Program and Abstracts
February 20-23, 2018

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

Katherine Masih, Editor
Anneliese Vitha, Editor

Eastern-Atlantic Student Research Forum
University of Miami Miller School of Medicine—P.O. Box 016960—Miami, FL 33101

http://research.med.miami.edu/esrf
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WELCOME FROM THE DIRECTORS

To all ESRF Participants:

It is our distinguished pleasure to welcome you to the 44th Annual Eastern-Atlantic Student Research Forum. We look back and reflect upon 44 years of providing an opportunity for medical students, graduate students, interns and residents to present their research before a group of peers and esteemed faculties. We hope that ESRF continues to promote the development of our future physician-scientists and researchers.

We are honored to host award winning Dr. David A. Hafler, a neurologist and clinical scientist with a research interest in the mechanism of multiple sclerosis, who is a co-founder of the International MS Genetic Consortium, co-founder of the Federation of Clinical Immunology Societies, and leads the NIH Autoimmunity Prevention Center Grant at Yale. Dr. Hafler received the University of Miami Annual Distinguished Alumni Award in 2010. He was also part of the founding group of ESRF and was the organizer of the 1978 Forum. He will be our keynote speaker this year, speaking of his experiences, challenges, and research in MS.

In addition to our student presentations throughout the forum, we will also have wonderful educational opportunities for our participants. We have a workshop entitled, “Career Development in Research: A Path or a Journey,” hosted by Dr. Jaime Rubin, who made landmark scientific history in describing the first identification and characterization of a human DNA repair gene in her PhD thesis first published in Nature. Dr. Rubin has had great experience with teaching and mentoring junior investigators, and educating others on misconduct in research and issues concerning publication, authorship, and peer review. We look forward to hearing her expertise in furthering young physicians’ and aspiring researchers’ career aspirations.

This year, our plenary session focuses on the concept of “Scientific Funding and Public Perception,” featuring a distinguished and interdisciplinary panel of guest speakers including Dr. Jaime Rubin (Vice Chair for Investigator Development in Columbia University), Dr. Claes Wahlestedt (Director of Therapeutic Innovation at UM), Dr. Ralph Sacco (Chair of Neurology at UM), Ms. Cindy Lerner (JD, Past Mayor of Pinecrest, Miami Climate Alliance), and Dr. Philip Stoddard (Mayor of South Miami, and Professor of Biology in FIU, Miami Climate Alliance).

We will conclude the conference with Dr. Dalton Dietrich, Scientific Director of The Miami Project and Kinetics Concepts Distinguished Chair in Neurosurgery, as our banquet address speaker. Dr. Dietrich’s work focuses on cellular and molecular injury mechanisms underlying various neurological disorders and neuroprotection in terms of correlating temperature of the brain and spinal cord with neuronal death and injury. He will speak of his latest research in using novel cellular and drug treatments to promote reparative processes and functional recovery after brain and spinal cord injury.

It is truly amazing that ESRF has reached its 44th anniversary, but it would not be possible without all of the wonderful presenters, committee chairs, faculty advisors, support staff and student volunteers 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 successful. Ms. Perez is a valued advocate of student research and without her, there would be no ESRF. It has been a wonderful 43 years, and we look forward to the continued success of ESRF in the future.

Sincerely,

Sandy Jiang
ESRF Co-Director

Owen Tan
ESRF Co-Director

Sophia Liu
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 2018 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 44th 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, MD/PhD 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,

Edward Abraham, M.D.
Executive Vice President for Health Affairs
CEO, UHealth
Dean and Chief Academic Officer, Miller School of Medicine
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 2017, U.S. News & World Report listed Bascom Palmer Eye Institute as the number one hospital in the country for ophthalmology for the fourteenth year in a row. Two other UM Miller School of Medicine specialties were also listed among the nation’s best: ear, nose and throat 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. This includes the UM Life Science and Technology Park, which recently opened and will continue to grow to add an additional two million square feet of space adjacent to the medical campus. The UM Life Science and Technology 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 fourteen 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 provides a program that permits spinal cord injured men to father children.

