulable in vitro system. However, current use of such devices focuses on modeling intravasation and neo-vasculogenesis in the metastatic niche. We sought to develop a competitive metastasis assay to determine why a particular melanoma line metastasizes to a certain niche. We hypothesized that biochemical and biomechanical factors influence this choice of target environment. To assess the influence of these factors, our hydrogel platform contained a central island of cancer cells surrounded by a ring-like compartment of four niche cells. Preliminary results demonstrated significant differences in the migratory behavior of metastatic vs. non-metastatic melanoma, lending support to the physiologic relevance of our platform. We also observed a qualitative difference in the preferential metastasis of melanoma to different niches. We speculate that statistically significant differences in migration patterns of metastatic cell lines will be documented when assay conditions are optimized. Differing matrix compositions, pH levels, oxygen tensions, and glucose concentrations will be tested to develop the most clinically relevant conditions prior to re-analyzing migration behavior. Migration assays will then be performed to confirm the physiologic relevance of these properties using cells that have been clinically documented to metastasize to each of our niches under study. We speculate we will discern a recapitulation of this clinically documented in vivo metastatic behavior in vitro. FACS will be used to confirm this biased migration pattern and RNA will be collected to correlate gene expression patterns with migration to particular niches. We hope to delineate precise molecular mediators of metastasis to facilitate the creation of targeted therapies.
VARIATIONS IN LEVELS OF MITF AND CELL CYCLE REGULATION. Samantha L. Schneider,
Andrew Ross and Dr. James M. Grichnik. Department of Dermatology, University of Miami School of Medicine,
Miami, FL 33101.

Melanoma, a neoplasm of melanocyte lineage, is an aggressive human skin cancer that is highly resistant to treatment. There has been debate within the field of melanoma research regarding the pathogenesis of melanoma. The traditional school of thought supports the evolution of an epidermal melanocyte into a melanoma whereas the stem cell model proposes that quiescent stem cell-like cells (qSCs) may develop into cancerous lesions. Furthermore, Nishimura et al have shown that melanocytic stem cells can activate and proliferate leading to transiently amplifying (TA) cells; and, they have shown that these new TA cells can also revert back into qSCs. MITF is a critical transcription factor in the commitment of neural crest cells to the melanocyte lineage that also regulates genes necessary for melanocyte survival, differentiation, function, and proliferation. In this study, we hypothesize that MITF is cell cycle regulated. We performed immunohistochemistry with immunofluorescence staining on melanoma tissue and identified heterogeneous MITF illustrating its relevance in the human system. Furthermore, using immunofluorescence microscopy, we confirmed heterogeneity of MITF in D1 melanoma cells and have also identified a change in localization of MITF from nuclear to cytoplasmic as cells progress through the cell cycle, particularly around M-phase. Immunofluorescence microscopy also illustrated heterogeneity in Ki-67, a marker of proliferation, which correlated with flow cytometry whereby increasing levels of MITF was associated with increasing levels of Ki-67. Because of these findings, we further hypothesized that after cellular division certain TA cells may "de-differentiate" into qSCs as evidenced by an MITF-low state, which will be evaluated using flow cytometry with EdU labeling of S-phase cells. While we have therapeutic options for patients with melanoma, we are still lacking in strong treatment choices that target the stem cell model of melanoma pathogenesis. This work is significant as it aims to identify a regulatory switch between qSC and TA tumor cells that could ultimately be the target of future therapeutic agents.

CIRCULATING NUCLEIC ACIDS AS INTERLEUKIN-2 THERAPY PREDICTIVE BIOMARKERS FOR MELANOMA. Sunali Shah and Izabela Panova, M.Sc; Byungwoo Ryu, PhD; Rhoda Alani, MD. Department of Dermatology, Boston University School of Medicine, Boston, MA 02118

Melanoma is the most dangerous type of skin cancer and the leading cause of death from skin disease. Currently interleukin-2 (IL2) therapy is one of two immunological therapies that are currently being used to treat advanced-stage melanoma patients. However, its therapeutic effects vary from patient to patient with only 10% of melanoma patients showing a favorable response to this therapy. Those who do have a favorable response experience a significantly longer remission compared to those who are treated with chemotherapy. Because the side effects of IL2 therapy are severe it would be beneficial to be able to select for patients who would show a therapeutic response to it. It is proposed that specific cancer genes, such as neuropilin-2 (NRP2), helicase, lymphoid specific (HELLS), and serine peptidase inhibitor (SPINT2) are correlated with IL2 therapy efficacy; therefore, using these genes as therapy predictive biomarkers for IL2 therapy represents a unique approach to cancer therapy and personalized medicine. Our research team evaluated mRNA levels of NRP2 (angiogenesis), HELLS (helicase), and SPINT2 (tumor suppressor gene) in both non-melanoma and melanoma human serum samples using quantitative real-time PCR (qRT-PCR). We confirmed upregulation of NRP2 and HELLS and downregulation of SPINT2 in melanoma human serum samples. Current analysis involves using qRT-PCR to compare mRNA levels of these genes in melanoma human serum samples pre-IL2 treatment to post-IL2 treatment. We predict that those who have a favorable response to IL2 therapy will show a decrease in NRP2 and HELLS levels and an increase in SPINT2 levels post-IL2 therapy compared to pre-IL2 therapy treatment. Additionally, we predict that current analysis will show that patients with a lower NRP2 and HELLS and a higher SPINT2 pre-IL2 treatment baseline are more likely to show therapeutic responsiveness to IL2 therapy. Collectively, these results will seek to better diagnose and treat patients with melanoma cancer.
Genomic sequencing and therapeutic approaches are rapidly advancing, providing clinicians with vital clues to more accurate diagnoses and potential targeted therapies for inherited immunodeficiency disorders (IID) with dermatologic manifestations but with relatively few published studies and a perceived low level of evidence for proposed treatments. A systematic PubMed search was conducted to identify treatments reported to be used in management of the following IID for which level of evidence (LOE) could be assessed using JAAD guidelines: chronic mucocutaneous candidiasis (CMC), cartilage-hair hypoplasia syndrome (CHHS), severe combined immunodeficiency disorder (SCID), hypohidrotic ectodermal dysplasia with immunodeficiency (HED-ID), ataxia telangiectasia (AT), Wiskott-Aldrich syndrome (WAS), chronic granulomatous disease (CGD), leukocyte adhesion deficiency (LAD), hyperimmunglobulinemia E syndrome (HIES), silvery hair syndromes (SHS--Chediak-Higashi and Griscelli), and antibody deficiencies disorders (ADDS--X-linked agammaglobulinemia, common variable immunodeficiency disorder, and hyper-IgM syndrome). The LOE for 156 treatments were determined from 406 citations. When more than one citation was available for a given treatment, the multiple citations were grouped and one determination for highest LOE was recorded for that treatment. A majority (75.6%) of the LOE assessments were Level III for all IIDs combined. The number of citations used to assess the LOE for the treatments related to CMC, CHHS, SCID, HED-ID, AT, WAS, CGD, LAD, HIES, SHS, and ADDs were 41, 11, 34, 17, 18, 41, 27, 35, 24, 33, and 80, respectively. Notably, the only disorders that had at least 1 treatment at LOE Level I were CMC, CGD, and ADDs, while HED-ID, HIES, and SHS had Level III as the highest assessed LOE for any given treatment. Nearly three-fourths of the LOE for treatments associated with IID is Level III--non-experimental descriptive studies. Understandably, higher LOE (randomized controlled trials) have been relatively rarely published, perhaps related to ethical and safety concerns in these populations. Nevertheless, the plight of patients with these inheritable immunodeficiency disorders underscores the need for new and novel targeted therapies and further controlled trials to better establish a LOE acceptable to practitioners and to provide a more optimized benefit to risk ratio for therapeutic approaches.


Melanoma, which has been increasing in incidence, is an aggressive malignancy with a high metastatic propensity. DNA methylation, which most frequently occurs at CpG loci in promoter regions, has become increasingly recognized as an important contributor to malignant transformation, and holds promise as a novel target for improvements in diagnosis, monitoring, and treatment of melanoma. High-throughput DNA-methylation array technology has emerged as a sensitive technique for simultaneously evaluating promoter methylation in many cancer-related genes. To date, tumor DNA-methylation studies have been able to distinguish primary melanomas from benign nevi, to uncover novel genes that may be important in melanoma progression, and as a potential prognostic aid. However, it is unclear whether methylation in primary melanomas is associated with tumor progression or defines a subtype. Characterizing the relationship between melanoma methylation patterns and clinicopathologic features could also impact selection of methylation markers in a diagnostic panel, and would be a step toward identifying potential prognostic biomarkers. The present study used the Illumina GoldenGate Cancer Panel I array, which has been previously validated for detecting DNA-methylation in tumors, to evaluate methylation at 1402 CpG sites in 47 primary melanomas. Methylation patterns were examined in relationship to tumor attributes, focusing on tumor features used in American Joint Committee on Cancer (AJCC) staging and somatic BRAF mutational status. On array-wide analysis, methylation levels tended to be higher with increasing Breslow depth and BRAF-positive tumors. In contrast, mitotic rate exhibited an opposite trend with methylation overall, while ulceration was weakly associated with methylation status. On analysis of methylation differences at the 235 most variant loci, K means clustering identified 3 methylation clusters, with one cluster exhibiting distinctly higher methylation across nearly all loci. These clusters differed significantly in Breslow thickness and mitotic rate, with the high-methylation melanoma cluster exhibiting the highest mean Breslow thickness. The observed high-methylation melanoma cluster suggests the existence of a CpG island methylator phenotype (CIMP) in melanoma.
**Public Health**

**PROJECT SERVE: ENGAGING MEDICAL STUDENTS AND PATIENT FAMILIES IN A NON-CLINICAL ENVIRONMENT.** Diana Botros, Samuel R. Beckerman, Emma Hollingsworth, Marissa Orenstein, Wanda Denise Castro and Margaret M. Byrne, PhD. Department of Public Health, University of Miami School of Medicine, Miami, FL 33101.

The Project Serve mission is to provide free, healthy, home cooked meals to the families residing at the Ronald McDonald House on a biweekly basis. In addition to cooking, students share the meal alongside the families. This unique environment allows for quality interactions between the RMH families, who have children seeking treatment at UM/Jackson Hospitals, and the medical students. The objectives of Project Serve are to (1) improve medical students’ ability to communicate with patients in a non-clinical environment, (2) enhance medical students’ understanding of obstacles facing families who have children with chronic health issues, and (3) improve medical students’ knowledge of diverse cultural beliefs. We hypothesized that these interactions could foster the development of communication skills, cultural competency, and an enhanced understanding about many of the challenges patients and their families face when seeking medical care away from their homes and community. To determine whether the Project Serve experience complemented existing medical school curricula, we administered surveys to participating students. Results from free response and Likert scale questions were analyzed and statistical analysis was performed in SPSS. Preliminary results show that Project Serve helps medical students gain an understanding of different cultures and increased awareness of the medical, financial, and psychosocial challenges faced by families staying at the Ronald McDonald House.

**HEALTH-RELATED QUALITY OF LIFE IN OLDER WORKERS AND NON-WORKERS.** Diana Kachan1, Lora E. Fleming1,2, Sharon Christ3, Peter Muennig4, Guillermo Prado1, and David J. Lee1.1Department of Public Health Sciences, University of Miami, Miller School of Medicine, Miami, FL 33136; 2European Centre for Environment and Human Health, University of Exeter Medical School, Truro Cornwall TR13HD UK; 3Department of Human Development and Family Studies and Statistics, Purdue University, West Lafayette, IN 47907; 4Mailman School of Public Health, Columbia University, New York, NY 10002

Adults aged 65+ are a rapidly growing group in the US workforce as well as the general US population, however their health-related quality of life (HRQL) has not been well characterized. We provide a comprehensive examination of the HRQL in this population using a representative sample of older US adults and controlling for known confounders. Medical Expenditure Panel Survey data were pooled for years 2000-2009 for adults aged 65+ (n=34,643, mean age 74.4). Structural equation modeling was used to examine the associations between socioeconomic and individual health factors (i.e. employment/occupation, gender, income, race/ethnicity, education, health insurance status, number of co-morbidities, age, smoking status) with three standard HRQL measures: 1) EQ-5D™ (range: -0.59 - 1.00), 2) mental health component of SF-12® (0.76 - 77.37), and 3) physical health component of SF-12® (5.85 - 69.22). Employed older adults demonstrated the highest HRQL scores, with farm workers having EQ-5D™ scores by 0.09 (95% Confidence Interval: 0.044; 0.127) higher than non-workers, and SF-12® mental health scores by 2.86 (0.595; 5.121) higher than non-workers. Poorer HRQL scores across all measures were associated with female gender, greater number of co-existing health conditions, and current smoking. Hispanics’ mental health SF-12® scores were by 1.79 lower than those of non-Hispanic whites (-2.379; -1.206), however were no different for other measures. While controlling for co-morbidities was aimed at eliminating some of the healthy-worker effect, employment was still the strongest predictor of higher HRQL scores. Better understanding of the effect of work on health at older age could assist in the development of policy measures aimed at improving older adults’ HRQL.
Oral Presentations II
Ophthalmology

COMPARATIVE PROFILES OF PHOSPHOLIPIDS OF HUMAN CONTROL AND GLAUCOMATOUS TRABECULAR MESHWORK. Katyayini Aribindi, Yenifer Guerra, Richard K. Lee, Sanjoy K. Bhattacharya. Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, FL 33136

Phospholipid species phosphatidylcholine (PC), phosphatidylserine (PS), phosphatidylethanolamine (PE), and phosphatidylinositol (PI) profiles of control and glaucomatous trabecular meshwork (TM) derived from human donors were compared to determine the changes occurring in phospholipid profiles with glaucoma development. Control TM, with a mean age of 57.8 ± 11.7, and most primary open angle glaucoma (POAG) TM, with a mean age of 64.3 ± 9.8, were collected from cadaver donors adhering to the tenets of declaration of Helsinki under IRB approved protocols. A select subset of POAG surgical TM samples also were collected for analyses. Lipid extraction was performed using a modification of the Bligh and Dyer method, protein concentrations were determined using the Bradford method, and for select samples confirmed with densitometry of PHAST gels. Lipids were analyzed using a TSQ quantum Access Max triple quadrupole mass spectrometric instruments with precursor ion scan (PIS) for PC, PI, and PE species and neutral ion loss scan (NLS) for PS species, using appropriate class specific lipid standards from previously determined studies. Lipids species were then identified using MZmine 2.10 and further quantified and analyzed using MATLAB in-house macros. The comparative profiles of phosphatidylcholine, phosphatidylserine, phosphoethanolamine, and phosphatidylinositol between control and glaucomatous TM showed several species common between them. A number of unique lipids in all four phospholipid classes also were identified in control TM that were absent in glaucoma TM and vice versa. A number of phospholipids were found to be uniquely present in control but absent in glaucomatous TM and vice versa. Compared to a previous study of control and POAG blood, a number of these phospholipids are absent locally (TM), as well as systemically (in blood).

MASS SPECTROMETRIC ANALYSIS OF PHOSPHOLIPIDS IN THE S334TER-3 RAT MODEL OF RETINAL DEGENERATION. Caroline Y. Chen, Mitchell Martinez, Byron Lam, Sanjoy K. Bhattacharya. Bascom Palmer Eye Institute, University of Miami, Miami, FL 33136

The purpose of this study was to profile the endogenous phospholipid species in the retinal tissue of the S334ter-3 rat model of retinal degeneration. Retinal tissue was collected from S334ter-3 rats at postnatal day 20, 30, and 60, while control retinal samples were collected from Sprague-Dawley (SD) rats at the same time points for comparison. Lipids were extracted using the Bligh and Dyer method, and resuspended in an acetonitrile/isopropanol (1:1) solution. For lipid analyses positive ion mode precursor ion scan (PIS) was used for phosphatidylcholines (PC; product m/z of 184), negative mode neutral loss scan (NLS) was used for phosphotidylserine (PS; product m/z of 87.1), and negative mode PIS for phosphotidylinositol (PI; product m/z of 241) and phosphotidylethanolamine (PE; product m/z of 196) with a TSQ Quantum Access Max mass spectrometer. The samples were infused and scanned for two minutes between 200 m/z to 1000 m/z. Ratiometric quantification was performed using quantitative standards for each lipid class. The comparative profiles of PC, PE, PS, and PI between S334ter-3 and control rats showed that there were a number of lipid species common to both groups, as well as several that were unique to the S334ter-3 group and vice versa. It was found that the total lipid amount of PC and PS was higher in the control retina as compared to the experimental, and that the total lipid amount of PE and PI was higher in the experimental retina as compared to the control.
OUTCOMES AND COMPLICATIONS OF PNEUMATIC RETINOPEXY OVER A 12-YEAR PERIOD. Aliza Epstein BA, Yasha S. Modi MD, Harry W. Flynn Jr. MD, Wei Shi MS, William E. Smiddy MD. Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, 33136.

Pneumatic retinopexy (PR) is a well-accepted technique for the repair of selected rhegmatogenous retinal detachments (RD). Compared to other repair techniques like scleral buckling and pars planavitrectomy, pneumatic retinopexyoﬀers the opportunity to avoid an operating room procedure and its incumbent surgical and anesthesia risks. It has been reported to be at least as cost eﬀective, and some studies show no disadvantage to final visual outcomes even if additional surgeries are required. The purpose of the current study is to evaluate both anatomic and clinical outcomes in a population that underwent pneumatic retinopexy for primary retinal detachment in an academic referral center. The study was a non-comparative, consecutive, interventional case series and was a single-center study evaluating all patients treated between 2000 and 2012. Patients with less than one month follow-up or coexisting neovascular age-related macular degeneration, uveitis, endophthalmitis, or prior posterior segment surgery were excluded. Sixty-three eyes from 63 patients with primary retinal detachment treated with pneumatic retinopexy were included in the current study with a median follow up of 10.3 months. Single-operation success (SOS), deﬁned as anatomic reattachment with pneumatic retinopexy alone, occurred in 40 (63%) eyes. The median time to additional surgery in the other 23 eyes was 20 days (range: 4 – 160 days); 21 (91%; 97% overall) were successfully reattached with one additional surgery. There was no diﬀerence in best-corrected visual acuity (BCVA) outcomes between eyes achieving SOS (mean BCVA 20/25) versus eyes requiring additional surgical intervention (median 20/27.5) (p=0.85). New or missed breaks were identiﬁed in 19/63 eyes (30%). At the last follow-up examination, the retina was fully attached in 97% of eyes. Pneumatic retinopexy remains a reasonably successful option in the management of primary retinal detachment. The current study did not demonstrate a difference in BCVA outcomes in eyes achieving SOS versus those requiring additional surgery.

MFRP REGULATES ACTIN POLYMERIZATION IN PATIENT SPECIFIC STEM CELL LINEs. Huy Nguyen, Yao Li, Wen-Hsuan Wu, Chun-Wei Hsu, Yi-Ting Tsai, Takayuki Nagasaki, Irene H. Maumenee, Lawrence A. Yannuzzi, Quan V. Hoang, HaiqingHua, Dieter Egli, Stephen H. TsangDepartment of Ophthalmology, Columbia University, New York, NY 10032.

Membrane frizzled-related protein (MFRP) is a newly identiﬁed gene that can cause autosomal recessive retinitis pigmentosa (RP). MFRP encodes a retinal pigment epithelium (RPE)-speciﬁc membrane receptor of unknown function. MFRP is one element in a dicistronic transcript which also encodes the complement C1q tumor necrosis factor-related protein-5 (CTRP5), whose mutations cause late-onset retinal degeneration and whose function is also unknown. In the current study, we aim to shed light on a novel mutation in the gene encoding MFRP and its putative association with RP using human induced pluripotent stem (iPS) cell technology. We hypothesize that RPE derived from patient-speciﬁc iPS will be representative of RPE taken from MFRP-deﬁcient patient retina and that adeno-associated virus (AAV)-mediated gene therapy will restore the phenotype in iPS-derived RPE. Five antibodies against standard pluripotency markers: Oct-4, Sox-2, TRA-1-60, SSEA4 and NANOG were applied to characterize the iPS cells reprogrammed from the ﬁbroblasts obtained from two MFRP patients. iPS cells were diﬀerentiated into morphological and functional RPE cells, as shown by immunohistochemical staining, transmission electron microscopy, and measurement of transepithelial resistance. AAV2/8(Y733F) vectors were transduced into iPS-derived RPEin vitro and into Mfrp<sup>+/−</sup>/Mfrp<sup>−/−</sup> mice via subretinal injection. Immunohistochemical studies showed MFRP and its dicistronic gene CTRP5 exist in an antagonistic relationship to regulate actin organization. Application of an AAV vector expressing human MFRP also rescued actin polymerization phenotype in patient-speciﬁc RPE lines. AAV-treated mutant RPE recovered pigmentation and transepithelial resistance. Eﬃcacy of AAV-mediated gene therapy was also evaluated in Mfrp<sup>+/−</sup>/Mfrp<sup>−/−</sup> mice. Significant improvement in retinal function as measured by electroretinogram and quantitative fundus autoﬂuorescence in AAV-treated mice was observed. This is the ﬁrst report of human iPS-derived RPE being successfully used to model this disease phenotype and as a recipient for gene therapy, and we present a new function for MFRP in actin polymerization in conjunction with CTRP5.
**Oncology**


The identification of multipotent stem cells in the postnatal mammary gland has provided an explanation for the unique regenerative capacity of this organ throughout adult life. However, it remains unclear what genes maintain mammary stem cells (MaSCs) and control their specification and differentiation into the two major epithelial cell lineages, luminal and basal. Limb-Bud and heart (LBH) is a novel transcription co-factor in the WNT pathway with hitherto unknown physiological function. LBH is expressed during normal mammary gland development and aberrantly overexpressed in aggressive, treatment-resistant ‘basal’ subtype breast cancers. Here we have explored the in vivo role of LBH in mammpoiesis. We show that in mammary epithelium of postnatal mice, LBH is predominantly expressed in the MaSC-enriched Lin-CD29hiCD24lo basal cell subpopulation. Upon conditional inactivation of LBH function, mice were found to exhibit a pronounced delay in pubertal mammary gland outgrowth, reduced terminal end bud cell proliferation, as well as increased luminal differentiation at the expense of basal myoepithelial differentiation. These defects could be traced to a severe reduction in the frequency and selfrenewal/differentiation potential of MaSCs. Mechanistically, LBH induces expression of the key epithelial stem cell transcription factor ΔNp63 to promote a basal stem cell state and repress expression of luminal lineage-specific genes, foremost hormone receptor ERα. Taken together, these studies identify LBH as an essential novel regulator of MaSC and basal epithelial lineage maintenance, raising important implications for its potential role in the pathogenesis of breast cancer.

**Geriatrics**

**THE RELATIONSHIP BETWEEN AGE, SCLEROSTIN, ESTRADIOL, AND TESTOSTERONE IN MEN OVER AGE 60**. 1, 2 **Darryl F. Cannady II**, 1, 2 **Joshua F. Yarrow**, 2 **Christine F. Conover**, 1, 3 **Stephen E. Borst**. 1Department of Applied Physiology and Kinesiology, University of Florida, Gainesville, FL; 2Malcom Randall VA Medical Center Gainesville, FL; 3Geriatrics, Research, Education, and Clinical Center Gainesville, FL.

Sclerostin is a protein secreted by osteocytes that inhibits the Wnt/β-catenin pathway leading to the inhibition of bone formation. The purpose of this study was to determine if there was a relationship between age and the serum concentrations of sclerostin, 17β-estradiol, and testosterone in men over age 60. Based on previous studies on sclerostin and the sex-steroid hormones, we hypothesized that there would be a negative relationship between sclerostin and 17β-estradiol, and that no relationship exists between sclerostin and testosterone. We also hypothesized that there would be a positive relationship between sclerostin and age and negative relationships between age and total testosterone as well as age and bioavailable testosterone. Serum samples from 168 men aged 67±7 years were analyzed for sclerostin and the circulating sex-steroid hormones using enzyme-linked immunosorbent assays (ELISAs) and radioactive tagging methods. The means and standard deviations for the hormones were: sclerostin (55 ± 23 pmol/L), total estradiol (22 ± 20 pg/ml), bioavailable estradiol (8.1 ± 7.5 pg/ml), total testosterone (355 ± 191 ng/dl), and bioavailable testosterone (57 ± 22 ng/dl). We observed no relationship between sclerostin and total estradiol (r = 0.015, p > 0.05), bioavailable estradiol (r = -0.024, p > 0.05), total testosterone (r = -0.031, p > 0.05) or bioavailable testosterone (r = -0.081, p > 0.05). A relationship was observed between age and sclerostin(r = 0.272, p < 0.05), age and total testosterone (r = -0.158, p < 0.05), and age and bioavailable testosterone (r = -0.282, p < 0.05). These data suggest that the circulating concentration of sclerostin increases with age and the endogenous sex-steroid hormones may not regulate sclerostin.
Biochemistry

BIOLUMINESCENCE ENERGY CAPTURE BY QUANTUM DOT. Michael Schoor, Manoj Kumar, and Sapna Deo. Department of Biochemistry and Molecular Biology, University of Miami Miller School of Medicine, Miami, Fl 33136

Bioluminescent proteins and Quantum dots are commonly used in molecular biology to detect target proteins and nucleic acids. In order to prove that bioluminescent protein can be utilized as the donor in an energy transfer system, we harvested the energy generated by luciferase from E. coli by exciting quantum dot (QD). With increasing concentration of QD in reaction, resonance energy transfer was observed by a new peak of light emission (λ_{max} 625 nm) and a decrease of luciferase emission (λ_{max} 485 nm). This proved the concept that luciferase and QD can be employed as an energy donor-acceptor pair. This finding suggests that luciferase expressed from E.Coli can be used with QD for resonance energy transfer (RET) with a wide range of applications. This research is important for future uses where bioluminescence energy could in theory be transferred to electrodes in order to produce electrical current.

Cell Biology

OCCLUDIN REGULATES GLUCOSE TRANSPORT IN THE BLOOD BRAIN BARRIER. Jane J. He, Victor Castro, and Michal Toborek. Department of Biochemistry and Molecular Biology, University of Miami Miller School of Medicine, Miami, FL 33136.

Diabetes mellitus (DM is the 8th leading cause of death in the world and is characterized by high blood sugar resulting from impaired insulin production or insulin resistance. In obese individuals, insulin resistance is triggered by an elevated production of the inflammatory molecule tumor necrosis factor alpha (TNFa). One of the most prevalent consequences of DM is impairment of blood-brain glucose transport associated with a decreased expression of the protein occludin in the blood-brain and -retina barriers. Using in cell ELISA and fluorescence spectrometry, we identified that occludin mediates the expression of glucose transporters GLUT1 and GLUT4, and glucose uptake in pericytes, astrocytes and endothelial cells of the human blood brain barrier (BBB), as well as the influence of TNFa on glucose uptake and tissue plasminogen activator (t-PA) expression in human astrocytes. These effects were accompanied by occludin mediated control of the master metabolic switch AMP-activated protein kinase (AMPK) and the activation of the stress response transcription factor nuclear factor kappa B (NF-kB). We also show in computer based analysis of normal human tissues that occludin mRNA expression is highest in skeletal muscle, the largest glucose consumer (by mass) in the body. Our work demonstrates how occludin plays a paramount role in controlling glucose uptake in the BBB under physiological and pathological conditions such as those associated with an increased level of TNFa (e.g. stroke, pain, systemic inflammation).
Obstetrics and Gynecology

COMBINATION INTRAPERITONEAL CARBOPLATIN AND INTRAVENOUS AND INTRAPERITONEAL PACLITAXEL IN THE MANAGEMENT OF OPTIMALLY CYTOREDUCED ADVANCED STAGE OVARIAN CARCINOMA: A PILOT STUDY. Mirelys Barrios, BS1, John P. Diaz, MD2, Eric D Schroeder, MD2, Richard Andrew Estape, BS3, Kristina Angel, RN, BSN2 and Ricardo E. Estape, MD2, (1)University of Miami Miller School of Medicine, Miami, FL 33136, (2)Dept. of OB/GYN, South Miami Gynecologic Oncology Group, Miami, FL 33143, (3)University of Miami-Jackson Memorial Hospital, Doral, FL 33178, (4)South Miami Gynecology Oncology Group, Miami, FL 33143, (5)Robotic Program, South Miami Hospital, Miami FL 33143.

Cisplatin-based intraperitoneal(IP) chemotherapy is known to be effective after optimal primary debulking surgery (PDS) for ovarian cancer (OC). However, a great portion of patients is unable to complete the six necessary IP chemotherapy cycles due to the cisplatin toxicity profile. Therefore, those patients discontinuing therapy prematurely cannot benefit from the above treatment. We conducted a pilot study in which we substituted carboplatin for cisplatin in an attempt to reduce the toxicities and make the treatment more feasible while still maintaining a survival advantage compared to standard therapy. A prospectively maintained database was utilized to identify all patients who received IP/IV chemotherapy following an optimal cytoreductive surgery for advanced epithelial ovarian carcinoma from May 2007 to June 2013. The regimen consisted of day 1 administration of IP carboplatin AUC 6 and IV paclitaxel 175 mg/m² over 3 hours, and day 8 IP paclitaxel 60 mg/m² over 1 hour. Common toxicity criteria for adverse events were utilized to classify toxicities. Protocol toxicities and oncologic outcomes were recorded. Twenty patients received the treatment protocol. The median age was 62 years, (range 42 – 88, years). The median CA-125 at presentation was 296 U/mL (range 31 – 4838, U/mL). Nineteen (95%) patients were stage IIIC. The median number of IP cycles completed was 6 (range 5-6, cycles). Grade 3 and 4 toxicities occurred in 11 (55%) and 10 (50%) of patients respectively. The following grade 3 and 4 toxicities occurred: neutropenia 14 (70%), patients, thrombocytopenia 5 (25%), anemia 4 (20%), nausea 2 (10%), fatigue 1 (5%). With a median follow up of 20 months, the median progression-free survival (PFS) has not yet been met. The 5-year overall survival rate was 80%. These results indicate that combination day 1 IP carboplatin, IV paclitaxel and day 8 IP paclitaxel following optimal cytoreductive surgery for advanced stage epithelial ovarian cancer is feasible, effective and safe.

ROBOTIC AND OPEN CYTOREDUCTIVE SURGERY IN COMBINATION WITH HYPERTERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) IN THE MANAGEMENT OF RECURRENT OVARIAN CARCINOMA. Johanna Kreafle, BS1, John P. Diaz, MD2, Kristina Angel, RN, BSN3, Richard Andrew Estape, BS2, Eric D Schroeder, MD2 and Ricardo E. Estape, MD2, (1)University of Miami School of Medicine, Miami, FL 33136 (2,3)Dept. of OB/GYN, South Miami Gynecologic Oncology Group, Miami, FL 33143, (4)University of Miami-Jackson Memorial Hospital, Doral, FL 33143, (5)Robotic Program, South Miami Hospital, Miami, FL 33143.

We aimed to evaluate the feasibility and tolerability of hyperthermicintraperitoneal chemotherapy (HIPEC) following robotic or open cytoreduction for recurrent ovarian cancer. In a single institution, pilot study, patients underwent optimal cytoreductive surgery in combination with HIPEC followed by consolidation chemotherapy from September 2011 to May 2013. Optimal cytoreduction was defined as no lesion > 1 cm. Adverse and oncologic outcomes were measured. Standard statistical analysis was utilized. Thirteen patients with a median age of 52 years (range 20 - 86, years) were identified. The median number of chemotherapy regimens prior to HIPEC was 3 (range 1-12, prior regimens). A median of 2 platinum containing regimens were administered prior to HIPEC (range 0-5, regimens). Median CA-125 at time of HIPEC was 256 U/mL (range 13 – 8543, U/mL). Seven (54%) of patients were platinum sensitive at the time of HIPEC. Six (46%) patients underwent a robotic optimal cytoreductive surgery. The following cytotoxic agents were utilized during HIPEC: mitomycin 6 (46%), cisplatin and paclitaxel 4 (31%), carboplatin 2 (15%), paclitaxel 1 (8%). There were no intra-operative complications or adverse events attributable to HIPEC-therapy. Hospital stay was a median of 8 days (range 1-25, days). All patients received consolidation chemotherapy following their cytoreduction and HIPEC. At a median follow-up of 4 months (range 1-7 months), the progression-free survival and overall survival have not been reached. In conclusion, select patients robotic and open cytoreductive surgery in combination with HIPEC is feasible and safe. The optimal candidate and chemotherapy regimen have yet to be defined. Preliminary survival data suggests efficacy. Further investigation for the role of robotic cytoreduction and HIPEC is warranted.
Oral Presentations III
Surgery

REGIONAL INFLAMMATION FOLLOWING LYMPH NODE TRANSPLANTATION IMPROVES SPONTANEOUS LYMPHATIC RECONNECTION AND FUNCTIONAL DRAINAGE. Walter J. Joseph, BS, Seth Z. Aschen, BS, and Babak J. Mehrara, MD. Department of Surgery – Division of Plastic & Reconstructive Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY 10065.

Lymph node (LN) transplantation has been shown to clinically improve lymphatic function and decrease lymphedema, a common and morbid condition. However, the results of these reports have been inconsistent as a consequence of inadequate lymphatic regeneration. Therefore, developing novel strategies that improve lymphatic regeneration after LN transplantation is clinically relevant and important. We have previously shown that lymphatic vessels spontaneously reconnect and restore lymphatic function after LN transplantation and that sterile inflammation increases lymphangiogenesis in a mouse model. We sought to determine if induction of sterile inflammation in transferred lymph node improves spontaneous lymphatic reconnection and function. To test the hypothesis, we performed LN transplants in three different groups. In the first group, we induced sterile inflammation in draining LNs by injecting a mixture of complete Freund’s adjuvant and ovalbumin (CFA/OVA) in the distal extremity of donor mice fourteen days prior to transplantation. In the second group, recipient mice were injected with CFA/OVA fourteen days following transplantation. A third group of animals served as controls and did not receive CFA/OVA. Four weeks after surgery, we compared lymphatic vessel regeneration, lymphatic function, and immunologic cell composition with sham-operated animals. Using 99Tc lymphoscintigraphy, we found that inflammation prior to LN transplantation was associated with impaired lymphatic regeneration. Interestingly, there was a 1.68-fold increase in 99Tc uptake in the post-transplant inflammation nodes as compared with pre-transplant inflammation LNs (p=0.0002). Furthermore, post-transplant inflammation animals had virtually normal lymphatic function as compared with sham-operated controls. These findings also corresponded to increased lymphatic vessel ingrowth (p=0.0442) as well as a predominance of pro-lymphangiogenic B cells in post-transplant inflammation LNs. This study demonstrates that sterile inflammation after LN transplantation may be used to augment lymphatic regeneration and function, facilitating functional drainage in transplanted LNs.

A NOVEL IMMUNE COMPETENT MURINE HYPERTROPHIC SCAR CONTRACTURE MODEL: A TOOL TO ELUCIDATE DISEASE MECHANISMS AND DEVELOP NEW THERAPIES. Kyle J. Miller, BA; Mohamed Ibrahim, MD; Jennifer Bond, PhD; Andrew Bergeron, BA; Tosan Ehanire, BA; Carlos Quiles, MD; Mark Fisher, MD; Elizabeth R. Lorden, BS; Manuel Medina, MD; Angelica Selim, MD; Bruce Klitzman, PhD; Kam W. Leong, PhD; Howard Levinson, MD. 1Departments of Surgery, 2Pathology, and 3Biomedical Engineering, Duke University, Durham NC 27710.

Hypertrophic scar contraction (HSc) following burn injury leads to contractures. Contractures are painful and disfiguring. Current HSc therapies are marginally effective. Thus, we developed an immune-competent murine HSc model. Third-degree burns were created on the dorsum of C57BL/6 mice. Three days later the tissue was excised and wounds were grafted with ear skin. Graft contraction was analyzed by computer planimetry. HSc outcomes were compared to the human condition up to day 168. Graft cellularity, collagen maturation, mast cells, and macrophages were assessed using fluorescent and immunohistochemical staining. Contractile protein RNA was quantified by qRT-PCR. Tissue mechanics were analyzed using microstrain analysis. The role of the panniculascarnosus (PC) in scar contraction was evaluated by tagging the PC with titanium clips and radiographically monitoring clip area. Graft survival was confirmed in GFP mice with dermal thickness and hair follicle density analysis. Skin grafts contracted by ~45% at day 14. The PC did not contract with the wound. Granulation tissue formed after day 3. Graft tissue cellularity, vascularity, macrophages, and mast cells were increased compared to unwounded skin. Collagen maturation increased over time. Grafts demonstrated upregulation of contractile proteins. Human skin and scar tissues were tougher than those in mice. In both species, scar tissue was more brittle than uninjured skin. Interestingly, hair follicles disappeared after grafting and regenerated by day 30. Thus, we have created a validated immune-competent murine HSc model. We found that murine HSc occurs independently of the PC. Graft hair follicles experienced a period of dissolution followed by regeneration, suggesting our model may also serve to study hair growth and development. This model will facilitate the study of HSc pathogenesis and accelerate its future therapies.
OPTIMIZING AUTOLOGOUS STEM CELL THERAPIES IN A DEVELOPED JUVENILE SWINE MODEL. Justin C. Morse, Alexandra E. Halevi, Omri Emodi, Montserrat Caballero, Jeyhan S. Wood, Michael R. Pharaon, John A. van Aalst. University of North Carolina School of Medicine, Division of Plastic and Reconstructive Surgery, Chapel Hill, NC 27599.

Reconstruction of craniofacial congenital bone defects has historically relied on autologous bone grafts. Engineered bone using mesenchymal stem cells (MSCs) from the umbilical cord (UC) on electrospun nanofiber scaffolds (NFS) offers an alternative to current treatments. This preclinical study presents a juvenile swine with surgically created maxillary cleft defect for autologous implantation of UC MSCs for bone generation. Swine UC MSCs were isolated by explant technique, labeled with adeno-associated fluorescence, seeded onto electrospun poly-lactic co-glycolic acid (PLGA) NFS, and cultured in either growth or osteogenic media. Four-week-old pigs (n=10) underwent surgically created maxillary defects to determine critical-sized defect, treatment outcomes with rib, hip cancellous bone, or autologous UC MCS-based therapies. Pigs were sacrificed at 1 month. Computed tomography (CT) scans were obtained at day 0 and sacrifice. Histology was performed on bone within the surgical defect. The 1 cm surgically created defect healed with no treatment; a 2 cm defect did not heal. Rib graft did not incorporate into adjacent bone; cancellous bone healed the 2 cm defect. Both differentiated and undifferentiated MSCs resulted in bone formation in a critical sized defect, though pre-induced MSCs demonstrated better bone by CT and histology. This work establishes a juvenile porcine maxillary cleft model with critical-sized defect between 1 and 2 cm. Autologous pre-differentiated UC MSCs improved bone formation in the surgical defect.