- 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 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.
## PROGRAM SCHEDULE

### Wednesday, February 21, 2018

<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>Registration for Non-UM Students</td>
<td>BPEI, Copper Spoon</td>
</tr>
<tr>
<td>7:00 AM – 8:00 AM</td>
<td>Breakfast for all presenters</td>
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<tr>
<td>8:15 AM – 8:45 AM</td>
<td>Welcome Address</td>
<td>BPEI, Berrocal 2nd Floor Auditorium</td>
</tr>
<tr>
<td>Carl I. Schulman, MD, MSPH, PhD</td>
<td>Executive Dean for Research</td>
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<tr>
<td>9:00 AM – 11:15 AM</td>
<td>Oral Presentations I</td>
<td></td>
</tr>
<tr>
<td>11:30 AM – 12:30 PM</td>
<td>Career Development Workshop</td>
<td>MCCD, 8th Floor Auditorium</td>
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<tr>
<td>Jaime S. Rubin, PhD</td>
<td>Vice Chair for Investigator Development, Department of Medicine</td>
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<tr>
<td>12:30 PM – 1:30 PM</td>
<td>Lunch</td>
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<tr>
<td>1:45 PM – 4:30 PM</td>
<td>Oral Presentations II</td>
<td>BPEI, Berrocal 2nd Floor Auditorium</td>
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### Thursday, February 22, 2018

<table>
<thead>
<tr>
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<th>Event</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00 AM – 9:00 AM</td>
<td>Breakfast</td>
<td>BPEI, Copper Spoon</td>
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<tr>
<td>9:15 AM – 11:30 AM</td>
<td>Oral Presentations III</td>
<td>BPEI, Berrocal 2nd Floor Auditorium</td>
</tr>
<tr>
<td>12:00 PM – 1:00 PM</td>
<td>Keynote Address</td>
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<tr>
<td><strong>David A. Hafler, MD, FANA</strong></td>
<td>William S. and Lois Stiles Edgerly Professor of Neurology and Professor of Immunobiology; Chair, Department of Neurology; Neurologist-in-Chief, Yale New Haven Hospital</td>
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<tr>
<td>1:00 PM – 2:00 PM</td>
<td>Keynote Luncheon</td>
<td>BPEI, Copper Spoon</td>
</tr>
<tr>
<td>2:05 PM – 3:00 PM</td>
<td>Plenary Session</td>
<td>BPEI, Berrocal 2nd Floor Auditorium</td>
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<tr>
<td>3:00 PM – 5:45 PM</td>
<td>Oral Presentations IV</td>
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### Friday, February 23, 2018

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<th>Location</th>
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<tr>
<td>8:00 AM – 8:45 AM</td>
<td>Breakfast</td>
<td>LPLC, Sidewalk Area</td>
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<tr>
<td>9:00 AM – 12:00 PM</td>
<td>Poster Session</td>
<td></td>
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<tr>
<td>12:30 PM – 1:15 PM</td>
<td>Lunch</td>
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<tr>
<td>1:30 PM – 2:30 PM</td>
<td>Distinguished Lecturer</td>
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<tr>
<td><strong>James DeGregori, PhD</strong></td>
<td>Deputy Director, University of Colorado Cancer Center</td>
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<tr>
<td>4:00 PM – 7:00 PM</td>
<td>Awards Banquet Address</td>
<td>Jackson Memorial Hospital</td>
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<tr>
<td><strong>W. Dalton Dietrich, III, PhD</strong></td>
<td>Scientific Director, The Miami Project to Cure Paralysis, University of Miami Miller School of Medicine</td>
<td>Diagnostic Trauma Center, DTC #263</td>
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1611 NW 12 Avenue
Miami, FL 33136
WELCOME ADDRESS

Carl I. Schulman MD, PhD, MSPH, FACS

Professor, Department of Surgery
Executive Dean for Research
Eunice Bernhard Endowed Chair in Burns
Director of the William Lehman Injury Research Center
University of Miami Miller School of Medicine

Dr. Carl Schulman is a Professor of Surgery and the Executive Dean for Research of the University of Miami Miller School of Medicine. He is also the Eunice Bernhard Endowed Chair in Burns and Director of the William Lehman Injury Research Center.

Dr. Schulman has a long and distinguished history of service to the Medical School and the community. He earned his medical degree from the University of South Florida College of Medicine and completed training in general surgery and received additional training in trauma and surgical critical care at the University of Miami/Jackson Memorial Medical Center. He also completed a Master’s of Science in Public Health and PhD in Epidemiology at the University of Miami School of Medicine. With research interests focusing on the epidemiology of burns and trauma, Dr. Schulman has been awarded grants from The Robert Wood Johnson Foundation, the Department of Defense and the CDC among others. He has authored over 140 peer-reviewed publications and is a reviewer for numerous journals.