Immunology

PROLONGATION OF MURINE CARDIAC ALLOGRAFT SURVIVAL BY ADOPTIVE TRANSFER OF ALLOGENEIC FOXP3+ T CELLS AND PLASMACYTOID DENDRITIC CELLS. Jared Gans, Dorothy Ndishabandi, Kazunobu Shinoda, Makoto Tonsho, Robert Colvin, Oren Madsen, and Alessandro Alessandrini. Transplantation Center, Massachusetts General Hospital, Boston, MA 02114

Chronic immunosuppression permits allograft survival but carries significant morbidity and mortality. We have found that without immunosuppression, life-sustaining, full MHC-mismatched mouse kidney allografts were spontaneously accepted in certain strain combinations (e.g., DBA/2 to B6) and in turn, induced tolerance of skin or heart grafts. Using B6. Foxp3\(^{DIR}\) mice, we have shown that Foxp3\(^{+}\) cells are necessary to maintain spontaneous kidney allograft tolerance. Pathological analyses of accepted kidney allografts from these animals demonstrated the development of unique, Treg-rich organized lymphoid structures (TOLS). TOLS are nodular lymphoid aggregates which are rich in Foxp3\(^{+}\) regulatory T cells (Tregs) and plasmacytoid dendritic cells (pDCs), and which are distinct from tertiary lymphoid structures. Plasmacytoid dendritic cells are important immune regulators postulated to be involved in tolerance induction, in part, by the promotion of FoxP3\(^{+}\) regulatory T cells (Tregs). To test whether pDCs in our accepted kidney allografts could promote the production of Tregs, we isolated pDCs from DBA mouse bone marrow and cultured them in vitro with naïve CD4\(^{+}\) CD25\(^{-}\) T cells from B6 mouse spleen in the presence of IL-2 and TGFβ. We observed an increased expression of Foxp3 in the co-cultured T cells as assessed by FACS analysis. These results were reproduced in non-human primates using bone marrow derived pDCs cultured with allogeneic naïve lymphocytes isolated from peripheral blood. ELISpot analysis revealed that murine Foxp3\(^{+}\) expressing T cell/pDC cultures produced large amounts of IFNγ, a known feature of newly induced Tregs. Adoptive transfer of the induced murine Foxp3\(^{+}\) T cell and pDC mixture into B6 recipients 2 weeks prior to heterotopic DBA/2 heart transplantation resulted in prolongation of allograft survival (MST = 15 days) compared to untreated controls (MST = 7 days). Induced regulatory cultures may have clinical utility in inducing long term cardiac allograft survival without the need for chronic immunosuppression.
CHITINASE-3-LIKE-1 PROTEIN EXPRESSION ASSOCIATED WITH PULMONARY INFLAMMATION ACCELERATES METASTASIS TO THE LUNG. Stephanie Libreros1, Ramon Garcia-Areas1, Roberto Carrio2 and Vijaya Iragavarapu-Charyulu1. 1Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL. 33431. 2University of Miami Miller School of Medicine, Miami, FL .33101

Disseminated metastasis accounts for majority of breast cancer deaths. Recently, elevated serum levels of a glycoprotein known as chitinase-3 like-protein-1 (CHI3L1) has been correlated with poor prognosis and shorter survival of patients with metastatic breast cancer. We have found that there are elevated levels of CHI3L1 in plasma of mammary tumor-bearing mice. In determining the cause of high plasma concentration of CHI3L1, we found that in addition to tumor cells, splenic macrophages and more interestingly pulmonary macrophages secrete CHI3L1. However, the biological and physiological functions of CHI3L1 are still unclear. We demonstrate that while CHI3L1 has an inhibitory role on the expression of interferon-gamma (IFN-γ), and up-regulate the production of pro-inflammatory mediators such MCP-1, IL-8 and MMP-9 all of which contribute towards tumor growth and metastasis. Thus, we hypothesize that CHI3L1 levels in the lung could enhance production of inflammatory mediators that may generated the proper environment to support the newly immigrated breast cancer cells and thus accelerated pulmonary metastasis. Towards the goal of understanding the role of CHI3L1 in enhancing pulmonary metastasis, we induced pulmonary inflammation in mice by sensitization with ragweed allergen. We found that asthmatic mice implanted with 4T1 or 67NR mammary tumors have a 5-fold increase in formation of metastatic foci in their lungs compared to non-asthmatic 4T1 mammary tumor-bearing mice. Further, asthmatic tumor-bearing mice showed accelerated tumor growth and shorter survival. Chitin (β-(1→4)-poly-N-acetyl D-glucosamine), the ligand for CHI3L1 was previously shown to enhance IFN-γ production. In vivo treatment of tumor-bearing mice with chitin microparticles was a substrate for CHI3L1 promoted immune effector functions with increased production of IFN-γ and decreased CCL2, IL-8 and MMP-9 expression. Significantly, in vivo administration of chitin microparticles decreased lung metastasis in mammary tumor-bearing mice. More interestingly CHI3L1 null mice showed a decreased in tumor volume, increased survival and a decreased in metastasis to the lungs compared to WT type mice. These studies suggest that CHI3L1 plays a role in tumor progression and that chitin microparticles can inhibit the pleiotropic effects of CHI3L1 giving support to the idea that CHI3L1 is a useful target for treatment of breast cancer.

Urology


Postobstructive Diuresis (POD) is a potentially life-threatening sequela of urinary retention (UR). Physicians caring for patients with UR often check serial serum chemistries to screen for this complication and may recommend hospitalization. Studies investigating the incidence of POD are scarce and outdated. We investigate the incidence of POD in patients with UR presenting to our Emergency Room (ER) in 2013. From 1/2013 to 9/2013, 168 patients presenting to the ER with UR were identified by diagnosis code and chart review. Parameters analyzed for these patients included: duration of UR, volume of retention, serum electrolytes, admission status, urine output, and diagnosis of POD by a practitioner. POD classification was made if daily urine output was > 4000 cc and: (1) a practitioner diagnosed POD and/or (2) electrolyte imbalance consistent with POD was present. Mean age of the 168 patients was 72 years (SD 14) and 86% were male. Mean duration of UR was 26.7 hours (SD 70) and mean volume of retention was 822 mL (SD 559). Initial electrolytes were checked in 95 patients (55%) and their mean serum creatinine was 1.01 MG/DL (SD 2.5). 45 patients (28%) had electrolyte levels checked; mean serum sodium and potassium levels were 137 MEQ/L (SD 6.8) and 4.4 MEQ/L (SD 0.9), respectively. 130 patients (77%) were discharged home, had no follow-up diagnosis of POD, and did not represent to the ER for electrolyte imbalance. 38 patients (23%) were admitted to the hospital. None met the criteria for a diagnosis of POD. The incidence of POD in patients with UR is exceedingly low. No patient in our series met the criteria for POD. Although serial monitoring of electrolytes and hospital admission may be a common tenet in the care of patients after relieving UR, this convention needs reconsideration. The incidence of POD may be decreasing as patients seek earlier medical attention.
**Medicine/Gastroenterology**

**PREDICTORS OF DETECTABLE INFlixIMAB TRough LEVELS AND ANTIBODIES IN INFLAMMATORY BOWEL DISEASES.** Ryan M. Dauer, Maria T. Abreu, Andres J.Yarur. University of Miami Division of Gastroenterology; Miami, Fl. 33136

Infliximab is a chimeric monoclonal IgG1 antibody against tumor necrosis factor(TNF). Clinical trials have shown that it’s an effective therapy for induction and maintenance of remission for both Crohn’s disease(CD) and ulcerative colitis(UC). Unfortunately, some patients don’t respond or lose effect. This was a retrospective cohort study performed in patients with either CD or UC treated with infliximab at the University of Miami and Jackson Memorial Hospital(Miami, FL). Predictive variables considered were demographics; hematological, nutritional and inflammatory markers;medications; history of previous biologic use; time on infliximab and disease phenotype. The primary outcome was the detection of infliximab and Human Anti-Chimeric Antibody (HACA)in serum. Continuous variables were compared using Student’s t-test and the χ2 test to evaluate distributions of categorical variables. Logistic regression models were used to assess associations between the studied predictors and the primary outcome. A total of 84 patients met inclusion criteria: 67.9% had CD, 60.7% were men,mean age was 42 years (SD:15.5). 65.5% of the patients had measurable infliximab trough levels, 20% had positive HACA. In the univariate analysis, factors that were found to be linked with detectable serum infliximab levels were higher hemoglobin levels(p<0.01), use of thiopurines combined with infliximab(p<0.0001), serum 25-hydroxyvitamin D levels(p=0.04), HACA concentration(p=0.01), history of IBD surgery(p=0.03) and end sedimentation rate (p=0.001). Two variables remained statistically significant in the multivariate analysis:hemoglobin level[OR:0.48;95%CI:0.20-0.88] and use of combination therapy with thiopurines[OR:42.95%CI:5.5-79]. Lower hemoglobin was associated with detectable infliximab trough level, which is unexpected, as anemia is more prevalent with active IBD. The use of azathioprine or 6-mercaptopurine was found to be associated both with detectable infliximab levels and negative HACA, which matches the results of other studies. We can conclude that few known factors affect infliximab levels or development of HACA and that there is variability in pharmacokinetics among individuals that warrants further investigation.

**Neurology**

**BIOMARKER EVIDENCE OF ACCELERATED AGING IN INDIVIDUALS WITH SPINAL CORD INJURY.** Joshua D. Parker and Rachel E. Cowan. Miami Project to Cure Paralysis, University of Miami Miller School of Medicine, Miami, FL 33136.

Physicians and researchers generally believe that persons with spinal cord injury (SCI) ‘age’ faster than the non-disabled population. Core evidence for this theory is the earlier onset and greater prevalence of chronic diseases, greater mortality rates, and reduced lifespans. We sought to identify cellular evidence that persons with SCI are indeed biologically older than similarly aged peers. Mean telomere length was selected as the aging biomarker of interest due to associations in non-disabled individuals with age, chronic diseases and disorders, the total number of diseases and disorders, and mortality. We compared mean telomere length of eight persons with SCI to eight age (+/-5y), gender, race, and smoking status matched non-disabled controls, with the hypothesis that persons with SCI would demonstrate shorter mean telomere lengths.DNA was extracted from blood samples,amplified by PCR, and analyzed to determine the telomere to single copy gene ratio (T/S), a measure of relative telomere length. There was no statistical difference in mean T/S ratio between the groups (p=0.95). The mean T/S ratio for the SCI group was 32, standard deviation (SD) of 17. In comparison, the mean T/S ratio for the control group was 38, SD of 22. Despite matching for confounders such as age, gender, race, and smoking status, it appears that ‘general health’ of the participants may need to be accounted for as well. The lack of statistical difference in the two groups may be attributed to the atypical healthiness of our SCI participants. Only SCI persons with low disease burdens were physically capable of traveling to the facility and participating in the study, essentially creating sample bias. Additionally, a panel of biomarkers may be more accurate than any single biomarker at determining an individual’s biological age. Discovery of such a biomarker/panel for ‘aging’ in persons with SCI could identify persons at greatest risk for functional decline and premature death, making early clinical intervention possible.
Neuroscience

AMYLOID-BETA PLAQUE DETECTION IN A MOUSE MODEL OF ALZHEIMER’S DISEASE. Anushi R. Patel and James M. Olcese. Department of Biomedical Sciences, Florida State University College of Medicine, Tallahassee, FL 32306.

Alzheimer's disease (AD) is a form of dementia that diminishes cognitive skills and memory. One of the major features of AD is formation of amyloid-beta plaques. The hormone melatonin, secreted by the pineal gland, has been found to reduce the formation of amyloid-beta plaques in various in vitro and in vivo models. We previously reported that long term melatonin administration to a mouse model of AD can provide protection from AD progression as assessed behaviorally, in terms of brain pathology, and in terms of mitochondrial dysfunction. The goal of this project was to develop reliable in-house techniques to detect amyloid-β plaques in the AD mouse model. These techniques will be used in our larger study that aims to define the mechanisms through which melatonin works. Staining techniques that were tested include Congo Red histochemistry and immunohistochemistry (IHC) with both infrared fluorescence and HRP-conjugated antibodies against the amyloid beta plaques. We determined that the commercial anti-amyloid beta antibody is functional, i.e. the images are suitable for quantification and reproducible for publication. After assessing the benefits and drawbacks to each method, we found the fluorescence technique to be the most sensitive of the three techniques and to yield the clearest images. We were also satisfied with the Congo Red and HRP staining. We determined that at 4 months of age, the cortices and hippocampi of AD animals do not yet exhibit the characteristic plaques of AD. Plaques accumulate with age and it is known that accumulation begins in the entorhinal cortex and hippocampus and then progresses to the prefrontal and frontal cortices. Thus, the effects of AD are seen later in life. This is why we then worked with tissues from AD animals that were 12 months old. Melatonin been shown to be safe for human administration. Thus, a critical barrier to clinical trials in the context of AD (e.g. safety) has already been bridged making melatonin a potential treatment for AD.

Cardiology

MODELING THE EFFECTS OF ANTI-HYPERTENSIVES ON THE PRESSURE WAVEFORMS IN A NORMAL AORTA. Scott Maddalo, Vittoria Flamini, Alison Ward, Abe DeAnda, Boyce E. Griffith. Division of Cardiology, New York University School of Medicine, New York, NY, 10016.

The relationship of hypertension and wall stress on the progression of aortic disease is well established. Pressure waveforms can be used to evaluate and compare the effects of medications on blood pressure and from this, on aortic wall stress. No analyses have compared the effect of pressures antihypertensive drugs exert on the aorta. We compared the hypothetical pressure waveforms of two commonly administered anti-hypertensive medications (esmolol and nicardipine) against a normal waveform using a 3D computer simulation model of a normal aorta. A literature search for trials on normotensive patients given esmolol or nicardipine was performed to identify relevant hemodynamic data. The changes in systolic and diastolic pressure, heart rate and mean arterial pressure were used to calculate the changes in a normal pressure waveform. CT-scans from clinical images were used to create a realistic 3D computational model of a healthy aorta for comparing the effects of these medications. Both medications were found to increase heart rate, but they had different effects on the systolic and diastolic pressure. Esmolol showed a decrease in systolic pressure compared with the normal waveform. Nicardipine demonstrated an increase in systolic pressure, which correlates with a higher wall stress because of an increase in pulse pressure. Increases in wall stress may increase the risk of enlargement or dissection of the aorta. Based on these findings, selective beta blockade would be a good strategy for pharmacologic management. This analysis affirms that pressure waveforms provided a non-invasive way to study the effects of medications on the aorta. With these initial results, pressure waveforms for other commonly used anti-hypertensive medications can be examined and compared to each other to find the optimal treatment methods for aortic disease.
Poster Presentations
**Cell Biology**

**POSTER #01:**  
LOSS OF PTEN EXPRESSION IN HUMAN ENDOTHELIAL CELLS PROMOTES ALTERED PROLIFERATION: IN VITRO MODELING OF VASCULAR ANOMALIES IN COWDEN SYNDROME.  
Natalie Klar; Qingxia Zheng; Kevin Pumiglia, Ph.D. Center for Cell Biology and Cancer Research, Albany Medical College, Albany, NY 12208.

PTEN is important in regulating cell growth, migration, and survival. Germline mutations in PTEN are found in Cowden syndrome (CS). CS patients are at risk of developing certain types of cancer, as well as developing vascular anomalies such as arteriovenous malformations. Given the links between vascular anomalies and loss of PTEN function, we sought to determine the effects of PTEN loss in human endothelial cells by investigating effects of PTEN loss on PI-3'K related signaling and cell proliferation. Specifically, we hypothesized that loss of PTEN in endothelial cells would be sufficient to deregulate AKT and mTOR signaling promoting altered cell proliferation. We screened unique mir-based shRNAlentiviral vectors for those that produced the best knockdown of PTEN. The most efficient vector was used to produce lentivirus and infect primary endothelial cells. Using these PTEN-deficient HUVECs, experiments investigating PI-3'K related signaling and cell proliferation were conducted. PTEN-deficient cells had higher phospho-AKT and phospho-S6 levels in the basal and stimulated states compared with HUVECs infected with a non-targeting virus. BrdU incorporation was used to assess proliferation in PTEN-deficient cells, under both basal and stimulated conditions. The PTEN-deficient cells had enhanced BrdU incorporation under both conditions. As enhanced proliferation and mTOR activation are traits that are known to be associated with vascular malformations, these effects could contribute toward inducing abnormal vasculature morphogenesis. We are currently conducting a co-culture in vitro angiogenesis assay to determine whether the loss of PTEN is sufficient to promote abnormal branching morphogenesis. These data provide insight into the manifestation of vascular anomalies in CS patients and provide a novel **in vitro** model to better understand the contributions of vascular endothelial dysfunction to this disease.

**POSTER #02:**  
THE NECL-4, PAR-3 AND 4.1G COMPLEX PROMOTES SCHWANN CELL MYELIN SHEATH FORMATION AND INTEGRITY. Xiaosong Meng and James L. Salzer. Department of Cell and Molecular Biology, New York University School of Medicine, New York, NY 10016.

Interactions between axons and Schwann cells in the peripheral nervous system induce myelination and result in the re-organization of axons into distinct domains. The largest domain by far is the internode - the portion of the axon located under the compact myelin sheath. The molecules that mediate the functional relationship between axon and myelinating glial cell along the internode include the Nectin-like (Necl) cell adhesion proteins. Previous studies have shown that Necl-4, which is expressed by myelinating Schwann cells and binds to Necl-1 expressed on axons, promotes myelination. An important question is how Necl-4 mediates these effects. Based on its structure, Necl-4 mediates cell adhesion through its extracellular Ig-like domains and interacts with PDZ-domain and 4.1 related cytoskeletal proteins via its cytoplasmic domain. Par-3, a member of the Par-aPKC polarity complex, was previously reported to be required for Schwann cell myelination. In this study, Necl-4 and Par-3 are found to co-localize along the internode in myelinated axons, driven by Necl-4 recruitment of Par-3 to sites of Necl-4/Necl-1 interaction through the first PDZ domain of Par-3. These findings suggest a model where Par-3 recruitment to the Schwann cell adaxonal membrane may target and activate signaling pathways that promote formation of a leading edge that drives spiral wrapping of the axon. Necl-4 also interacts with members of the 4.1 family of cytoskeletal proteins, notably co-localizing with 4.1G along the internode and Schmidt-Lanterman incisures (SLI). Mice deficient in 4.1G have a dramatic loss of Necl proteins along the internode, abnormal clusters of proteins at the paranodal loops, and disorganized SLI. Intriguingly, segmental demyelination in aging 4.1G−/− mice appears to trigger propagation of demyelination, resulting in remyelinated fibers with shortened internodes along their full length. Taken together, these results indicate that interactions of the Necls with Par-3 and 4.1 proteins promote myelination and that the 4.1 proteins are essential for myelin sheath organization and integrity.
POSTER #03:
TNFα CAUSES PODOCYTE CHOLESTEROL ACCUMULATION AND APOPTOSIS IN DIABETIC KIDNEY DISEASE. Christopher Pedigo1, Armando Mendez2, Matthias Kretzler3, Robert G Nelson4, George W Burke III2,5, Alessia Fornoni2,3, Sandra Merscher-Gomez1. 1Division of Nephrology and Hypertension and 2Diabetes Research Institute, University of Miami Miller School of Medicine, Miami, FL. 3University of Michigan, Ann Arbor, MI, 4NIDDK Phoenix, Arizona and 5Department of Surgery, University of Miami.

Diabetic Kidney Disease (DKD) remains the most common cause of end-stage renal disease in the United States, and serum concentrations of Tumor Necrosis Factor alpha (TNFα) and TNFα Receptor (TNFR) 1 and 2 correlate with the development and progression of DKD. In DKD, decreased podocyte number and glomerular cholesterol accumulation are both associated with albuminuria. We tested the hypothesis that TNFα or TNFR1/R2 induce apoptosis in podocytes and determined if this is mediated by cholesterol accumulation. We demonstrated that TNFα (10ng/mL, 24 hours) but not TNFR1/R2 induce apoptosis in cultured human podocytes (p<0.05). TNFα-induced apoptosis was associated with a significant increase in the number of lipid droplets as determined by Opera High Content Screening analysis of Bodipy 493/503 stained cells (p<0.01). ApoA1 mediated cholesterol efflux was decreased in TNFα-treated podocytes (p<0.05) and was accompanied by decreased ATP-binding cassette transporter A1 (ABCA1) protein (p<0.01) and mRNA expression (p<0.001). Down-regulation of ABCA1 expression was also demonstrated in glomeruli of type 2 diabetic patients with DKD (N=70) when compared with healthy living donors (N=32). In order to determine if TNFα-induced apoptosis was mediated by cholesterol accumulation, we depleted podocytes from cholesterol using cyclodextrin prior to exposure to TNFα. We showed that cyclodextrin partially prevented TNFα-induced podocyte apoptosis (p<0.05). In summary, TNFα attenuates reverse cholesterol transport in podocytes leading to increased cholesterol accumulation and apoptosis. Our data suggest that strategies targeting the TNFα-cholesterol axis in podocytes may protect from the development of DKD.

Dermatology

POSTER #04:
TOPICAL MEVASTATIN AND SIMVASTATIN ACCELERATE ANGIOGENESIS AND WOUND CLOSURE IN VIVO. Shailee Patel1, I. Pastar1, O. Stojadinovic1, N. Yin1, A. Sawaya1, H. Ramirez2, G. Ji1, S.C. Davis2, M. Tomic-Canic1. 1Wound Healing & Regenerative Medicine Research Program, University Of Miami Miller School Of Medicine, Miami, FL 33132; 2Department Of Dermatology & Cutaneous Surgery, University Of Miami Miller School Of Medicine, Miami, FL 33132

Statins, 5-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, are used to reduce circulating cholesterol levels. Statins also exert cholesterol-independent effects including targeting the mevalonate pathway and inhibiting synthesis of farnesyl pyrophosphate (FPP), a known wound healing inhibitor. We have previously shown that naturally occurring mevastatin, a HMG-CoA reductase inhibitor, blocks FPP formation and promotes epithelialization in human wound healing models. Furthermore, another hypolipidemic drug, simvastatin, significantly increased angiogenesis in murine wound model. In the current study we investigated the effects of topically applied mevastatin or simvastatin alone or in combinationon wound healing closure of porcine full thickness wound model. Biopsies were collected from 60 wounds from each of the three animals for histology, protein and RNA isolation on days 4, 6, 8 and 10 after wounding. Using histology we determined the optimal dose of topical mevastatin, simvastatin, and their combination that accelerated wound healing in vivo. Histological assessment of blood vessel formation was performed by staining with endothelial cell marker PECAM-1 (CD-31). The vascularization rate was quantified for each condition by determining the ratio of CD31 positively stained endothelial cells to the total wound area. We found that the topically applied mevastatin and simvastatin showed increased angiogenesis compared to the untreated control. Furthermore, the combination of mevastatin and simvastatin had a greater rate of vascularization compared to mevastatin or simvastatin alone. These findings were in accordance with enhanced epithelialization rate observed in wounds treated with both statins. Our in vivo study suggests that combinatorial therapy using mevastatin and simvastatin simultaneously improves angiogenesis and wound closure and may have considerable therapeutic potential for patients with chronic wounds that do not respond to standard treatment modalities.
POSTER #05: NEUROPATHY AND ANKLE MOBILITY ABNORMALITIES IN PATIENTS WITH CHRONIC VENOUS DISEASE. Elizabeth Yim MPH, Alejandra Vivas MD, Andrea Maderal MD, Robert S. Kirsner MD, PhD. Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL 33101

How complications associated with chronic venous insufficiency (CVI) develop is not clearly known. Possible mechanisms include the dysfunction of the calf muscle pump, which includes veins and their valves, the gastrocnemius and other lower leg and foot muscles, the nerves supplying the muscles, in addition to ankle mobility limitations. Least well studied is the relationship between range of ankle movement (ROAM), neuropathy, and the clinical severity of the disease. Our objective was to study sensory neuropathic changes and ankle mobility in CVI patients to help elucidate the pathophysiologic development of venous ulcers. We performed a cross-sectional study at the outpatient wound clinic and the wound healing research clinic at University of Miami Hospital. 64 limbs from 42 subjects were evaluated and individually classified according to the clinical aspect of the Clinical-Etiology-Anatomy-Pathophysiology classification (CEAP) for CVI. ROAM was measured using goniometry, measuring active ankle plantar-dorsiflexion and inversion-eversion. Peripheral neuropathy was measured subjectively through the Neuropathy Symptom Score (NSS) and objectively through the Neuropathy Disability Score (NDS). Results showed that patients with severe CVI had reduced plantar-dorsiflexion ROAM compared to mild CVI (89.3% v. 30.6% P<0.001) and reduced inversion-eversion ROAM (78.6% v. 11.1%, p<0.001). Patients with worse CVI had significantly worse neuropathy with higher NSS and NDS scores compared to less severe CVI. In conclusion, we found a relationship between reduced ankle movement and worsening neuropathy with increased severity of CVI. Future management in patients with CVI should include testing for neuropathy and improving ankle mobility.

Emergency Medicine

POSTER #06: IS THE RIVERMEAD POST-CONCUSSION QUESTIONNAIRE A VALID TOOL FOR DIAGNOSING BRAIN INJURY IN THE ACUTE SETTING? Nina Osafo, School of Medicine, Meharry Medical College, Nashville, TN 37208. Lawrence M. Lewis, Division of Emergency Medicine, Washington University School of Medicine, St. Louis, MO 63105

The Rivermead Post-Concussion Symptoms Questionnaire (RPQ) is a 16-item, 5-point Likert scale survey that measures severity of symptoms of traumatic brain injury (TBI). The objective of this study is to determine if the RPQ can differentiate between TBI and non-TBI subjects in the acute setting. A previous study split the RPQ into two separate scales, RPQ 3 and RPQ 13. Taken separately, the RPQ 3 appeared to be a more reliable determinant of acute TBI. We compared RPQ scores between patients presenting to the Emergency Department with TBI and those presenting for any complaint with no history of TBI (control subjects). Patients were excluded for the following: Degenerative neurologic disorders, psychiatric disease, recent (in the past 3 months) TBI, organ failure, severe pain, pregnancy, incarceration, or unable to understand English. The RPQ was administered by trained study personnel to 57 consenting subjects with TBI and 68 without TBI who met the remaining selection criteria. Mean total RPQ scores, as well as mean scores for the RPQ 3 and RPQ 13 were calculated for both groups and compared using a two-sided t-test. The mean total RPQ score was not significantly different between TBI and controls (13.6 vs. 11.0; p=0.2), nor was the RPQ 13 (10.4 vs. 9.0; p= 0.41). However, RPQ 3 mean scores were significantly different between groups (3.26 vs. 2.02; p=0.03). The results confirmed our hypothesis that the RPQ will not reliably distinguish TBI from non-TBI subjects in the acute setting and also suggest the RPQ 3 might be a better test for diagnosing TBI than the complete RPQ. The project described was supported by a grant from the Office of Medical Student Research at Washington University School of Medicine.
Genetics

POSTER #07: NOVEL ANKRD11 MUTATIONS IN KBG SYNDROME AND DELINEATION OF THE PHENOTYPE. Devon Cohen1, Joseph Foster II1, Korcan Demir2, Richard Fisher3, Michelle Moffat4, Nienke Verbeek4, Kathrine Bjørgo5, Mustafa Tekin6, John P. Hussman Institute for Human Genomics and Dr. John T. Macdonald Department of Human Genetics, University of Miami Miller School of Medicine, Miami, FL 33136, USA; 7Pediatric Endocrinology Unit, Gaziantep Children’s Hospital, MucahitlerMh., 27090 Gaziantep, Turkey; 8Northern Genetics Service Teesside Genetics Unit, The James Cook University Hospital Marton Road Middlesbrough TS4 3BW; University Medical Center Utrecht, Heidelberglaan 100, 3584 CX Utrecht, Netherlands; 9Dept. of Medical Genetics Oslo University Hospital, Kirkeveien 166 0450 Oslo, Norway

KGB syndrome is a rare cause of intellectual disability associated with craniofacial anomalies, macrodontia of upper central permanent incisors, skeletal abnormalities, and short stature. Heterozygous mutations in ANKRD11 encoding ankyrin repeat domain 11 have recently been reported to cause KGB syndrome in five families. In this study we aimed to find the mutation spectrum and associated phenotypes in four additional simplex cases. Sanger sequencing revealed four novel ANKRD11 mutations: c.1785_1786delGCinsT (p.R595_A2663delinsS), c.6817_6833delGGCCCCGCCCCGAACAC (p.G2273Cfs*17), c.7535G>A (p.R2512Q), and c.4283_4286delAAGA (p.K1428Ifs*13). Testing of both parents suggested the first three mutations were de novo. Parents were not available for the last mutation. Phenotypic evaluation of patients in this study along with previously published data suggests that patients with ANKRD11 mutations present with the most salient phenotypic features distinguishing KGB syndrome. These features include short stature, developmental delay/intellectual disability, brachycephaly/turricephaly, triangular face, synophrys, anteverted nostrils, prominent nasal bridge, and macrodontia. Three of the reported mutations here lead to truncation leaving only a varying length of the N-terminal intact, while the remaining missense mutation was located in the C-terminal repression domain that is highly conserved in different species. This raises the possibility that the disruption of the function of the amino acids located in this repression domain is sufficient to cause KGB syndrome. The combined genotypic and phenotypic manifestations of these four mutations provide further support for the causative role of ANKRD11 point mutations in KGB syndrome.

POSTER #08: CHARACTERIZATION OF FRAGILE X SYNDROME CAUSED BY FMR1 DELETIONS. Kaitlin Young1; Abigail Rupchock Deppen, MS, CGC1; Monica Dowling, PhD1; HerminiaPuerta, MD2; Mislen Bauer, MD2; Deborah Barbouth, MD1 University of Miami, Miller School of Medicine, Miami, FL 33136. Miami Children’s Hospital, Miami, FL 33155

Fragile X syndrome, the most common form of inherited intellectual disability, is typically caused by an expansion of CGG trinucleotide repeats within the FMR1 gene. This expansion leads to silencing of the FMR1 gene and the absence of the gene product, Fragile X mental retardation protein (FMRP), which ultimately causes the symptoms associated with Fragile X. However, deletions of the FMR1 gene may also cause Fragile X syndrome, as both deletions and expansion of CGG repeats into the full mutation result in a deficiency of FMRP. Here we describe three patients with microdeletions of less than 1000 kb that include the FMR1 gene. Although prior case reports suggest that the phenotype associated with FMR1 deletions is similar to that seen in individuals with typical Fragile X syndrome, this has not been well characterized. Furthermore, as illustrated in our cases, individuals with an FMR1 deletion cannot be diagnosed through typical Fragile X testing, which consists of PCR analysis with reflex to Southern Blot analysis. Without the use of chromosomal microarray (CMA) testing, the diagnosis of Fragile X syndrome would not have been made in these patients. Several genetic societies are now recommending the use of CMA as a first line technique in the diagnosis of developmental disorders in an effort to identify smaller chromosomal abnormalities that cannot be detected by other modalities. Establishing an accurate diagnosis can be particularly important in securing services and treatments for the patient, supporting families, and providing additional information about the expected course of the disorder, the recurrence risk in future pregnancies and its inheritability. Therefore, physicians should consider using CMA to aid in the diagnosis of individuals with developmental disabilities whose prior genetic testing has not yet elucidated a cause.
**Hematology**

**POSTER #09:**

**BOTH HEMOPHILIA HEALTH CARE PROVIDERS AND HEMOPHILIA A CARRIERS REPORT THAT CARRIERS HAVE EXCESSIVE BLEEDING.** Olatunde Oso, Allison Paroskie, Michael R.DeBaun and Robert F Sidonio. Department of Pediatric Hematology – Oncology397 PRB, 2220 Pierce Ave, Nashville, TN 37209

Hemophilia A, the result of reduced factor VIII (FVIII) activity, is an X-linked recessive bleeding disorder. Previous reports of Hemophilia A carriers suggest an increased bleeding tendency. Our objective was to determine the attitudes and understanding of the Hemophilia A carrier bleeding phenotype, and opinions regarding timing of carrier testing from the perspective of both medical providers and affected patients. Data from this survey was used as preliminary data for an ongoing prospective study. An electronic survey was distributed to physicians and nurses employed at Hemophilia Treatment Centers (HTC), and Hemophilia A carriers who were members of Hemophilia Federation of America. Questions focused on the clinical understanding of bleeding symptoms and management of Hemophilia A carriers, and the timing and intensity of carrier testing. Our survey indicates that 51% (36/51) of providers compared to 78% (36/46) of carriers believe that Hemophilia A carriers with normal FVIII activity have an increased bleeding tendency (p<0.001); 72% (33/36) of Hemophilia A carriers report a high frequency of bleeding symptoms. Regarding carrier testing, 72% (30/46) of medical providers recommend testing after 14 years of age, conversely 65% (29/45) of Hemophilia A carriers prefer testing to be done prior to this age (p<0.001). Hemophilia A carriers self-report a higher frequency of bleeding than previously acknowledged, and have a preference for earlier testing to confirm carrier status.

**Immunology**

**POSTER #10:**

**RELATIONSHIP BETWEEN DIMINISHED NATURAL KILLER CELL ACTIVITY AND ELEVATED MENTAL FATIGUE.** Young Jo1, Zachary Barnes1, Mary Ann Fletcher1,2, Nancy Klimas1, 2. 1Miller School of Medicine, University of Miami, Miami, FL, 33136; 2Institute for Neuro-Immune Medicine, Nova Southeastern University, Fort Lauderdale, FL, 33314.

MylagicEncaphalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating disorder affecting over 1 million individuals in the US alone. Natural Killer Cell cytotoxicity (NKCC) is significantly decreased in these patients and constitutes a well-documented biomarker for ME/CFS. One of the key presenting symptoms for ME/CFS is severe, prolonged fatigue. The components of this fatigue can be assessed using the Multidimensional Fatigue Inventory (MFI), a self-report survey originally developed to assess fatigue in cancer patients but found to be broadly applicable. In an ongoing study by our research group, NKCC data from ME/CFS patients was collected. Blood was drawn when n=25 female patients were assessed in clinic and administered the MFI. NKCC was quantified by a bioassay that uses a gamma counter to measure radioisotope release after incubation ofCr51 labeled target K562 cells with whole blood collected from patients. These patients were sorted according to their scores on several MFI components. There was no statistically significant correlation between mental, physical, and general MFI subscores with percent NK or NKCC. Due to the study being limited to a small group of female subjects with ME/CFS, the range of MFI scores was much greater than that of NKCC. Patients’ perceived general, physical or mental fatigue levels cannot be attributed directly to their diminished NKCC. The two major symptoms of ME/CFS, extreme fatigue and impaired NKCC are most likely related to other inflammatory response and immune irregularities that are still being studied by our research group.
POSTER #11:
THE MINIMUM CLINICALLY IMPORTANT IMPROVEMENT AND PATIENT ACCEPTABLE SYMPTOM STATE IN BASDAI AND BASFI IN PATIENTS WITH ANKYLOSING SPONDYLITIS. Milla J. Kviatkovsky, 1,*, S. Ramiro 2, R. Landewé 2, F. Tubach 3, M. Dougados 4, D. van der Heijde 5. 1COM, Nova Southeastern University, Miami, United States, 2Clinical Immunology & Rheumatology, AMC, Amsterdam, Netherlands, 3INSERM, Universite Paris Diderot, 4Department of Rheumatology B, Paris-Descartes University, Paris, France, 5Rheumatology, LUMC, Leiden, Netherlands

The minimum clinically important improvement (MCII) and patient acceptable symptom state (PASS) are clinically relevant measures that report the patient response and condition. We aimed at estimating the MCII and PASS cut-off values for the Bath Ankylosing Spondylitis Index (BASDAI) and for the Bath Ankylosing Spondylitis Functional Index (BASFI) in patients with Ankylosing Spondylitis (AS). A multinational study including patients with AS receiving NSAIDs for 4-weeks has been used to define PASS and MCII, by using external anchor questions for patient global assessment for BASDAI and functional impairment for BASFI. For PASS, patients were asked to consider the ways AS has affected them during the last 48 hours and if this would be an acceptable state for the rest of their life. Patients who answered “acceptable” met criteria for PASS analysis. For MCII, patients were asked to compare how they felt in the past 48 hours to the start of the study. Secondly, if they felt improved, to consider how important the improvement was. Those reporting moderate or slightly important improvement met criteria for MCII analysis. Subgroup analysis was performed for gender, age, baseline BASDAI and BASFI scores, disease duration, HLA-B27 status and presence/history of SpA extra-articular manifestations. Continuous variables were stratified according to the median value. For MCII in BASDAI, a separate analysis was done on patients with a baseline BASDAI≥4 to represent patients recommended to receive treatment in clinical practice. The 75th percentile approach was used to establish cut-off values. 283 patients with AS (76% males, 64% HLA-B27 positive, mean (SD) age: 43(14) years and mean disease duration:13(10) years) were included. Mean baseline BASDAI and BASFI values were 5.0 and 4.6 respectively. Cut-off values for PASS values were 4.1 for BASDAI and 3.8 for BASFI (Table 1). The MCII cut-off was an absolute change of 0.7 BASDAI and 0.4 in BASFI. Subgroup analyses revealed differences between groups if stratified for age, disease duration and baseline value, with differences larger for PASS than MCII. Subgroup analysis was performed for gender, age, baseline BASDAI and BASFI scores, disease duration, HLA-B27 status and presence/history of SpA extra-articular manifestations. Continuous variables were stratified according to the median value. For MCII in BASDAI, a separate analysis was done on patients with a baseline BASDAI≥4 to represent patients recommended to receive treatment in clinical practice. The 75th percentile approach was used to establish cut-off values. 283 patients with AS (76% males, 64% HLA-B27 positive, mean (SD) age: 43(14) years and mean disease duration:13(10) years) were included. Mean baseline BASDAI and BASFI values were 5.0 and 4.6 respectively. Cut-off values for PASS values were 4.1 for BASDAI and 3.8 for BASFI (Table 1). The MCII cut-off was an absolute change of 0.7 BASDAI and 0.4 in BASFI. Subgroup analyses revealed differences between groups if stratified for age, disease duration and baseline value, with differences larger for PASS than MCII. For the sub-analysis of the patient group with a baseline BASDAI score≥4, the MCII was 1.1 in BASDAI and 0.6 in BASFI for absolute change. PASS for both BASDAI and BASFI are highly variable based on important patient characteristics such as age, disease duration and baseline value. Frequently the PASS value is even higher than the recommended cut-off for start of treatment. Therefore, no uniform PASS can be proposed and this makes this instrument less useful. This applies similarly to the MCII but to a lesser extent. As MCII will mostly be applied in patients who start with new treatment (and a BASDAI ≥4), we recommend a cut-off value for MCII of 1.1 for BASDAI and 0.6 for BASFI.

a: median Baseline BASDAI = 4.9  b: median baseline BASFI = 4.6
Medical Education

POSTER #12:
CAN TEACHING DOCTORS ABOUT DECISION TREES IMPROVE THE INFORMED CONSENT PROCESS? Lucas Marinacci and Herbert Chase. Department of Biomedical Informatics, Columbia University Medical Center, New York, NY, 10032.

When doctors engage in medical decision making with patients and their families, such as during the informed consent process, they often omit important risks, benefits, and alternatives to the treatment being discussed. Omission of these options and outcomes can make it difficult for patients or their surrogates to make a truly informed decision. Decision trees are analytical constructs which allow for a systematic approach to complicated decision-making scenarios; when employed properly, they may be a simple and reproducible way to train student doctors to explicitly address all reasonable options and outcomes when discussing treatment plans with patients. This pilot project had two parts. To better quantify student performance in this area, 71 seniors were instructed to counsel a hypothetical patient facing a complicated medical decision. Their written responses were compared to a gold standard list of 3 major options and 3 major outcomes. The overall omission rate was calculated for each item and ranged from 32-86%, justifying an educational intervention. A short written primer on the fundamentals of decision trees was developed by the research team, with the hypothesis that students exposed to the primer would list more options and outcomes than those who were not. Ten medical students were given 2 clinical scenarios and asked to write out everything they would tell the patient to help them make an informed decision, using any external resources they wished. The half randomly assigned to the intervention arm also received the primer; those in the control arm did not. The number of options and outcomes listed by each participant was counted and the mean and range calculated for each arm for each vignette. The means of the two arms were compared using a one-tailed student T-test. Subjects in the intervention arm listed significantly more risks and benefits than those in the control arm for both vignettes (10.8 vs 5.8, p=0.01; 11.6 vs 3.8, p=0.04). These results support the conclusion that educating future physicians about the basics of decision trees may be a simple and inexpensive way to improve the informed consent process by offering a systematic way to reduce inadvertent omissions.

Medical Humanities

POSTER #13:
THE IRONIES OF LEO KANNER: A HISTORICAL ANALYSIS OF AUTISM FROM 1943-1980. Melissa D. Stone and Jeffrey P. Brosco. Department of Pediatrics, University of Miami School of Medicine, Miami, FL 33101.