Dr. Schulman has also been involved in undergraduate and graduate medical education and served as the Associate Program Director for the General Surgery Residency Program. He has mentored many surgical residents and graduate students in his clinical laboratory including advisory roles on their MPH and PhD thesis and dissertation work. He is also the director of a federally funded international Telemedicine Program and leads the medical content creation team for the Defense Health Agency.

Dr. Schulman has been involved in motor vehicle crash-related research for his entire career and is currently the Principal Investigator for the BMW Crash Research Program at the University of Miami. He serves on the Board of Directors of the Association for the Advancement of Automotive Medicine (AAAM) and is the past Chair of the Scientific Program Committee. Dr. Schulman was recently elected to the Burn Science Advisory Panel of the American Burn Association (ABA) - this panel oversees all ABA-affiliated clinical trials, functioning to guide and support all aspects of the clinical research enterprise. He is the Principal Investigator on a DOD funded Phase 1 and 2 human clinical trial, which is the first trial to look at the use of allogeneic mesenchymal stem cells in the treatment of deep second degree burns.

Dr. Schulman has served on numerous University of Miami faculty and search committees, and was one of the inaugural recipients of the Miller School's Citizenship Award. He was elected by the Faculty and served as first Vice-Speaker of the Medical School Faculty Council from 2008-2013 and then as Speaker from 2013 until 2017. He is also a member of Iron Arrow, the highest honor attained at the University of Miami.
KEYNOTE SPEAKER

David A. Hafler, M.D., FANA

William S. and Lois Stiles Edgerly Professor of Neurology and Immunobiology
Chairman, Department of Neurology
Yale School of Medicine
Neurologist-in-Chief, Yale New Haven Hospital

How to Cure a Disease, or Never Give In,
Never Give In. Never, never, never…

Dr. Hafler is the William S. and Lois Stiles Edgerly Professor and Chairman Department of Neurology and Professor or Immunobiology, Yale School of Medicine, and is the Neurologist-in-Chief of the Yale-New Haven Hospital. He is among the most highly cited living Neurologist. He graduated magna cum laude in 1974 from Emory University with combined B.S. and M.Sc. degrees in biochemistry, and the University of Miami School of Medicine in 1978. He then completed his internship in internal medicine at Johns Hopkins followed by a neurology residency at Cornell Medical Center-New York Hospital in New York. Dr. Hafler was trained in immunology at the Rockefeller University and then at Harvard where he joined the faculty in 1984 and later became the Breakstone Professorship of Neurology at Harvard and was a founding Associated Member of the Broad Institute at MIT. In 2009, he moved to Yale as the Chair of the Department of Neurology. Dr. Hafler is a clinical scientist with a research interest in the mechanism of multiple sclerosis with over 370 publications in the field of MS, autoimmunity and immunology. He is a co-founder of the International MS Genetic Consortium a group that identified the genes causing MS. Dr. Hafler has been elected to membership in the American Society of Clinical Investigation, the Alpha Omega Society, and was a Weaver Scholar of the NMSS. He has served as a member of the editorial boards for Journal of Clinical Investigation and the Journal of Experimental Medicine, and is co-founder of the Federation of Clinical Immunology Societies and leads the NIH Autoimmunity Prevention Center Grant at Yale. Dr. Hafler was a Jacob Javits Merit Award Recipient from the NIH and has won many awards including 2010 Dystel Prize for MS research from the American Academy of Neurology, the Raymond Adams Prize in 2015 from the American Neurologic Association and the 2016 Frontier Lecturer at the AAN. Dr. Hafler received the University of Miami Annual Distinguished Alumni Award in 2010, but perhaps of greatest note, he was part of the founding group of the Eastern Student Research Forum and was the organizer of the 1978 Forum.
W. Dalton Dietrich Ph.D.

The Miami Project to Cure Paralysis, Scientific Director, Professor, Neurosurgery, Neurology, Biomedical Engineering and Cell Biology

New Insights into the Pathophysiology and Treatment of Brain and Spinal Cord Injury

Dr. Dalton Dietrich received his Ph.D. in Anatomy from the Medical College of Virginia in 1979 and completed a postdoctoral fellowship in the Department of Pharmacology at Washington University, St. Louis, MO, 1981. In 1981, Dr. Dietrich joined the Department of Neurology at the University of Miami, with a joint appointment in Cell Biology and Anatomy, and in 1993 attained the rank of Professor. Dr. Dietrich served as Vice-Chairman for Basic Science in the Department of Neurology from 1995 to 1997, when he accepted the position of Scientific Director of The Miami Project to Cure Paralysis. Dr. Dietrich also serves as the Senior Associate Dean for Discovery Science at the University of Miami Miller School of Medicine.