This past year, the American Psychiatric Association unveiled the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), the first major revision in ten years for the manual that dictates the entire field of mental illness. With hundreds of diagnoses in the DSM-V, one of the most controversial diagnoses is autism spectrum disorders. Leo Kanner first identified autism spectrum disorders in 1943 as a distinguished mental illness of childhood. The two key features that Kanner used for diagnosing autism, abnormal social interaction and insistence on sameness, are the same diagnostic criteria used in the DSM-V. However, the 70-year journey from Kanner’s 1943 paper to the 2013 DSM-V was complicated by academic debate, public outrage, and controversy. In modern day, many celebrate Kanner as the father of autism, a hero in fighting for parents and children of autism, but Kanner’s story is much more convoluted. Through analyzing medical journals, archival sources, popular periodicals, oral histories, historical texts, and personal letters over the past century, I will argue that there are ironies surrounding the story of Leo Kanner. In modern day, there are many disagreements surrounding autism’s cause, diagnosis, and management but debate and incongruent school of thought about autism have persisted since 1943. This history of medicine research will show that though much previous research has championed Kanner as the father of autism, Kanner was just as confused about autism as anyone else.
Kaposi’s Sarcoma Associated Herpes Virus (KSHV) causes Kaposi’s sarcoma (KS), an angiogenic spindle-cell sarcoma associated with AIDS. KSHV-encoded viral G-protein coupled receptor drives initiation and progression of KS by regulation the hypoxia inducible factor 1 alpha (HIF-1α) that leads to secretion of vascular endothelial growth factor. HIF-1α is an oxygen-sensible subunit part of the HIF transcription factor complex essential for adaptation of cells and tissues to low oxygen and inflammation. Interestingly, KSHV lytic gene expression of Primary Effusion Lymphoma, a lymphoproliferative disease associated with KSHV, is induced by low oxygen and HIF-1α expression. This suggests a role for the HIF pathway in the KS life cycle. In this study, we employed the murine gammaherpesviruses virus 68 (MHV68) to investigate the role of HIF-1α in gammaherpesviruses replication and pathogenesis. MHV68 is biologically and genetically similar to KSHV and infects laboratory mice providing a valuable small animal model of gammaherpesvirus infection. Here, we show that MHV68 infection activates HIF transcriptional activity in vitro when assessed by luciferase activity of a HIF-1α-dependent promoter, stabilizes HIF-1α mRNA when observed by qRT-PCR and protein expression by western blot. HIF activation was dependent on viral gene expression since UV-irradiated MHV68 did not elicit the same response. Moreover, MHV68 in vitro infection of mouse embryonic fibroblasts lacking HIF-1α results in a 7.5-fold increase of virus released in the supernatant when quantified by plaque assay. We conclude that HIF-1α activation is conserved among gammaherpesviruses including MHV68. Also, HIF-1α regulates MHV68 in vitro infection in a restrictive manner. Based on these conclusions we hypothesize that HIF-1α plays a role during gammaherpesvirus infection and latency establishment. Understanding the interaction between viral and cellular genes leading to KS oncogenesis is a crucial step towards the development of therapies for KS.

Food availability positively regulates thyroid hormone secretion through leptin stimulation of thyrotrophin-releasing hormone (TRH) and thyroid-stimulating hormone (TSH) expression. However, the biologically active thyroid hormone triiodothyronine (T3) is largely produced outside of the thyroid gland via activation of thyroxine (T4) by the type II deiodinase (D2). To understand how nutritional signals affect D2 expression, we studied a mesothelioma cell line, MSTO211H, which endogenously expresses D2. Our data show the finding that D2 activity is transcriptionally upregulated by nutrient availability via insulin signaling through the mammalian target of rapamycin complex 2 (mTORC2) signaling pathway. Specifically, insulin at a dose of 300-600nM was found to upregulate D2 by 2-fold in 4h in cells that were serum starved for 48h. Our novel discovery is that the upregulation of D2 activity is dependent on (mTORC2) by the use of dual mTORC1/2 inhibitor PP242, which caused complete inhibition of D2 activity. Further downstream of mTORC2, the inhibition of protein kinase C (PKC) using GO690693 and RO318220 also downregulated D2 activity; conversely, stimulation with TPA resulted in 3-fold upregulation of D2 activity after 4h. MTOR signaling impacts critical aspects of cell biology such as cell proliferation and energy homeostasis. Therefore, because D2 is so critical for T3 generation, we show that aberrant signaling of mTOR affects D2 activity, a process critical for local thyroid hormone activation. Herein, we have thoroughly examined effects of major targets of the PI3K/AKT/mTOR signaling pathway on D2 activity and expression levels in MSTO211H cells.
Molecular Biology

POSTER #16:
In vivo PROXIMITY LABELING FOR THE DETECTION OF PROTEIN-PROTEIN AND PROTEIN-RNA INTERACTIONS. David B. Beck1, William Drury1, Ryan Casey1, Varun Narendra1, Pascal W.T.C. Jansen2, Michiel Vermeulen2, and Roberto Bonasio1. 1Howard Hughes Medical Institute and Department of Biochemistry, New York University School of Medicine, 522 First Avenue, New York, NY 10016, USA. 2University Medical Center Utrecht, Department of Molecular Cancer Research, Universiteitsweg 100, 3584CG Utrecht, The Netherlands

Accurate and sensitive detection of protein–protein and protein–RNA interactions is key to understanding their biological functions. Traditional methods to identify these interactions require cell lysis and biochemical manipulations that exclude cellular compartments that cannot be solubilized under mild conditions. Here, we introduce an in vivo proximity labeling (IPL) technology that rapidly identifies polypeptides and RNAs in the vicinity of a protein of interest using affinity tags and photoactivatable groups. Using quantitative mass spectrometry and deep sequencing, we show that IPL identifies novel, as well as known, protein–protein and protein–RNA interactions in the nucleus of mammalian cells. Thus, IPL provides additional temporal and spatial information for the characterization of biological interactions in vivo.

POSTER #17:
INSULIN RECEPTOR IS TUMORIGENIC IN BREAST CANCER: POSSIBLY LINKED VIA CD24 EXPRESSION. Inna Genkin, Ran Rosto, Derek LeRoith. Diabetes and Metabolism Clinical Research Center of Excellence, Clinical Research Institute at Rambam and the Faculty of Medicine, Technion, Haifa, Israel

Hyperinsulinemia is associated with breast cancer progression and mortality. Both the Insulin receptor (IR) and the insulin-like growth factor-I receptor (IGF-IR) were found to be involved in mediating hyperinsulinemia’s mitogenic effect. Recently we found non-uniform expression of the mucin-like cell surface protein, CD24, which is considered a prognostic marker in breast cancer on the murine mammary Mvt1 (c-myc/vegf oncogene) cell line. Here, we aimed to determine whether hyperinsulinemia induce accelerated tumor growth by maintaining CD24+ expression. Moreover we looked for a correlation between CD24 and the expression of the two receptors tyrosine kinase (RTK): IR and IGF-IR. We found that CD24+ cells are widely dispersed in culture, displaying spindle-like cytoplasm. Furthermore, IGF-IR was expressed in significantly higher levels in the CD24+ cells which showed accelerated growth rate and higher migratory capacity compared to the CD24- cells. Based on these findings we compared breast tumor progression following inoculation of CD24+ vs CD24- cells in both FVB/N mice and the unique hyperinsulinemic MKR female mice. We found that CD24+ formed larger tumors in both models. To further understand the linkage between IR, IGF-IR and CD24 expression, we determined the percentage of CD24+ and CD24- cell population following IR and IGF-IR KD. Our results demonstrate a significant decrease in the percentage of CD24+ population following IR-KD. Inoculation of the Mvt1 IR-KD cells into the mammary fat pad of FVB/N mice significantly inhibited tumor growth rate compared to the control group, whereas only moderate trend was observed following inoculation of Mvt1 IGF-IR KD cells, similar trend was observed when either of the KD cells was innoculated into the hyperinsulinemic MKR female mice. Taken together, this study shows a significant role for IR in the progression of mammary tumors, not only through mediating insulin’s mitogenic effect but also by a crosstalk with IGF-1. These results place in doubt the efficiency of specific strategies aiming toward IGF-1 while sparing the IR. We suggest that both IR and IGF-1R should be targeted to accomplish a desired inhibitory effect on tumor growth; however with constant monitoring of blood glucose level. In addition to the current strategies, the development of new strategies targeting both receptors in a tissue specific manner should be considered, as it may achieve anti-tumor effect with minimum side-effects. Furthermore, we show here for the first time, a link between IR expression and CD24. This may reveal a novel mechanism for IR mitogenic effects, however further studies are required to obtain clearer picture about the relationship between the two.
Notch signaling has an indispensible role during vertebrate development and in maintenance of tissue homeostasis. A generally accepted scheme for the Notch mediated transcriptional regulation is that of turning ON transcription or enhancing transcription by recruiting co-activators to the target promoters. Here, using p19ARF as an example, we for the first time demonstrate the mechanism in which Notch functions as a repressor. We have observed that the Notch-driven mouse T-ALLs have no detectable expression of ARF. This result has been confirmed on lymphoma cell-lines and MEFs. This repression is a transcriptional effect of Notch since exogenous expression of a transcriptionally inactive form of Notch in MEFs does not result its repression of ARF. Besides, Notch binding to the ARF promoter in mouse T-ALL as well as in MEFs by infected with NICD detected by ChIP suggests the same. This repression is accompanied by reduction of activation mark (H3K4me3) and increase in the repression mark (H3K27me3) across the promoter. Ezh2 (H3K27 methyl transferase) then has been shown to be a transcriptional target of Notch in T-ALL and is recruited to the ARF promoter in a Notch dependent manner. The recruitment of Ezh2 and the increase in H3K27me3 are dependent on LSD1(a H3K4 demethylase) activity as the enrichment is reduced in the presence of an inhibitor to LSD1. DNA pull down experiments show that Notch, Ezh2 and LSD1 can form a complex on DNA harboring binding sequences for CSL in a CSL-dependent manner. Our study for the first time demonstrates that Notch can directly inhibit gene transcription by recruiting epigenetic modulators such as Ezh2. Given that p19ARF is a tumor suppressor, this study also gives insight into the mechanisms of Notch mediated tumorigenesis. It opens up the possibility of using epigenetic therapy in combination with GSI in treating Notch dependent cancers for a better outcome.

Arterial occlusive diseases are major causes of morbidity and mortality in industrialized countries and represent a huge economic burden. The extent of the native collateral circulation is considered to be the most important determinant of the magnitude of tissue damage and subsequent functional impairment that ensues following an arterial occlusive event. Therefore, understanding the mechanisms responsible for collateral artery development may provide avenues for the design of strategies to enhance the collateral circulation in patients at risk for arterial occlusive diseases. Here, we identify a critical requirement for cJun-NH2-Terminal Kinase (JNK) in collateral artery development. Indeed, using immunofluorescence, microfil perfusion and three dimensional high resolution micro computed tomography (µCT) imaging techniques, we demonstrate that mice with compound JNK-deficiency in the vascular endothelium display abnormal collateral arteries, which are unable to restore blood perfusion following occlusion of a major artery leading to severe tissue necrosis in animal models of femoral and coronary artery occlusion. Furthermore, employing constitutive and inducible conditional deletion strategies we demonstrate that endothelial JNK acts during the initial development of collateral arteries to ensure proper patterning and connectivity, but is, for the most part, dispensable for angiogenic and arteriogenic responses in adult mice. The defects in collateral arterial development may reflect an enhanced sensitivity of JNK-deficient endothelial cells to cell death in specific contexts. This study introduces JNK as a major regulator of vascular development and highlights the crucial importance of the collateral circulation as the main defining factor in reducing the severity of tissue damage and functional impairment following arterial occlusive events.
Neurology

POSTER #20:
THE AGE OF AMBULATION IN BOYS WITH DUCHENNE MUSCULAR DYSTROPHY AND ITS USE AS AN END-POINT IN CLINICAL TRIALS. Jacob J. Gissy, Teresa Johnson, Michele Yang, Emma Ciafaloni, Deborah J. Fox, Anil Kumar, Sunkyung Kim, Anthonie J. van Essen, Richard Finkel. 1University of Central Florida College of Medicine, Orlando, FL 32832; 2University of Colorado, Denver, CO 80202; 3University of Rochester, Rochester, NY 14627; 4New York State Department of Health, NY; 5Center for Disease Control, Atlanta, GA 30333; 6University of Groningen, Netherlands; 7Nemours Children’s Hospital, Orlando, FL 32832.

Duchenne muscular dystrophy (DMD) is an X-linked recessive disease that affects 1 in 3600-6000 newborn males. Mutations in the dystrophin gene cause absent or defective dystrophin in muscle. Genetic testing confirms the diagnosis of a dystrophinopathy and allows for newborn screening and identification of presymptomatic patients. Affected males exhibit delayed musculoskeletal development, with older age when independent ambulation is achieved, and eventual muscle deterioration, with loss of ambulation, restrictive lung disease and cardiomyopathy, leading to reduced survival. Data on age when loss of independent ambulation occurs is well established for DMD, however age when ambulation is first achieved in boys with DMD has not been well reported nor used as an endpoint for clinical trials. In preparation for a clinical drug trial to investigate the effectiveness of drug treatment in infants with DMD, a clinically meaningful primary outcome measure needs to be established. Our hypothesis is that infants with DMD walk later than normal, have an innate desire to walk as soon as the motor system permits this task, and that an effective drug for DMD would reduce the age when independent ambulation is reached. As such age of independent ambulation is a discrete dichotomous event that may serve as an effective primary outcome measure in a clinical trial. This study uses MDSTARnet (Data Set 1) and a Dutch natural history survey (Data Set 2), to report the age of ambulation. Mean ±Standard Deviation of age of ambulation in Data Set 1 was 17.0 ± 5.1 (CI 16.5, 17.5) months. Median age of ambulation was 16.0 (IQR 13.0, 18.0) months. Mean age of ambulation in Data Set 2 was 21.8 ± 7.1 (CI 21.0, 22.7) months. Median age of ambulation was 20.0 (IQR 18.0, 24.0) months. Hypothetical clinical trial study design and power analyses are presented based upon these data.

Neuroscience

POSTER #21:
PROTEIN KINASE C EPSILON-MEDIATED EXPRESSION OF THE NEUROPROTECTIVE PROTEIN ARC IS AGE-DEPENDENT IN RATS. Charles H. Cohan, Kahlilia Morris-Blanco, Jake T. Neumann, Clinton B. Wright and Miguel A. Perez-Pinzon. Evelyn F. McKnight Brain Institute and Cerebral Vascular Disease Research LaboratoriesDepartment of Neurology, University of Miami Miller School of Medicine Miami, FL 33136.

Cerebral ischemia is a leading cause of death and disability in the United States, primarily affecting individuals 50 and over. Survivors often suffer from permanent brain damage. This brain damage can impair memory due to cellular damage to the CA1 region of the hippocampus, an area highly susceptible to ischemic injury that is necessary for memory formation. Protein kinase C epsilon (PKCe) activation protects the CA1 region against ischemic injury in young rats. However, as a majority of ischemic injuries (~80%) occur in people over the age of 50, this animal model may not be representative of the population most at risk. Due to this, using aged animal models in ischemic injury research may be more appropriate. We uncovered that in young animals, activation of PKCe using a specific activator of PKCe, ψε-Receptor for Activated C Kinase (ψεRACK), triggers the expression of a potentially neuroprotective protein, activity-regulated cytoskeleton-associated protein (arc). Also, we uncovered that PKCe activation decreased AMPA receptor currents, a known function of arc. Additionally, we determined neuroprotection against oxygen and glucose deprivation (an in vitro model of ischemic injury) was dependent upon arc expression in organotypic hippocampal cultured slices. Finally, we observed that PKCe-mediated arc expression is age-dependent. We determined that although this mechanism is activated in juvenile and young rats(27 days and 4 months), there was no increase in arc expression in animals 9, 12, or 24 months of age. This research identifies a novel mechanism of arc expression, a novel mechanism of arc-mediated neuroprotection, and indicates that some neuroprotective therapies may be least effective in the age group that often needs them the most, the elderly.
POSTER #22:
MODULATING POST-INJURY GLIOTRANSMITTER LEVELS LEADS TO IMPROVED SYNAPTIC FUNCTION. Enmanuel J. Perez, Maria L Cepero, Daniel J. Liebl. Department of Neurosurgery, The Miami Project to Cure Paralysis, Neuroscience Program, University of Miami Miller School of Medicine, FL 33136.

Traumatic brain injury (TBI) results in a number of acute pathological alterations including the extracellular release of glutamate. This acute transmitter release is thought to play a significant role in early neuronal cell death. However, cell death after injury is progressive, and unfortunately our understanding of transmitter regulation in the days and weeks after TBI is limited. Glial cells, in particular astrocytes, play an important role in maintaining synaptic integrity and function after injury by regulating transmitter levels in the synaptic cleft. In addition, our laboratory has shown that a family of receptor tyrosine kinases, Eph receptors, and their cognate ligands, ephrins, regulates synaptic function and formation as well as transmitter synthesis and release from astrocytes. We hypothesize that neurons communicate with astrocytes through ephrinB3-EphB3 signaling to regulate GT levels in the synapse, and through enhancement of EphB3 signaling we can improve synaptic stability and function after TBI. In this study, we will examine how varying transmitter levels through genetic manipulation of transmitter enzymes (i.e. serine racemase) and ephrinB3-EphB3 signaling in astrocytes and/or neurons affects synaptic stability and function post-TBI. We will take a comprehensive approach and make use of cutting-edge techniques to measure synaptic transmission, transmitter release, biochemical alterations in protein expression, and learning and memory behavior using gain-of-function and loss-of-function mouse models. Our preliminary findings suggest that there is an acute increase in D-serine levels after injury that can be regulated by EphB3-ephrinB3 signaling, and results in deficits in synaptic function and learning.

POSTER #23:
NEUROPROTECTIVE PROPERTIES OF ANTIOXIDANTS IN STROKE CORRELATE WITH THEIR EFFECTS ON ISCHEMIC RELEASE OF GLUTAMATE. Aarshi Vipani, Preeti Dohare, Maria C. Hyzinski-Garcia, Nicole H. Bowens, Julia W. Nalwalk, Paul J. Feustel, Richard W. Keller, Jr, David Jourd’heuil, and Alexander A. Mongin.

Antioxidant agents potently protect against ischemic brain damage in animals, but show no clinical benefits in humans. In the present study we tested the hypothesis that potency of antioxidants in preventing pathological glutamate release can predict their ability to reduce ischemic infarction. Transient focal ischemia in rats was induced by 2-hr occlusion of the middle cerebral artery. Antioxidants Tempol and Edaravone (500 nmols) were injected into the lateral ventricles prior to ischemia. 72 hrs later, control and antioxidant-treated animals were evaluated for behavioral deficits and brain damage. Tempol, but not Edaravone, reduced infarction volumes by ~60% and improved neurological outcomes. In parallel microdialysis experiments, Tempol but not Edaravone reduced extracellular levels of the excitatory neurotransmitter glutamate. Paradoxically, when tested in antioxidant assays in vitro, Edaravone was more effective in scavenging the majority of the ischemia related free radicals and oxidants. The only exception was scavenging of superoxide anion, in which Tempol was superior to Edaravone. Overall, these results suggest that neuroprotective properties of Tempol are determined by its ability to scavenge superoxide and prevent pathological glutamate release.
Neurosurgery

POSTER #24:
SURROGATE FITNESS MEASURES’ ASSOCIATION WITH FUNCTIONAL INDEPENDENCE IN PEOPLE WITH SPINAL CORD INJURY. 1Darryl Cannady, B.S., 1Jochen Kressler, Ph.D., 1,2,3Mark S. Nash, Ph.D, FACSM and 1,2Rachel E. Cowan, Ph.D. 1The Miami Project to Cure Paralysis, 2Department of Neurological Surgery, and 3Department of Rehabilitation Medicine, Miller School of Medicine, University of Miami, Miami, Miami, Florida USA.

Laboratory-derived fitness assessments of aerobic capacity (VO\textsubscript{2peak}) and anaerobic power (AP) are associated with functional independence in persons with spinal cord injury (SCI). To provide simple, easily conducted field-tests, surrogate fitness assessments (SFAs) for VO\textsubscript{2peak} and AP have been developed, i.e., the 6-minute (6MPT) and 30-second push tests (30sPT), respectively. However, the relationship between surrogate fitness measures and functional independence is unknown. The purpose of this study was to evaluate whether SFAs are associated with functional independence in people with chronic SCI who use wheelchair as their primary mobility mode. 63 persons with chronic SCI aged 18-65y completed the Spinal Cord Independence Measure (SCIM). VO\textsubscript{2peak} was then assessed via an incremental arm crank exercise test to exhaustion with 3 min stages and injury level-dependent workload increments. AP was assessed with a table mounted cycle ergometer using the Wingate protocol. SFAs were a 6-minute (N=63) and 30-second push test (n=51) using a 15m loop in a flat linoleum surfaced hallway. VO\textsubscript{2peak} and anaerobic power were 1239±526.4mL/min and 2.7±1.1W/kg, respectively, and 6MPT and 30sPT distance travelled was 487±142 and 43.7±17.1m, respectively. Demographics (BMI, age, injury level, and injury duration) were associated with 33.8% of SCIM score variability (p<0.001). 6MPT was associated with an additional 33.6% (p<0.001). Comparatively, the VO\textsubscript{2peak} (when entered instead of the 6MPT) was associated with additional 12.5% (p=0.001) of the variability in the SCIM score. Demographics for those who performed the 30sPT and Wingate were associated with 29.0% (p=0.015) of SCIM score variability. The 30sPT was associated with an additional 42.8% (p<0.001), while the Wingate test (when entered instead of the 30sPT) was associated with an additional 38.0% (p<0.001). These data suggest that the surrogate fitness measures could provide substantial predictive power (beyond common demographics) for functional independence of those individuals with SCI who depend on wheelchairs as primary means of ambulation.