Dr. Dietrich’s laboratory is focused on clarifying the pathophysiology of brain and spinal cord injury with the ultimate goal of developing new therapies to protect and enhance recovery of function. Over the last 35 years, Dr. Dietrich and colleagues have studied the cellular and molecular injury mechanism underlying various neurological disorders including stroke, cardiac arrest, traumatic brain and spinal cord injury. In terms of neuroprotection, he and his colleagues provided the initial preclinical data indicating that small differences in the temperature of the brain and spinal cord critically determine whether neurons die or not following neurological injury. These preclinical studies of therapeutic hypothermia have now been successfully translated to the clinical arena, where patients are being cooled following out-of-hospital cardiac arrest, strokes, traumatic brain injury, and more recently spinal cord injury. Most recently, Dr. Dietrich and colleagues have investigated the importance of abnormal inflammasome activation in the brain and spinal cord after injury. These studies have uncovered a new therapeutic target for modifying the immediate immune response to injury. In addition to these studies, Dr. Dietrich and colleagues are using novel cellular and drug treatments to promote reparative process and functional recovery after brain and SCI. He is currently the Sponsor of a first-in-man FDA approved clinical trial testing the safety of human Schwann Cell transplants in people with severe subacute SCI.
James DeGregori, PhD

Courtenay C. and Lucy Patten Davis Endowed Chair in Lung Cancer Research Professor, Department of Biochemistry and Molecular Genetics Deputy Director, University of Colorado Cancer Center University of Colorado Anschutz Medical Campus

The Ecology of Cancer: How Changes in Tissue Microenvironments Drive Cancer Evolution

Dr. DeGregori received a B.A. in Microbiology from the University of Texas at Austin in 1987 and a Ph.D. in Biology from the Massachusetts Institute of Technology in Cambridge in 1993. From 1993 to 1997, as a postdoctoral fellow at Duke University Medical Center, he studied how the E2F transcription factor family controls transcription and cell fate decisions. Since 1997 he has been a faculty member in the Department of Biochemistry and Molecular Genetics at the University of Colorado School of Medicine.

Studies to better understand the conditions that foster the initiation of leukemias and lung cancers are a major thrust of the lab. The DeGregori lab has developed an evolutionary based model for cancer development, called Adaptive Oncogenesis. The lab is currently exploring how reduced stem cell fitness resulting from carcinogen exposure (such as smoking) or aging can select for adaptive cancer-causing mutations and thereby promote cancer. The focus is on how changes to tissue microenvironments with aging or carcinogenic exposures leads to selection for cells with oncogenic mutations adaptive to this new environment. Additionally, the lab seeks to understand how tumor suppression has evolved in animals, with the ultimate goal of maximizing reproductive success. Other studies in the lab are geared towards the development of novel therapeutic strategies to treat leukemias and non-small lung cancers. The lab performs genome-wide screens to identify genes whose inhibition will synergize with current targeted therapeutics to eliminate cancer cells. These studies could lead to discovery of novel combination therapies that will more effectively treat or possibly even cure common malignancies.
Jaime S. Rubin, Ph.D. received a B.S. in physics *sigma pi sigma* in 1977 from The Cooper Union for the Advancement of Science and Art (New York, N.Y.). She then received the M.Sc. and Ph.D. degrees from the Ontario Cancer Institute/University of Toronto (Canada) 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 Vice Chair for Investigator Development in the Department of Medicine where she also holds a faculty position. All of these positions have allowed for the teaching and mentoring of junior investigators, including medical, public health, nursing, and graduate students, postdoctoral fellows, and assistant professors. In 1995, she founded and continues as Director of the graduate-level course "Funding for Research Activities: Basic Issues in Obtaining Support" (http://grantscourse.columbia.edu). She served as the Associate Program Director for the Doris Duke Clinical Research Fellowship Program, having helped initiate this program at Columbia in 2000. In 1994, she founded and continues as one of the Directors of the Medical Center's course on "Responsible Conduct of Research and Related Policy Issues" (http://researchethics.cumc.columbia.edu/), lecturing on misconduct in research as well as on issues concerning publication, authorship, and peer review. Other career development roles include serving as Associate Director for Career Development on a number of NIH-funded predoctoral and postdoctoral training grants, fellowships, and junior faculty career development awards, as well as an Advisory Board member of Columbia’s Patient-Oriented Research (POR) Master of Science Program and the Clinical and Translational Science Award (Education). She has also given presentations on these and related topics at national conferences and peer institutions.
PLENARY SESSION