Oncology

POSTER #25:
KSHV-DEPENDENT ACTIVATION OF PDGF RECEPTOR-α SIGNALING IS AN ONCOGENIC DRIVER IN KAPOSI’S SARCOMA. Lucas E. Cavallin1, Qi Ma1, Sachin Gupta1, Paolo Romanelli2, Pascal J. Goldschmidt1 and Enrique A. Mesri1. 1Department of Microbiology and Immunology, 2Department of Dermatology, University of Miami, Miami, FL 33136

Kaposi’s sarcoma (KS), an AIDS-associated cancer caused by the KS Herpesvirus (KSHV), is a vascular sarcoma characterized by intense angiogenesis and spindle cell proliferation. KS is the most common malignancy among HIV-infected individuals, and specific KS treatments are needed. KSHV causes tumorogenesis via autocrine and paracrine mechanisms. Defining the critical host pathways subverted by the virus is essential to identify new therapeutic targets. KSHV encodes a G protein-coupled receptor (vGPCR) that is critical for tumorogenesis. We previously found that reactive oxygen species (ROS), via vGPCR and Rac1, are critical for oncogenesis. Since vGPCRand Rac1 are powerful activators of paracrine responses, we set out to investigate host pathways activated by KSHV and assess the in vivo impact of their inhibition. Kinome analysis showed that PDGF receptor alpha (PDGFR\alpha) was the only activated receptor tyrosine kinase in KS. KSHV vGPCRupregulated PDGF ligands. IHC analysis of mouse KS displayed prominent PDGFR\alpha phosphorylation in KSHV-positive areas. PDGFR activation induced c-Myc and VEGF expression in a Rac1/ROS-dependent manner. The following results point to PDGFR\alpha as an oncogenic driver in KS: 1) Inhibition of KSHV tumorogenesis by the RTK inhibitor Imatinib; 2) Constitutively active PDGFR\alpha mutation D842V conferred resistance to Imatinib; 3) A PDGFR\alpha dominant negative construct completely blocked tumorogenesis in mice; 4) Analysis of human KS biopsies showed high expression of phosphorylated PDGFR\alpha and PDGFR ligands only in areas where KSHV was present, indicating that the viral mechanisms of PDGFR\alpha signaling revealed in our mouse model of KS are present in human KS. This work identifies PDGFR\alpha as a critical player in Kaposi’s sarcoma, pointing to pharmaco-oncogenomic targeting of
PDGFRA signaling as a key potential therapeutic approach for KS. Furthermore, PDGFRA and downstream signaling molecules can serve as valuable biomarkers to assess current AIDS-KS trials with Imatinib.

### Ophthalmology

**POSTER #26: CORRELATION OF PHENOTYPIC EXPRESSION OF METHICillin RESISTANCE WITH GENOTYPE AND IN VITRO SUSCEPTIBILITY FOR mecA+ STAPHYLOCOCCUS EPIDERMIS ENDOPHTHALMITIS ISOLATES.** Laura C. Huang; James Wong; Jack Stringham; Jorge Maestre; Darlene Miller; Harry W. Flynn. Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL 33136.

Our purpose was to correlate genotypic methicillin resistance conferred by the mecA gene with phenotypic expression of methicillin resistance among *Staphylococcus* (*S.* epidermidis) isolates from endophthalmitis and in vitro susceptibility to commonly used antimicrobials including cefaroline, a new fifth generation cephalosporin. Methods: Etests and the VITEK2 system were used to detect the presence and phenotypic expression of methicillin resistance among *S. epidermidis* isolates recovered from endophthalmitis. Results were compared with mecA genotype using polymerase chain reaction (PCR) and in vitro susceptibility to cefaroline and vancomycin (Etests) and gentamicin, daptomycin, linezolid, tigecycline, levofoxacin, and moxifloxacin (VITEK 2). Additionally, antibiotic susceptibility was analyzed following the following subgroups: mecA+ with methicillin resistance (group A) and isolates that were mecA+ though clinically methicillin sensitive (group B). All isolates recovered from 2010-2013 were mecA-genotype positive (100%), however, only 21/32 (65.6%) expressed methicillin resistance by conventional laboratory tests. Isolates were 100% susceptible to vancomycin (MIC < 3 μg/mL, N=32), cefaroline (MIC < 0.38 μg/mL, N=32), linezolid (N=20), and tigecycline (N=20). The susceptibility of daptomycin (N=20) was 95%. Gentamicin susceptibility overall was 86.7% (26/30) of which group A had 78.9% (15/19) susceptible compared to 100% (11/11) ingroup B. A correlation between the phenotypic expression of mecA genotype and in vitro susceptibility was demonstrated for the fluoroquinolones. For levofloxacin, group A had 21.1% (4/19) susceptible in contrast to 81.8% (9/11) (p=0.001) ingroup B. For moxifloxacin, group A had 30% (3/10) susceptible compared to 80% (8/10) (p=0.025) in group B. Conclusions: Routine laboratory methods may fail to detect heterogeneous and or low level expression of methicillin resistance among mecA+ S. epidermidis genotypes. This may have important implications for the correct selection and administration of S. epidermidis endophthalmitis. The new fifth generation cephalosporin, cefaroline, demonstrated low MIC values and may show promise as a therapeutic agent for methicillin resistant *S. epidermidis*.

**POSTER #27: KNOCKDOWN OF INNATE IMMUNITY PRESERVES RETINAL FUNCTION IN THE rd1 MOUSE.** Sarah Syeda, Amit K. Patel, Abigail S. Hackam. Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL 33136

Innate immune response and its dysregulation have been implicated in the pathogenesis of retinal degeneration. What is currently not well understood is how it contributes to the progression of the disease. Toll-Like Receptors (TLR) form a key branch of the innate immune system, and TLR signaling occurs in response to damage-associated molecular proteins including those released from injured cells. Most TLRs operate through the adaptor protein Myeloid differentiation primary response gene 88 (Myd88) whose downstream mediators lead to the induction of pro and anti-inflammatory genes. The purpose of this study is to examine the role of the TLR branch of innate immunity on the retinal degeneration1 (rd1) mouse in whom early photoreceptor cell dysfunction and death occurs. This study used rd1 mice crossed with Myd88+/− mice to produce mice homozygous for the rd1 mutation, and Myd88+/−, Myd88+/+ and Myd88−/− genotypes. Electroretinograms (ERG) were performed at different time points to investigate our hypothesis that knockdown of this innate immunity pathway would protect retinal function. ERGshow preservation in function at postnatal day 13/14 in rd1/Myd88−/− mice (n=14) compared with rd1/Myd88+/+ (n=11, p<0.05). Outer nuclear layer cell counts in sections of mouse eyes revealed less cell death in Myd88−/− mice (n=3). To elucidate the mechanism behind preservation of function and cells, retina cross-sections were stained with a marker for microglia, IBA-1. These pivotal retinal immune cells have previously been shown to increase in number during retinal degeneration and have been suggested to enhance photoreceptor death in the rd1 mouse. Preliminary data shows a 60.1% reduction in the number of microglia in the outer retina of rd1/Myd88−/− (n=2) mice compared with rd1/Myd88+/+ (n=2) suggesting that the TLR/Myd88 signaling pathway is involved in pathological microglial response during retinal degeneration. In summary, this study reveals that knocking down the TLR branch of innate immunity is protective, thus highlighting a novel pathway regulating retinal degeneration and providing a potential target for therapy.
**POSTER #28:**
PREVALENCE OF ACCESSORY GENE REGULATOR (AGR) SUBTYPES, DELTA-HEMOLYSIN (HLD) TOXIN, AND CORRELATION WITH BIOFILM PRODUCTION AMONG STAPHYLOCOCCUS EPIDERMIDIS ENDOPTHALMITIS ISOLATES. James Wong; Laura C. Huang; Jack Stringham; Jorge Maestre; Darlene Miller; Harry W. Flynn. Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, FL 33136.

The accessory gene regulator (AGR) of staphylococci is a global regulator of biofilm and staphylococcus virulence. Our purpose was to determine the presence of AGR subtypes and correlation with known coagulase negative staphylococcus virulence factors: biofilm production and delta toxin among Staphylococcus (*S*) epidermidis endophthalmitis isolates. A multiplex polymerase chain reaction (PCR) assay with four primer sets was used to characterize AGR (1-4) types among *S*. epidermidis endophthalmitis isolates. Separate PCR assays were run to detect the presence of the HLD gene loci. Biofilm production was evaluated qualitatively by staining test tubes inoculated with the isolates with crystal violet dye and grading the level of staining on a scale of 0 to 3 with 0 (non-adherent), 1 (weakly adherent), 2 (moderately adherent), and 3 (strongly adherent). *S*. epidermidis isolates (n=33), were recovered from the anterior chamber (10) and vitreous (23) of endophthalmitis cases between 2010 and 2013. Three AGR subtypes, AGR1 (n=12, 36.4%), AGR2 (n=16, 48.5%), and AGR3 (n=3, 9.1%) were documented amongst isolates. The HLD toxin was documented in 32 (97%) samples. The mean biofilm grade of AGR subtypes were as follows: AGR1 was 2.33, AGR2 was 2.44, and AGR3 was 2.75. One-way analysis of variance indicated that there were no significant differences among the three groups F(2,29) = 0.57, p > 0.05. To our knowledge, this is the first study determining AGR subtypes of *S*. epidermidis isolated from endophthalmitis. While isolates from infections in medical devices have been found to be AGR1 most commonly, the predominant profile among this group was AGR2 which may constitute a subtype unique to *S*. epidermidis endophthalmitis. All samples with AGR1 expressed HLD and were associated with a lower level of biofilm production than respective subtypes although this was not statistically significant. This may indicate that AGR, as a regulator of quorum sensing system, in particular AGR1, may downregulate biofilm production and upregulate toxin production.

**POSTER #29:**

Experience in the clinic shows that the rate of glaucoma in the Haitian population is among the highest, resulting in the greatest level of blindness at the youngest ages. The purpose of this study was to determine the incidence of glaucoma suspects in the Afro-Caribbean population of South Florida at community screenings. A retrospective chart review from October 2011 to October 2013 was conducted. A total of 939 patient charts were reviewed from 5 separate health screenings held at the Center for Haitian Studies within the Little Haiti district in Miami, Florida. Measurements of intraocular eye pressure (IOP), cup-to-disc ratio, and visual acuity (VA) were performed on all patients. Glaucoma suspects were defined as having either an IOP of 24 mm Hg or greater or a cup-to-disc ratio of 0.6 or greater in either eye. The incidence of glaucoma suspects was calculated as well as the severity of pathology based upon IOP, cup-to-disc ratio, and visual acuity. A total of 331 patients were newly identified as glaucoma suspects in the Afro-Caribbean community of South Florida. The incidence of a glaucoma suspect diagnosis was 35.3%. Among patients diagnosed as glaucoma suspects, the median IOP was 22.0 mmHg (SD 19-25), the median cup-to-disc ratio was 0.60 (SD 0.4-0.8), and the median logMAR VA was 0.22 (SD 0.20-0.24, Snellen equivalent 20/30). The median age of patients diagnosed as glaucoma suspects was 56 years. Community health screenings alone have led to an increase in the number of people diagnosed with glaucoma. The incidence and severity of optic nerve cupping and ocular hypertension in the Afro-Caribbean population of South Florida is very high even though the median visual acuity of these patients is close to normal. The data from these community screenings suggest the Afro-Caribbean population is a high-risk population for glaucoma in line with our impression in our clinics. Further follow-up will be required to determine the incidence and severity of glaucoma.
POSTER #30:
NATURAL HISTORY OF CIRCUMSCRIBED CHOROIDAL HEMANGIOMAS. Angelica Ortiz, Marco Gonzalez, William Harbour, and Bernadete Ayres. Bascom Palmer Eye Institute, Miami, FL, 33136.

Circumscribed choroidal hemangiomas are rare, benign vascular tumors of the choroid. The most frequent sight-threatening complication of these intraocular tumors are exudative retinal detachments. An understanding of the natural history of circumscribed choroidal hemangiomas is important for predicting disease trends and determining the timing of treatment. The aim of this work is to evaluate the natural course of the clinical and ultrasonographic characteristics of circumscribed choroidal hemangiomas. This is a non-comparative consecutive case series from January 2000 through July 2013. Patients presenting with circumscribed choroidal hemangiomas at the Bascom Palmer Eye Institute were identified. Data was collected on demographics, clinical features, treatments, and visual outcomes. A total of 78 eyes in 78 patients were identified. The mean age at presentation was 54.9 years (range: 19 to 88). The mean follow up after presentation was 42.8 months. Presenting visual acuity was equal or better than 20/50 in 37 of 87 patients (43%). 42 patients had an associated serous retinal detachment. The mean height on initial ultrasonography was 2.4 mm (range 1 to 5 mm). Treatment included photodynamic therapy in 40 eyes. Final visual acuity was equal or better than 20/50 in 38 of 87 patients (44%). In spite of the benign nature of this tumor, many patients in the present study developed sight-threatening complications requiring treatment. Despite the effectiveness of current treatment modalities, visual prognosis remains guarded.

POSTER #31:
EMERGING TRENDS IN PEDIATRIC IDIOPATHIC INTRACRANIAL HYPERTENSION (IIH): IS THE CHILDHOOD OBESITY EPIDEMIC AFFECTING THE PREVALENCE AND PATIENT CHARACTERISTICS OF PEDIATRIC IIH? Sastry Ananth,1,2 Shields Rebecca1, Cavuoto Kara1. Bascom Palmer Eye Institute. 900 NW 17th St. Miami, FL 33136. University of Miami Miller School of Medicine. 1600 NW 10th Ave #1140, Miami, FL 33136.

Idiopathic intracranial hypertension (IIH) commonly presents in obese females of child-bearing age. Our multi-center study investigates epidemiologic trends in children with specific regard to age and sex. A retrospective multi-center chart review identified children between 4-17 years from 2002-2012 diagnosed with IIH. Gender, age, body mass index (BMI), opening pressure, grade of optic nerve head (ONH) edema and management were analyzed. Fifty-four patients were divided into group 1 (4-8 years), group 2 (9-12 years) and group 3 (13-17 years). The average age was 11.5 years, differing significantly between males and females (males: 9.7 years, females: 13.3 years, p=0.001). Females represented 67% of patients across all age groups (26/54) and 86% of patients in group 3 (18/21). Group 2 represented the most patients overall (23/54), evenly split between males and females (52% versus 48%, respectively) and with similar BMI (26.7 versus 28.1, respectively). The BMI in group 3 differed between males and females (23.6 versus 33.5). Opening pressure was highest in group 2 (42.8) and lowest in group 1 (30.9). ONH edema was most severe in group 3 and higher in females (median grade 4). Thirteen children underwent surgical intervention, of which 70% were female (9/13). The results showed that female patients have similar clinical appearances to their adult counterparts, whereas males present at younger ages with lower BMI suggesting an alternate disease mechanism. From these results, we concluded that the epidemiology of IIH differs in children and depends on age. The steep rise in childhood obesity may correspond with the increasing frequency of pubescent women diagnosed with IIH.
LONG-TERM EFFECTS OF CATARACT SURGERY ON TEAR FILM PARAMETERS. Vincent D Venincasa BS1,2, Anat Galor MD1,2, William Feuer MS2, David J Lee PhD3, Hermes Florez MD, PhD1,2, Michael J Venincasa3. Miami Veterans Administration Medical Center, 1201 NW 16th St, Miami, FL 33125; 2Bascom Palmer Eye Institute, University of Miami, 900 NW 17th Street, Miami, FL, 33136; 3Department of Epidemiology and Public Health, University of Miami, 1801 NW 9th Avenue, Miami, FL 33136; 4Department of Endocrinology and Geriatrics, University of Miami, 1611 Northwest 12th Avenue, Miami, FL, 33136;

To examine the differences in tear film parameters more than 3 months post-surgery in eyes with cataract surgery (surgical eyes) versus eyes without cataract surgery (non-surgical eyes), 29 patients seen at the Miami Veterans Affairs Medical Center (VAMC) who had cataract surgery by phacoemulsification in one eye more than 3 months prior to the study date and had no history of surgical intervention in their fellow eye. Tear film parameters were measured in both eyes and compared using McNemar tests for dichotomous variables and paired and single sample t-tests for continuous variables. Mean patient age was 73 (standard deviation (SD): 11); 26 patients (90%) identified themselves as white and 7 (24%) as Hispanic. The mean number of days between surgery and this study was 952 (SD: 1109). There were no statistical differences between the surgical eye and the non-surgical eye with respect to any of the measured tear film parameters. Confidence intervals around these differences were narrow enough to exclude a substantial effect of cataract surgery. The elapsed time between cataract surgery and measurement of the tear parameters did not appear to affect the difference in parameters between the two eyes. We found that eyes that had cataract surgery more than 3 months prior to testing had no differences in their tear film parameters compared to eyes without a history of surgery.

POSTER #33:
LONG-TERM OUTCOMES OF POST-PENETRATING KERATOPLASTY ASTIGMATIC KERATOTOMY PERFORMED USING 30kHz FEMTOSECOND LASER FLAP MODE SOFTWARE VS 150kHz FEMTOSECOND LASER ENABLED ASTIGMATIC KERATOTOMY SOFTWARE. *Priyanka Chhadva BS, 1Florence Cabot MD, 1Vardhaman Kankariya MD, 3Sonia H Yoo MD. *University of Miami Miller School of Medicine, 1Bascom Palmer Eye Institute, 900 NW 17th St, Miami, FL 33136

This study assesses the long-term outcomes of astigmatic keratotomy (AK) performed with two different techniques in patients with post-penetrating keratoplasty (post-PK) residual astigmatism. This retrospective study included 11 eyes of 11 patients who underwent post-PK AK performed using either 30kHz femtosecond laser flap mode software (IntraLase/AMO, Irvine, CA) -Group 1- or using 150kHz femtosecond laser enabled AK software (IntraLase/AMO, Irvine, CA) -Group 2- to create two anterior arcuate corneal incisions. Preoperative and postoperative follow-up data, including uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), spherical equivalence (SE), average keratometry (avgK), and corneal cylinder (CC) were recorded and analyzed to determine visual outcomes and long-term results of these procedures. The student t-test was used to compare the two groups, and p<0.05 was considered statistically significant. The results showed no complications using either technique. In Group 1 (n=5), the preoperative mean UCVA was 0.99LogMAR, mean BCVA was 0.48LogMAR, mean SE was -0.89 diopters (D), mean avgK was 45.45D, and mean CC was 10.82D. The postoperative mean UCVA was 0.48LogMAR, mean BCVA was 0.27LogMAR, mean SE was -1.53D, mean avgK was 46.67D, and mean CC was 5.48D. In Group 2 (n=6), the preoperative mean UCVA was 1.03LogMAR, mean BCVA was 0.52LogMAR, mean SE was -0.08D, mean avgK was 45.38D, and mean CC was 9.35D. The postoperative mean UCVA was 0.77LogMAR, mean BCVA was 0.15LogMAR, mean SE was -3.18D, mean avgK was 57.43D, and mean CC was 3.24D. In Group 1, the difference between preoperative and postoperative BCVA was not statistically significant (p=0.63). In Group 2, postoperative BCVA showed clinical improvement, even though the difference between preoperative and postoperative BCVA was not statistically significant (p=0.06). In conclusion, AK performed with both techniques are safe and efficient procedures to correct post-PK residual astigmatism.
Orthopedic Surgery

POSTER #34:
RECONSTRUCTION OF THREE AND FOUR PART PROXIMAL HUMERUS FRACTURES UTILIZING PATIENT SPECIFIC THREE DIMENSIONAL CT MODELING. Krishn Khanna, Charles M Jobin MD, William N. Levine MD, Christopher S Ahmad MD. Department of Orthopaedic Surgery, Columbia University College of Physicians and Surgeons, New York, NY 10032

Though a very effective treatment for proximal humerus fractures, the hemiarthroplasty is the most technically challenging and unpredictable surgery a shoulder specialist performs, as there is very little original shoulder anatomy preserved on which to base the placement of the prosthesis. Usage of 3-D computer modeling may play a role in the pre-operative planning for these difficult surgeries. The purpose of this study is to determine whether it is possible to accurately and reliably reconstruct the pre-injury proximal humerus using 3-D computer modeling on post-injury CT scans. 28 patients who received hemiarthroplasty for a proximal humerus fracture, and had adequate pre-operative CT imaging were selected. These CT scans were converted into patient specific three-dimensional computer models of the shoulder using the Materialise's Interactive Medical Image Control System software. The individual bony fragments of the fractured humerus were separated from each other using the voxel selecting capabilities of the software. These bony fragments were reassembled in 3-D space to recreate an approximation of the pre-injury proximal humerus. These reconstructions were conducted with two fellowship-trained surgeons in separate trials. Measurements were made on these models to assess the reliability and validity of the reconstruction. The average measured dimensions from all trials fell within the range of dimensions of a normal healthy proximal humerus specified in literature. The reconstructions of the 28 humerus fractures showed very good to excellent inter- and intra-observer reliability for all measurements, with Inter-Class Correlation Coefficients ranging from 0.71 – 0.93 for a single observer and from .82 – 0.98 between two different observers. These findings suggest that the techniques used to reconstruct the CT generated computer models of the fractures were both valid and reliable. The use of reconstructive 3-D CT modeling shows promise in reconstructing native humeral anatomy and providing a surgeon with pre-operative information which may yield a more anatomically accurate hemiarthroplasty.

POSTER #35:
PHOTOGRAPH-BASED CLINICAL GONIOMETRY: A COMPARISON OF TECHNIQUES. Arash Sayari, Jared Crasto, Robert Gray. Department of Orthopedic Hand Surgery, University of Miami Miller School of Medicine, Miami, FL, 33101

Assessment of joint motion is an accepted evaluation of disability as well as an indicator of recovery from musculoskeletal injuries. Many goniometric techniques have been described to evaluate joint motion, almost all of which are valid, though each has a varying degree of inter-rater reliability. Such reliability is important as a single orthopedic injury is treated by multiple healthcare providers. This study examined clinical, approximated, and photograph-based measurements to assess the range of motion of joints of the upper extremity in 70 patients who visited the Orthopedic Hand Surgery Clinic at the Bascom Palmer Eye Institute. When tested against manual goniometry, we found visual approximations and photograph-based goniometry to be both clinically valid and require less time than traditional manual goniometry (visual approximations require 2 minutes, photograph-based measurements require 3 minutes, and clinical measurements require 8 minutes). Furthermore, photograph-based measurements afforded a promising degree of inter-rater reliability. Our study therefore supports photograph-based goniometry as the new standard goniometric technique as it has been clinically validated, is performed more rapidly than manual goniometry, and does not require surgeon presence to obtain reliable measurements. This results in a more efficient system, where the surgeon can spend more time managing the orthopedic patient, rather than recording measurements.
Otolaryngology

POSTER #36:
PIK3CA\textsuperscript{H1047R} MUTANT SYNERGIZES WITH P53\textsuperscript{H172R} TO PRODUCE NOVEL MOUSE MODEL FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA. Andrew HY Lee, Dario Garcia-Carracedo, Ilias Stratikopoulos, Ramon Parsons, Argiris Efstratiadis, Angela J. Yoon, Gloria H. Su. Departments of Pathology, Otolaryngology/Head and Neck Surgery, Columbia University College of Physicians and Surgeons, New York, NY 10032

The phosphatidylinositol 3-kinase (PI3K) signaling pathway regulates many normal cellular processes, such as cell proliferation, survival, apoptosis and glucose metabolism. Deregulation of this pathway and aberrant changes to its genetic components have been associated with cancer development in a wide variety of cancers, including that of head and neck squamous cell carcinoma (HNSCC). Notably, mutations of the PIK3CA gene, encoding for the catalytic subunit of PI3K, have been reported in up to 20% of head and neck tumors. Currently, a major limitation in HNSCC has been the lack of animal models to test current genetic paradigms and explore the effectiveness of new treatment modalities and chemopreventative strategies. Therefore, to better understand the role of mutant PIK3CA in tumor initiation and progression, a novel PI3K mutant knock-in mouse was generated carrying a gain of function allele (\textit{LSL-PIK3CA}\textsuperscript{H1047R}). Conditional expression of the mutant PI3K in the squamous epithelium of the upper digestive tract was driven by \textit{Keratin14-Cre} (K14Cre). These mice were crossed with heterozygous p53\textsuperscript{H172R} mutants to yield PIK3CA\textsuperscript{H1047R};p53\textsuperscript{H172R};K14-Cre double mutants. Upon tumor induction with 4-nitroquinoline-1-oxide (4NQO) and follow-up for 8 and 16 weeks, PIK3CA\textsuperscript{H1047R};p53\textsuperscript{H172R};K14-Cre mice developed tumors which histologically mimic human HNSCC. Furthermore, PIK3CA\textsuperscript{H1047R};p53\textsuperscript{H172R};K14-Cre mice presented significant gross and histological differences compared to single mutants and wild-type control mice. Moreover, molecular analysis of primary cell lines derived from tumors revealed activation of the PI3K pathway only in cancer cells harboring the \textit{H104R} mutation. Our data showed that an activating PIK3CA mutation could synergize with mutant p53 to enhance susceptibility to carcinogen-induced oral tumorigenesis. These results underscore the importance of PIK3CA-in oral neoplastic development and provide a model to explore the cross-talk between the PI3K pathway and p53. To the best of our knowledge, this is the first time PIK3CA mutant has been applied to HNSCC.

POSTER #37:
COCHLEAR IMPLANTATION OUTCOMES IN PATIENTS WITH INNER-EAR ANOMALIES. Phi T. Ho, Raphael Nwojo, Brian J. Simmons, Yeunjung G. Kim, Denise Yan, and Xue Z. Liu. Department of Otolaryngology, University of Miami Miller School of Medicine, Miami, FL 33101.

Cochlear implants (CI) for patients with an inner ear malformation (IEM) were once contraindicated. It was shown that as many as 20% of patients with sensorineural hearing loss are associated with anomalies of the temporal bone; they were previously underreported. With advances of radiological imaging, the diagnosis of IEM is becoming more common. Recent studies have shown safe and effective implantation of cochlear implants in patients with an IEM. However, few studies have been published on outcomes. In order to assess the outcomes of CI placement for IEM patients, we assessed common surgical complications, genetic diagnosing, and epidemiologic data in a retrospective chart review of a single tertiary institution. A total of 657 patients enrolled between seen in 2004 - 2009 were identified as having sensorineural hearing loss and a subset of them have received a cochlear implant. 20 of those patients with CI had radiological evidence of having an IEM. The epidemiological results of the study revealed that 70% of the CI recipients have postlingual deafness versus 30% showed prelingual deafness showed a 70/30 breakdownbetween postlingualv prelingual patients, with the average age being35 years old when receiving CI. Vestibular Aqueduct Syndrome and Internal Auditory Canal anomalies comprise 35% and 30% of IEM patients receiving CI, respectively.Additionally, two of the patients had genetic anomalies: one with a translocation of 5:13in a prelingual patient and one with Waardenburg Syndrome. Outcomes of the procedure revealed 10% of patients havinginaoperative complications including electrode bending and a mini-gusher. However, all 20 patients had successful implantation, 19 of which had functional implants on the last follow-up visit, which averaged 53 months post-operation. This study shows evidence that CI can be implanted safely and remain functional in patients with an IEM, regardless of epidemiological or genetic conditions.
POSTER #38: ORBITAL EXENTERATION FOR ADVANCED PERIORBITAL SKIN CANCER: PROGNOSTIC FACTORS AND SURVIVAL. Cody T. Ott, Robert Gerring MD, Sara TullisWester MD, and Zoukaa Sargi, MD. Department of Otolaryngology, Head and Neck Surgery. University of Miami School of Medicine, Miami, FL 33101.

Orbital exenteration refers to complete excision of orbital contents, periorbital tissues, and eyelids in order to remove locally invasive malignancies not controlled by less aggressive methods. Cancer recurrence rates as low as 7% have been reported in cases where all margins are negative. However, the presence of clear margins has not been shown to be a significant predictor of survival. Orbital invasion of cutaneous basal cell carcinoma is the most common indication for exenteration, but invasive squamous cell carcinoma and sebaceous gland carcinoma are also frequently encountered. Few studies specifically address advanced sinonasal and periorbital cutaneous malignancies resulting in orbital exenteration. The goal of this study is to describe survival outcomes, prognostic factors, follow up, and complications of patients with sino-nasal and cutaneous malignancies who have undergone orbital exenteration. This case series utilized a retrospective, single institution design to examine 49 patients (mean age 70.3) who underwent orbital exenteration over a 10 year period. Thirty-five of the patients presented with recurrent disease. Many patients with recurrent disease underwent prior Mohs surgery, and 13 patients received neoadjuvant radiation. Several additional resections were necessary in the study group. We hypothesized that additional resection requirements, disturbed vision, erosion of bone on pre-operative imaging, preoperative pain, and positive final margins will predict worse prognosis. Utilizing univariate analysis, multiple potential prognostic factors were examined. It was determined that erosion of bone on pre-operative imaging (p=.003), positive final margins (p=.001), eye discharge at presentation (p=.045), and additional resection requirements beyond orbital exenteration (p=.043) all conferred a worse prognosis. The 5 year overall survival was 74% and the 5 year disease free survival was 56%. Patient follow-up revealed that recurrences were most common in the first 24 months after surgery.

POSTER #39: CHANGING TRENDS OF SPEECH OUTCOMES AFTER TOTAL LARYNGECTOMY IN THE 21ST CENTURY. Francesca Raffa, Seo Moon, Rosemary Ojo, Mario A. Landera, Donald T. Weed, Zoukaa Sargi, Donna Lundy. Department of Otolaryngology, University of Miami Miller School of Medicine, Miami, FL 33136

Management of laryngeal cancer has evolved significantly in the past few decades. Although total laryngectomy (TL) was once the standard for initial treatment of advanced laryngeal cancer, organ preservation approaches have become more common and TL is now primarily reserved for patients with recurrence or failure after chemoradiation (salvage TL). Tracheoesophageal puncture (TEP) continues to be the gold standard for speech rehabilitation, but the increase in salvage TL raises a question regarding the current TEP success rate. This study described the TEP success rates of patients undergoing TL in the 21st century. Retrospective chart review was performed on 167 patients who underwent TL from June 2000 to February 2012 with a minimum of one year follow-up. Demographics, disease variables, previous treatment, and surgical factors were reviewed. TEP complication rates and speech outcomes were assessed. Patients were considered to have successful speech if they had good/fair intelligibility with rare/occasional repetition and failed speech if they had poor intelligibility requiring frequent repetition. This study showed that there was no significant difference in TEP success rates between primary TL versus salvage TL groups or primary versus secondary TEP. However, the overall speech success rate for TEP (primary or secondary) was lower than historically reported. TEP may continue to be a superior option for speech rehabilitation in patients with TL, including those undergoing salvage TL, but this warrants further evaluation.
POSTER #40: ISOLATED GANGLIONEUROMAS OF THE TONGUE. Kiran Sethi, B.S. and Jason M. Leibowitz, M.D. Department of Otolaryngology, University of Miami Miller School of Medicine, Miami, FL 33101

Ganglioneuromas are generally benign tumors derived from the ganglion cells of the sympathetic and parasympathetic nervous system. We describe the case of a 78-year-old man who presented to our clinic with dysphonia, dysphagia, and biopsy-proven oral ganglioneuroma of the base of the tongue. This rare case of an isolated, tongue ganglioneuromahelps explain how to identify these tumors, the unique complications associated with such neoplasms, and how best to treat such patients. Immunohistochemical staining with S100 of the biopsied tongue mass was positive. MRI showed no lesions in the cerebellum and brainstem, but demonstrated a right-sided enhancing lesion of the tongue. The case was reviewed with the tumor board and the patient was further evaluated by neurology to ensure that there was no central pathology. Surgical excision was deemed to have high morbidity considering that damage to the right hypoglossal nerve was likely irreversible and surgery could further worsen speech and swallow function. The patient decided he could live with his current speech and swallow dysfunction and felt his symptoms had stabilized. He will be followed with biannual clinic visits and annual MRIs. Ganglioneuromas of the tongue are very rare tumors. Given the benign nature of these tumors and high morbidity associated with surgical excision, treatment should be conservative by observing patients biannually in clinic and with annual MRIs to check growth of the tumor to prevent possible mass-effects.

Pediatrics

POSTER #41: ASSESSING THE EFFICACY OF A STANDARD PROTOCOL ON IMPROVING SYMPTOMS OF ENURESIS IN PEDIATRIC PATIENTS. Yassmeen Abdel-Aty BS; Carla Holder, MD; Teresa Johnson, PhD; Lloyd N. Werk, MD, MPH. College of Medicine, University of Central Florida and Nemours Children’s Hospital, Orlando, FL 32827.

Enuresis is the recurrent involuntary passage of urine in an individual who is older than five years of age. This can occur during the daytime or nighttime and is very difficult on parents and embarrassing for the children. Although most children outgrow their enuresis, 1% of nocturnal and 5% to 10% of diurnals will not and many of them will continue to have related complications, sometimes into adulthood. We evaluated the effectiveness of Nemours Children’s Hospital’s Bladder Clinic (BLCC) and the standard protocol that it implements to treat children ages 6 to 18 years old with enuresis. This study is a cohort study completed by analyzing abstracted medical records (retrospective component) and a telephone interview (prospective). This study is outcomes research (Phase T4) investigating the effectiveness of a standard evidence based approach in practice. A standardized protocol was adopted by the Nemours Bladder Control Clinic to treat children between 6 and 18 years of age who are referred to this subspecialty clinic with diurnal and/or nocturnal enuresis. The outcomes of this study will be used to improve the BLCC in order to give the children the best treatment possible.
POSTER #42:
CHANGES IN EDUCATIONAL DEMANDS INCREASE THE PREVALENCE OF ADHD IN YOUNG CHILDREN. Anna Bona, Jeffrey P. Brosco, MD PhD. Department of Pediatrics. University of Miami Miller School of Medicine, Miami, FL 33101.

The prevalence of Attention Deficit Hyperactivity Disorder (ADHD) doubled during the second half of the twentieth century. Factors previously implicated in the increase in prevalence include greater access to pharmaceuticals, loosening of diagnostic criteria, and national legislation that provides benefits to children diagnosed with ADHD. Few scholars have suggested that the number of children with ADHD may truly have increased, as it is unlikely that a genetically based neurocognitive disorder would change in prevalence so rapidly. We hypothesized that increased educational demands on young children may also account for the increase in diagnosis. Most children with ADHD are diagnosed before 8 years of age, and the diagnostic criteria require that a child have difficulty functioning in his or her environment. We used existing longitudinal population studies to document changes since 1970 in the amount of time children spent on studying, reading, and doing homework. Time diaries from 1971 through 1997 showed that the time 3- to 5-year-old children spent on studying increased 44%. 6- to 8-year-old children’s studying time increased 146%, and 9- to 11-year-old children’s studying time increased 9%. Time spent on reading for 3- to 5-year-olds increased from 29 to 84 minutes a week, a 190% increase. From the 1970s to the 1990s, the only age group with a notable and sustained increase in time spent on homework was the 6- to 8-year-olds. The increased educational demands on young children correlate with the increased prevalence of ADHD in the US in the second half of the twentieth century. This research suggests that attempts to improve academic performance at young ages will adversely affect a significant portion of elementary-aged children.

POSTER #43:
EFFECT OF COLON TRANSECTION ON SPONTANEOUS HIGH-AMPLITUDE-PROPAGATING CONTRACTIONS IN CHILDREN. Sharon Wolfson*, Courtney Jacobs*, Carlo Di Lorenzo, Jose Cocjin, Javier Monagas, Paul Hyman. Pediatric Gastroenterology, Hepatology and Nutrition, Children’s Hospital New Orleans, New Orleans, LA, 70118. University of Miami Miller School of Medicine, Miami, FL, 33136*These authors contributed equally to this work

After Hirschsprung’s disease (HD) surgery, many children suffer fecal incontinence caused by increased high amplitude propagating contractions (HAPCs). The aim of this study was to determine whether children with HD have more HAPCs than children with colon transections for reasons other than HD. We reviewed 500 colon manometries. Children (7.6±5.1 yrs; 275 male) with functional constipation (n=237; 7.4±5.0yrs; 126 male) and chronic abdominal pain (n=48; 9.8±5.8yrs; 25 male) served as controls compared to subjects with HD (n=56; 6.9±4.1yrs; 44 male) and colon transection for other reasons (n=24; 6.1±5.8yrs; 12 male). We excluded 139 subjects without HAPCs. We documented HAPCs during 1 h fasting and 1 h postprandial. Results are mean ± SD. During fasting, HD subjects had more HAPCs (2.2±3.4/h) vs. functional constipation (0.8±2.2/h, p=0.0004) and chronic pain (0.5±1.1/h, p=0.001), but not more than colon transection (1.9±3.2/h, p=1.0). HD showed more postprandial HAPCs (4.0±5.4/h) than functional constipation (1.5±2.5/h, p<0.0001) and chronic pain (0.9±1.6/h, p<0.0001), but not more than colon transection (2.4±3.0/h, p=0.6). There were more HAPCs fasting and postprandial after colon transection (1.9 ± 3.2/h and 2.4±3.0/h) than functional constipation (0.8±2.2/h, p=0.3 and 1.5±2.5/h, p=1.0) and chronic pain (0.5±1.1/h, p=1.0 and 0.9±1.6, p=1.0). HD subjects were divided by chief complaint: fecal incontinence or constipation. HD subjects with incontinence (n=23) only had more HAPCs fasting (p=0.01) and post-prandial (p=0.01) than HD subjects with constipation (n=28) only. Increased HAPCs followed colon transection, regardless of cause. HD subjects with incontinence had more HAPCs than subjects with colon transection for other reasons. These results confirm that colon transection for any reason, including HD treatment, increases HAPC numbers. It would be interesting to determine if genetics play a role in the pathophysiology of defecation disorders in HD.
Public Health

POSTER #44:
FEASIBILITY OF FECAL IMMUNOCHEMICAL TESTING (FIT) IN A COMMUNITY SETTING. Vikye Beauport and Dr. Erin Kobetz. Public Health Department, University of Miami School of Medicine, Miami FL, 33136.

Colorectal cancer (CRC) is the second leading cause of cancer-related death in the United States for both men and women. Fecal immunochemical test (FIT), a home based test which looks for blood in the stool has been used as an annual screening tool for colorectal cancer. Previous research has shown that 72% of colorectal cancers diagnosed in residents of Little Haiti were in late stage disease compare to 57% in the state of Florida. If FIT is a culturally-appropriate method, more people in little Haiti will take the test. In this research, we 1) examined the number of consented individuals recruited from Little Haiti between June and July 2013 who returned their FIT; 2) analyzed baseline data to determine whether FIT return was associated with participant socio-demographic characteristics or knowledge of colorectal cancer. 39 eligible participants were recruited from different local venues in Little Haiti from June to July 2013 and consented to FIT. During the process 53 questionnaires were completed to look at different characteristics of participants. If blood was found in the stool, follow up would be needed. The return rate of the FIT in Little Haiti was 82%. Of all screened individuals, less than 50% had prior knowledge of CRC. Participants who return the test were more likely to be married and between the age group of 50-59; they also resided in the US for more than five years. Analysis of participant socio-demographic characteristics and knowledge of colorectal cancer from June to July 2013 is ongoing. This data suggest that FIT is a culturally-appropriate method of colorectal cancer prevention for Haitian immigrants, and likely other racial/ethnic minorities disenfranchised from the formal healthcare systems.

POSTER #45:
ASSOCIATION BETWEEN NUTRIENTS, SPECIFIC FOOD CONSUMPTION AND PANCREATIC CANCER RISK AMONG MIDWEST POPULATION IN US. Jiali Zheng, Baojiang Chen, Simon Sherman. Department of Biostatistics, University of Nebraska Medical Center, Omaha, NE68198, USA.