Science Funding and General Public Interest

Ralph L. Sacco, MD, MS, is the Chairman of Neurology, Olemberg Family Chair in Neurological Disorders, UMMSM professor of Neurology, Epidemiology, Human Genetics, and Neurosurgery, Executive Director of the Evelyn McKnight Brain Institute, and Chief of the Neurology Service at Jackson Memorial Hospital. A graduate of Cornell University in Bio-electrical Engineering and a cum laude graduate of Boston University School of Medicine, he also holds an MS in Epidemiology from Columbia University, Mailman School of Public Health. He was previously Professor of Neurology, Chief of Stroke and Critical Care Division, and Associate Chairman at Columbia University before taking his current position as Chairman of Neurology at the University of Miami, Miller School of Medicine.

Jaime S. Rubin, Ph.D., received the M.Sc. and Ph.D. degrees from the Ontario Cancer Institute/University of Toronto (Canada). Her Ph.D. thesis, published in the journal, *Nature*, described the first molecular identification and characterization of a human DNA repair gene. 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 Vice Chair for Investigator Development in the Department of Medicine where she also holds a faculty position.

Claes Wahlestedt, M.D., PhD, is the director of the Center for Therapeutic Innovation and associate dean for therapeutic innovations at the University of Miami. Dr. Wahlestedt has a long-standing interest in non-protein-coding RNA (epigenetics) and pioneered various uses of antisense RNA, siRNA and small molecules that target RNA. He spent four years as assistant professor in the Division of Neurobiology at Cornell University Medical College in New York, and was subsequently adjunct professor of biochemistry, and pharmacology and therapeutics at McGill University in Montreal. He also spent more than a decade directing drug discovery and genomics efforts in the pharmaceutical industry for Astra-Zeneca, Pharmacia & Upjohn, and Pharmacia Corporation.
Mayor Philip Stoddard was first elected to office in 2010 and is currently serving his fourth term as Mayor of South Miami. In 2015, Mayor Stoddard was appointed by the White House to the Governance Coordinating Committee of the National Ocean Council, where he developed national policy for sea level rise. In 2016, Mayor Stoddard was named by Politico Magazine on the Politico-50 guide to the “thinkers, doers and visionaries transforming American politics in 2016”. He was named the Green Municipal Official for 2016 by the Florida Green Building Coalition. In addition, he has been a professor of biology at Florida International University since 1992.

Cindy Lerner was elected Mayor of Pinecrest, Florida in November 2008 and was subsequently re-elected for a second four year term in 2012. Throughout her eight year term, Mayor Lerner led the Village in being a leader in sustainable practices, and has been a nationally recognized leader on Climate Change policies. She was invited by the White House to the US-China Climate Leaders Summits in Los Angeles in 2015 and in Beijing in 2016 as a presenter.

Caroline Lewis is the founder and executive director of the CLEO Institute, a non-profit that advances civic engagement on climate issues. She worked for 22 years as a school teacher and principal, then joined the staff of Fairchild Garden, created the Fairchild Challenge, and as Director of Education, expanded programs and partnerships by 800%. In addition, she serves or has served on boards and committees for the National Environmental Education Advisory Council, American Public Garden Association, Miami-Dade Executive Board for Science Curriculum and Instruction, White House Summits on Climate and Energy and on Women & the Environment, and the Conservation Fund’s National Forum on Children and Nature. In 2013, Ms. Lewis was one of twelve individuals, nationally, recognized as White House Climate Resilience Champions of Change.
FACULTY JUDGES

The directors and staff of the 2018 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 presentation:

Monica Alba-Sandoval, MD
Ibolya Edit Andras, MD
Fotios Andreopoulos, PhD
Taghrid Asfar, MD, MSPH
Heidi Bahna, MD
Zinzi Bailey, ScD, MSPH
Andre Barreto Bruno Wilke, PhD
Georgeta Basturea, PhD
Sanjoy Bhattacharya, PhD
Scott Brown, PhD
Nicolas Brozzi, MD
Alberto Caban-Martinez, PhD DO, MPH
Tongyu Cao, PhD
Jose Carugno, MD
Angela Maria C. Rodriguez, MD
Tsung-Han Chou, PhD
Kunjan Dave, PhD
Sapna Deo, PhD
Seth Dodds, MD
Lundy Donna, PhD
Vikas Dudeja, MD
Derek Dykxhoorn, PhD
Ananth Eleswarapu, MD

John Ford, PhD
Irman Forghani, MD
Sophia George, PhD
Mousumi Ghosh, PhD
Ayodele Gomih, PhD, MSPH
Lisa Gwynn, DO
Abigail Hackam, PhD
Victor H. Hernandez, MD
Barry Hudson, PhD
Michael Hughes, MD
Chukwuemeka Ikpeazu, MD, PhD
Ivan Jozic, PhD
Mariano Kanamori, PhD
Sebastian Koch, MD
Ana Leda, PhD
Sandra Lemmon, PhD
Argentina Leon, PhD
John Lew, MD
Matthias Loebe, MD, PhD
Donna Lundy, PhD
Micheline McCarthy, MD, PhD
Carlos Medina, MD
Sandra Merscher, PhD
Charles Mitchell, MD

Mehrdad Nadji, MD
Ozcan Ozdamar, PhD
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ALVING AWARD

BARBARA & CARL ALVING, M.D.

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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ACKNOWLEDGMENTS

The directors and staff of the 2018 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:

Carl Schulman, MD, MSPH, PhD, Dushyantha Jayaweera, MD, and Alex Mechaber, 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 the ESRF is unwavering.
You truly make the ESRF a success year after year.
ORAL PRESENTATIONS I  
FEBRUARY 21, 2018  
9:00 AM – 11:15 AM
PREDICTORS OF UPSTAGING FOR NON-MUSCLE INVASIVE BLADDER CANCER: RESULTS FROM THE NATIONAL CANCER DATABASE

Felix V. Chen, Shuo-Chieh Wu, Mahmoud Alameddine, Chad Ritch, Mark Gonzalgo, Department of Urology, University of Miami Miller School of Medicine, Miami, FL 33136

Introduction: Despite recent advances in detection and management of bladder cancer (BC), accurate staging remains challenging. In this study, we determined clinical parameters for predicting the risk of upstaging from non-muscle invasive bladder cancer (NMIBC) to muscle invasive bladder cancer (MIBC) using the National Cancer Database (NCDB). Methods: A total of 7,091 patients diagnosed with NMIBC (CIS, cTa, or cT1) and underwent radical cystectomy from 2004 to 2014 were identified in the NCDB. Patients with non-urothelial and unknown histology, race/ethnicity, pathologic T or N stage, or patients with prior chemotherapy and/or radiation therapy were excluded. Patients were subcategorized by clinical stage: cTa (n=515), and CIS (n=327), cT1 (n=3,319). Upstaging from NMIBC to MIBC was defined as CIS, cTa, or cT1 to pT2-4. Multivariable logistic regression analysis was performed to identify predictors of pathologic upstaging. Results: A total of 1,403 patients (33.7%) were upstaged from NMIBC to MIBC. Patients with initial cT1 status were more likely to become upstaged compared to patients with cTa or CIS (37.3% vs 20.0% vs 18.7%, respectively). Upstaging was significantly associated with age, clinical stage, tumor size (>3 cm) and type of treatment facility. On multivariate analysis, the strongest predictors of NMIBC upstaging were high grade (2.49, 1.79-3.45) and age >65 (1.49, 1.28-1.74). Interestingly, patients treated at a non-academic facility were more likely to be upstaged after radical cystectomy (1.24, 1.07-1.43). Negative lymphovascular invasion status was the strongest negative predictor of NMIBC upstaging (0.16, 0.12-0.22). Race, immunotherapy history, and Charlson-Deyo score did not predict NMIBC upstaging. Conclusion: We present a large scale analysis assessing parameters that may guide treatment decision-making for NMIBC. Elderly patients, presence of lymphovascular invasion, high tumor grade, stage, and size >3 cm were strong predictors of upstaging from NMIBC to MIBC at the time of radical cystectomy. More aggressive treatment options should potentially be considered for patients with NMIBC who have multiple positive predictors.