168 cases from Pancreatic Cancer Collaborative Registry(PCCR)-University of Nebraska Medical Center(UNMC)database and 168 normal controls extracted from Great Plains Health Informatics Database (GPHID)and thyroid cancer collaborative registry (TCCR)who live in Midwest areas in US that matched cases by age (<=50 and >50) and gender were used in our study to identify nutrients,food consumption risk factors for Pancreatic Cancer(PC) development and to explore significant interactions between nutrients,food consumption and other previously confirmed risk factors of PC among US Midwest population. Multiple imputation method and energy adjusted residual model were respectively used to impute missing dietary frequency data and calculate energy-adjusted value for each nutrient variable.Each nutrient and food variable was treated as both continuous and categorical variables in separate multivariate logistic model after adjusting for total energy intake, other food items analyzed in the study and confounding factors for PC. Our study showed that smoking, low education level, and diabetic status were risk factors for PC while one or more cups of wine (white or/and red wine) consumption per day significantly decreased PC risk. We found existence of significant interactions between coffee consumption and the following variables: total energy,cholesterol,saturated fatty acid (SFA), monounsaturated fatty acid (MUFA),polyunsaturated fatty acid (PUFA) and margarine consumption. The odds ratio of developing PC associated with 1 gram increase in aforementioned nutrients and margarine consumption per day except cholesterol was higher among high-levelcoffee consumption group(>=3.5 cups/day)than among low-level coffee consumption group(<3.5 cups/day). Fruit consumption was shown to have a significant protective effect on PC risk (OR=0.91, 95% CI: 0.848-0.978) while caffeinated beverages exerted significantly increased risk on PC (OR=1.18, 95% CI: 1.05-1.32). Linear trend test showed that PC risk decreased linearly when proteins, fruits, and wine consumption levels increased (All P<0.0001). According to the results of our study, people living in Midwest US are suggested to drink less than 3.5 cups of coffee every day, especially for those who have high-calorie or high-fat diet habit and are encouraged to consume more fruit and less fat in order to prevent PC.
POSTER #46:
PERSPECTIVES ON CIGARETTE SMOKING FROM LATINO SMOKERS LIVING WITH HIV.
Alexandra C. Bicki1,2 and Cassandra A. Stanton1,3,1.Cancer Prevention and Control Program, Georgetown University Medical Center, Washington, DC 20007; 2University of Miami Miller School of Medicine, Miami, FL 33136; 3 Schroeder Institute for Tobacco Research and Policy Studies, American Legacy Foundation, Washington, DC 20036

The shift toward treating the human immunodeficiency virus (HIV) as a chronic illness has made it important for people living with HIV (PLWH) to manage comorbidities to improve quality of life. Over half of PLWH in the US smoke cigarettes. Latinos are not only disproportionately affected by HIV as compared to other ethnic groups, but also express smoking behaviors that vary by subgroup characteristics. In preparation for a randomized clinical trial comparing a culturally-tailored cessation intervention to standard care, focus groups were conducted among 27 Latino smokers living with HIV (26 of Puerto Rican descent, 52% female, age range 28-53 years). Two facilitators used a pre-determined agenda to conduct six mixed-gender focus groups in English and/or Spanish. Session transcripts were qualitatively coded with NVivo software for themes related to smoking triggers, motivators to quit, and preferences regarding ideal intervention design. Stress and anxiety were the most and second-most commonly cited smoking triggers, respectively (more than half of participants). Stress related to uncertainty about disease progression was the most common HIV-related theme. Thus, many participants believed discussing emotional management strategies would be important in an intervention. Over half of participants cited health concerns as their primary motivation to quit and were amenable to the idea of “health tests” (e.g., carbon monoxide testing) that could demonstrate how smoking had affected their health. Prevalent themes of willpower and individualism may help explain why participants were not interested in the idea of bringing a social-support “buddy” to intervention sessions. Approximately two-thirds of respondents expressed interest in nicotine replacement therapy patches (but not gum), largely based on past personal quit attempts. Three-quarters of respondents were interested in group-style, mixed-ethnicity counseling sessions. Participants were interested in the idea of speaking with a health educator; being an ex-smoker was considered a more important characteristic than the educator’s ethnicity. Although generalizability of results to other ethnic subgroups is low, results may help healthcare providers understand attitudes toward cessation among Latino smokers living with HIV and how best to reach this diverse group. Themes highlighted here will be considered while designing a smoking cessation intervention for this population.

POSTER #47:
LEPTIN: AN OBESITY BIOMARKER IN PRE-MENOPAUSAL VS. POST-MENOPAUSAL WOMEN.
Paige Deichmann and Larry Webber. School of Public Health and Tropical Medicine, Tulane University, New Orleans, LA, 70112.

Leptin is a protein hormone that induces satiety and regulates energy expenditure. It is secreted by adipose tissue and binds to receptors in the hypothalamus. BMI is a strong predictor of serum leptin levels in both males and females; however, serum leptin levels are consistently higher in females as compared to males, regardless of BMI. Leptin is also involved in reproductive function in females and serum leptin levels have been shown to increase with the onset of menarche. Estrogen may stimulate leptin synthesis. The objective of this retrospective data analysis was to test the hypothesis that post-menopausal females will have lower fasting serum leptin levels than pre-menopausal females, which would manifest through an inverse relationship between leptin and age. SPSS Statistics Software was used to analyze a sample of 3197 female participants ranging in age from 20 to 89, obtained from an existing dataset, The NHANES III Household Adult Questionnaire Data File. Descriptive statistics were obtained and Pearson product moment correlation coefficients were estimated to determine the relationship between fasting serum leptin levels, age, and BMI. Next, the dataset was stratified by age groups and analyzed. The descriptive statistics of the entire sample revealed mean age=46.1 years, mean BMI=26.6 kg/m², and mean leptin=17.9 ng/mL. This data was consistent with findings in the literature review. As expected, there was a positive correlation between leptin and BMI (r=0.673). There was no significant correlation between leptin and age (r=0.087). The average age of menopause in American females is 51. The mean leptin level of the 40-49 year old age group (n=525) was 19.6 ng/mL, while the mean leptin level of the 50-59 year old age group (n=391) was 19.1 ng/mL. From this study, it can be concluded that there was no significant change in leptin level as a direct result of change in age in our sample of females. Further research is needed to investigate the complex relationship between estrogen and leptin.
Surgery

**POSTER #48:**
**SURGEON-PERFORMED ULTRASOUND ACCURACY OF ABNORMAL PARATHYROID GLAND LOCALIZATION YOUNGER PATIENTS WITH SPORADIC PRIMARY HYPERPARATHYROIDISM.**

Surgeon-performed ultrasound (SUS) is commonly used for preoperative parathyroid localization for targeted parathyroidectomy (PTX) with intraoperative parathormone monitoring (IPM) in patients with sporadic primary hyperparathyroidism (SPHPT). A retrospective review of prospectively collected data of 453 patients who underwent targeted PTX guided by IPM or SUS was performed. Patients with confirmation of elevated calcium and PTH levels, preoperative SUS and ≥6 month postoperative follow up were stratified into younger (≤50, n=110) and older (>50, n=343) age groups. SUS accuracy was determined by localization of all abnormal parathyroid glands intraoperatively verified by IPM that resulted in operative success. Operative success was defined as eucalcemia for ≥6 months after PTX and operative failure as elevated calcium and PTH levels within 6 months of PTX. Among the 453 patients, SUS localization of a single abnormal parathyroid gland was more accurate in patients ≤50 years compared to patients >50 years old (81% vs. 70%, respectively; P=0.03). Univariate analysis of patients ≤50 years indicated SUS accuracy was significantly associated with preoperative PTH levels ≥175 pg/ml (91% vs. 75%, P=0.04) as well as the presence of an inferiorly located abnormal gland (88% vs. 69%, P=0.02) compared to patients ≤50 years. Multivariate analysis of both combined predictors within the younger group had significantly higher SUS accuracy compared to members of the same cohort with ≥1 predictors (97% vs. 75%, P=0.01). Combination of all 3 predictors yielded comparable operative success rates (97% vs. 97%, P=0.81) between both age groups at 25 months follow-up. These findings suggest that younger age, elevated preoperative PTH levels, and localization of an inferior parathyroid gland are significant predictors of SUS accuracy in SPHPT caused by a single abnormal parathyroid gland, and may mitigate the further use of additional localization studies in such patients.

**POSTER #49:**
**LAPAROSCOPIC ANTRECTOMY: A SAFE AND DEFINITIVE TREATMENT IN MANAGING TYPE 1 GASTRIC CARCINOIDS.**
Hillary E. Jenny, BS, Kenji Fujitani, BA, Sapna Rustagi, MD, Richard R.P. Warner, MD, Celia M. Divino, MD FACS. Department of Surgery, Icahn School of Medicine at Mount Sinai, New York, NY 10029.

Type 1 gastric carcinoids (T1GC) develop due to excess gastrin production, which causes hyperplasia of enterochromaffin cells (ECL), which may then progress to tumor. Various T1GC treatments exist, including esophagogastroduodenoscopy (EGD) observation, polypectomy, and antrectomy, but studies comparing treatment outcomes have been limited. A retrospective review of 52 T1GC patients (ages 30-88; 75% female) who presented to the Mount Sinai Medical Center between 2004-2012 was conducted. All patients underwent one or more of the following procedures: EGD surveillance and/or polypectomy, and antrectomy. Patient demographics, surgical procedures, pathologic findings, recurrence, and outcomes were reviewed. All statistical analyses were performed using SPSS v20 software. Of the 52 patients, 38.5% received laparoscopic antrectomy, 30.75% received EGD surveillance, and 30.75% received EGD surveillance with polypectomy. Morbidity and mortality following antrectomy was 11% and 0% respectively. The two post-operative complications included retained antrum and respiratory decompensation requiring intubation with no long-term sequelae. Average number of total EGDs per antrectomy patient was 1.85, compared to 2.88 for non-antrectomy patients. The number of EGDs needed post-antrectomy (1.35) was statistically significantly lower than the total number of EGDs needed for polypectomy or EGD surveillance treatments (p-value=0.019). In addition, antrectomy patients had decreased risk of recurrence compared to polypectomy patients (10% vs. 44%, p=0.049), despite having a significantly longer average follow-up time than nonantrectomy patients (74.1 vs. 45.6 months, p=0.009). The average number of EGDs needed for post-antrectomy patients is lower than for those treated with polypectomy or EGD surveillance. Antrectomy represents a safe way to effectively treat T1GC with lower risk of recurrence and less post-intervention monitoring necessary. Patients who elected for antrectomy often cited wishing to avoid further treatment complications as a reason for their decision; antrectomies allow patients to avoid the side effects of medication like octreotide and the pain and discomfort of repeated EGD surveillance.
Urology

POSTER #50:
THE ASSOCIATION BETWEEN SOCIOECONOMIC STATUS AND RENAL CANCER PRESENTATION. Matthew R Danzig, James M McKiernan, Ketan K Badani. Dept of Urology, Columbia University Medical Center, New York, NY, 10032.

Recent research indicates that most renal cancers in the United States are now diagnosed incidentally on abdominal imaging. Such tumors present with smaller size and more localized stage than symptomatic tumors. Discrepant access to and usage of health care resources may lead to reduced incidental detection in socioeconomically disadvantaged counties. We sought to determine if socioeconomic indicators predict the size and stage of renal cancers, as well as overall survival. The NCIs Survival, Epidemiology, and End-Results registries were queried for patients diagnosed with renal cancers between 2001 and 2010. Presentation, survival, and county-level socioeconomic data for these patients were obtained. Cancers with stage T0 and with histologic codes inconsistent with renal cell carcinoma were excluded. A socioeconomic index (SEI) was created based on median income, percentage of the population in poverty, and percentage of high school graduates. Regression analyses were used to assess the impact of a patient’s SEI score on cancer presentation and survival while controlling for age, gender, race, and tumor grade. 89,632 renal cancer cases were identified. On multiple linear regression SEI was a significant predictor of larger tumor size (p<0.001). On multinomial regression SEI was a significant predictor of T stage (T2 vs. T1, p = 0.008. T3 vs. T1, p = 0.001. T4 vs. T1, p = 0.002). On binary logistic regression SEI was a significant predictor of positive nodal status (p = 0.045), but was not predictive of metastasis at diagnosis (p=0.132). On multiple linear regression, SEI was a significant predictor of fewer months of survival when controlling for year of diagnosis, gender, race, grade, age, nodal status, and metastasis at diagnosis (p<0.001). These findings suggest that lower socioeconomic status may be correlated with cancers that are more advanced at diagnosis, leading to poorer outcomes in these patients. Higher levels of access and more frequent medical care for patients in higher SEI counties may serve as a de facto screening system for kidney cancer.

POSTER #51:
UTILIZATION OF PSA TESTING AND PROSTATE BIOPSY OUTSIDE OF AUA RECOMMENDED AGE GROUPS. Rajiv Jayadevan, Kristian Stensland, Michael Leapman MD, Gregory Baldwin, Martin Casey, Simon Hall MD, Michael Palese MD. Urology Department, Icahn School of Medicine at Mount Sinai, New York, NY 10029

The incidence of prostate cancer (PCa) increases with age; however, the usefulness of PSA-based screening appears limited to younger men with favorable life expectancy. Hazards to mortality limit the ability to offer definitive treatment, and detection of non-lethal tumors may expose aging or unfit patients to unnecessary toxicities. Healthy older patients may undergo testing, though the value of screening beyond a certain age is controversial. We evaluated the rates of PSA tests and prostate biopsy (PBx) in patients who may not be optimally suited for PCa screening according to AUA recommendations. An institutional data warehouse was queried for all men with PSA test results from 7/1/2005 to 6/30/2013. Data collected included the presence of comorbidities at the time of PSA, as well as progression to PBx. Statistical analysis assessed the associations between clinical variables, PSA testing and PBx among age groups. 27,078 men underwent serum PSA tests, of whom 7,895 (29.2%) were ≥70 years old, and 5,585 (20.6%) had a serious comorbidity including congestive heart failure (CHF), chronic kidney disease (CKD) or end-stage renal disease (ESRD). Of those ≥70 years old who had PSA screens, 1306 (17%) had CHF, 1551 (20%) had CKD, and 409 (5%) had ESRD. Of 790 men (2.8%) who went on to have PBx, 299 (38%) were ≥70 years old, and 111 (14.1%) had a serious comorbidity (CHF, CKD, ESRD). On multivariate analysis, CHF and ESRD decreased the likelihood of PBx (OR 0.634 and 0.435 respectively, p<0.001, 95% CI) while the presence of DM and CKD had no effect on PBx. Many patients with multiple comorbidities still underwent PSA screening and PBx. Conclusions: PSA testing and prostate biopsies were commonly performed in men outside the current age range (55 to 69 years) according to AUA recommendations. In the midst of controversy surrounding over-detection and overtreatment of PCa, clinicians must be more selective in identifying patients in whom a PSA test and PBx is necessary and appropriate.
INDEX OF PRESENTERS

<table>
<thead>
<tr>
<th>Presenter</th>
<th>Index</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdel-Aty, Yassmeen</td>
<td>60</td>
<td>47</td>
</tr>
<tr>
<td>Aribindi, Katayini</td>
<td>28</td>
<td>58</td>
</tr>
<tr>
<td>Barrios, Mirelys</td>
<td>32</td>
<td>36</td>
</tr>
<tr>
<td>Beauport, Vikye</td>
<td>62</td>
<td>30</td>
</tr>
<tr>
<td>Beck, David</td>
<td>48</td>
<td>47</td>
</tr>
<tr>
<td>Bicki, Alexandra</td>
<td>63</td>
<td>38</td>
</tr>
<tr>
<td>Bishop, Brian</td>
<td>64</td>
<td>46</td>
</tr>
<tr>
<td>Bloom, Romi.docx</td>
<td>25</td>
<td>40</td>
</tr>
<tr>
<td>Bokman, Christine</td>
<td>54</td>
<td>34</td>
</tr>
<tr>
<td>Bona, Anna</td>
<td>61</td>
<td>35</td>
</tr>
<tr>
<td>Botros, Diana</td>
<td>26</td>
<td>29</td>
</tr>
<tr>
<td>Cannady, Darryl</td>
<td>30, 52</td>
<td>55</td>
</tr>
<tr>
<td>Cavallin, Lucas</td>
<td>52</td>
<td>42</td>
</tr>
<tr>
<td>Chen, Caroline</td>
<td>28</td>
<td>44</td>
</tr>
<tr>
<td>Chhadva, Priyanka</td>
<td>56</td>
<td>59</td>
</tr>
<tr>
<td>Cohan, Charles</td>
<td>50</td>
<td>37</td>
</tr>
<tr>
<td>Cohen, Devon</td>
<td>43</td>
<td>38</td>
</tr>
<tr>
<td>Cox, Audrey</td>
<td>23</td>
<td>41</td>
</tr>
<tr>
<td>Danzig, Matthew</td>
<td>66</td>
<td>41</td>
</tr>
<tr>
<td>Dauer, Ryan</td>
<td>36</td>
<td>51</td>
</tr>
<tr>
<td>Deichmann, Paige</td>
<td>63</td>
<td>59</td>
</tr>
<tr>
<td>Epstein, Aliza</td>
<td>29</td>
<td>49</td>
</tr>
<tr>
<td>Gans, Jared</td>
<td>35</td>
<td>55</td>
</tr>
<tr>
<td>Genkin, Inna</td>
<td>48</td>
<td>57</td>
</tr>
<tr>
<td>Gissy, Jacob</td>
<td>50</td>
<td>24</td>
</tr>
<tr>
<td>Han, Xiaqing</td>
<td>49</td>
<td>31</td>
</tr>
<tr>
<td>He, Jane</td>
<td>31</td>
<td>60</td>
</tr>
<tr>
<td>Ho, Phi</td>
<td>58</td>
<td>24</td>
</tr>
<tr>
<td>Huang, Laura</td>
<td>53</td>
<td>25</td>
</tr>
<tr>
<td>Jayadevan, Rajiv</td>
<td>37, 65</td>
<td>46</td>
</tr>
<tr>
<td>Jenny, Hillary</td>
<td>64</td>
<td>53</td>
</tr>
<tr>
<td>Joseph, Walter</td>
<td>34</td>
<td>57</td>
</tr>
<tr>
<td>Kachan, Diana</td>
<td>26</td>
<td>51</td>
</tr>
<tr>
<td>Khanna, Krishn</td>
<td>57</td>
<td>61</td>
</tr>
<tr>
<td>Klar, Natalie</td>
<td>40</td>
<td>54</td>
</tr>
<tr>
<td>Kouillas, Yiannis</td>
<td>23</td>
<td>42</td>
</tr>
<tr>
<td>Kreafl, Johanna</td>
<td>32</td>
<td>44</td>
</tr>
<tr>
<td>Kviatkovsky, Milla</td>
<td>45</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td></td>
<td>62</td>
</tr>
<tr>
<td>Lartey, Lattoya</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee, Andrew</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Libreros, Stephania</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lindley, Linsey</td>
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<tr>
<td>Lopez, Darlah</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maddalo, Scott</td>
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<tr>
<td>Marinacci, Lucas</td>
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<tr>
<td>Meng, Xiaosong</td>
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<tr>
<td>Miller, Kyle</td>
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<td>Morse, Justin</td>
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<td>Nguyen, Huy</td>
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<td>Ortiz, Angelica</td>
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<td>Parker, Joshua</td>
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<td>Patel, Anush</td>
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<td>Patel, Shailee</td>
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<td>Pedigo, Christopher</td>
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<td>Perez, Enmanuel</td>
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<td>Raffa, Francesca</td>
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<td>Ramo, Kasmir</td>
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<td>Sastry, Ananth</td>
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<td>Sayari, Arash</td>
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<td>Schneider, Samantha</td>
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<td></td>
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<tr>
<td>Schoor, Michael</td>
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<tr>
<td>Sethi, Kiran</td>
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<td></td>
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<tr>
<td>Shah, Sunali</td>
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<td>Slater, Nathaniel</td>
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<td>Stone, Melissa</td>
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<tr>
<td>Syeda, Sarah</td>
<td></td>
<td></td>
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<tr>
<td>Venincasa, Vincent</td>
<td></td>
<td></td>
</tr>
<tr>
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