NEoadjuvant Versus Adjuvant Chemotherapy for Muscle-Invasive Bladder Cancer

Joshua S. Jue, Maria Camila Velásquez, Luis Felipe Sávio, Mahmoud Alameddine, Tulay Koru-Sengul, Feng Miao, Chad R. Ritch and Mark L. Gonzalgo, Department of Urology, University of Miami Miller School of Medicine, Miami, FL 33101

Introduction: Neoadjuvant (NAC) or adjuvant (AC) chemotherapy have become increasingly utilized for management of muscle-invasive bladder cancer (MIBC) in combination with radical cystectomy (RC). We directly compared survival outcomes among patients who received either NAC or AC and RC. Methods: We identified patients in the National Cancer Data Base (NCDB) diagnosed with clinical T2-T4, N0, M0 urothelial cell carcinoma who underwent RC. Patients who received NAC were propensity matched by age, race, ethnicity, sex, insurance type, academic/research program, comorbidity, and clinical stage to patients receiving AC within 90 days of RC. Median survival was calculated using Kaplan-Meier analysis. Adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI) were calculated from multivariable Cox regression models to compare overall survival (OS), downstaging to non-MIBC (NMIBC), and N upstaging. Results: A total of 509 patients treated with NAC and 283 patients treated with AC were identified from 2004-2013. Patients who received NAC had better 5 year OS (50.3%, 95% CI: 43.2%-57.0%) compared to patients who received AC (38.0%, 95% CI: 32.0%-44.0%). NAC was a significant predictor of decreased mortality, decreased progression to node positivity, and downstaging to NMIBC (0.68, 0.54-0.86, p=0.001; 0.18, 0.12-0.26, p<0.001; 12.75, 6.06-26.81, p<0.001). Increasing clinical T stage was a significant predictor of decreasing probability of pathologic node positivity in patients who received AC. Conclusions: The use of NAC+RC was associated with better OS compared to RC+AC for patients diagnosed with T2-T4, N0, M0 bladder cancer. The increased survival benefit associated with NAC compared to AC among patients undergoing RC may be due to decreased progression to node positivity and pathologic downstaging.
WEEEKEND VS. WEEKDAY APPENDECTOMY FOR COMPLICATED APPENDICITIS, EFFECTS ON OUTCOMES AND OPERATIVE APPROACH

Rebecca S. Lane BS, Jun Tashiro MD MPH, Brandon Burroway BS, Eduardo A. Perez MD, Juan E. Sola MD. Division of Pediatric Surgery, DeWitt-Daughtry Department of Surgery, Leonard M. Miller School of Medicine, University of Miami, Miami, FL, 33136

Introduction: The “weekend effect”, a phenomenon in which patients have higher mortality and complication rates on weekends compared to weekdays, has been studied in many fields. However, few studies have examined the weekend effect in the pediatric population, specifically for appendectomy patients and especially on a national scale. We hypothesized that laparoscopic (LA) or open appendectomy (OA) outcomes in complicated appendicitis are associated with weekend vs. weekday procedure complication rates.

Methods: We queried the Kids’ Inpatient Database (1997-2012) for complicated (540.0, 540.1) appendicitis treated with LA or OA. Propensity score (PS)-matched analysis compared outcomes associated with weekend vs. weekday LA and OA.

Results: Overall, 103,501 cases of complicated appendicitis were identified. On 1:1 propensity score (PS)-matched analyses of complicated appendicitis, weekday OA had increased wound infection rates (1.3) vs. weekend OA, p=0.003. Weekend OA had higher pneumonia rates (1.4) and longer LOS, but lower home healthcare requirement following discharge vs. weekday OA, p<0.05. Weekend and weekday LA had no significant outcome differences.

Conclusion: On a PS-matched comparison of appendectomies performed for complicated appendicitis on weekends and weekdays, procedure day is associated with different complication rates and resource utilization for OA. For LA, no weekend effect was noted for complicated appendicitis. To ensure the optimal patient care, prospective studies should be sought to identify causes of complications dependent on the day of procedure.

ANATOMIC ASSESSMENT OF THE AORTIC ARCH: RELATIONSHIP BETWEEN ARCH ANATOMY AND AGE

Sinan Jabori, Brian DeRubertis, Ali Alktaifi, Paul Finn, Roya Saleh, Wesley Moore, Peter Lawrence, UCLA School of Medicine, Division of Vascular Surgery, Los Angeles, CA 90095. UCLA School of Medicine, Department of Radiology, Los Angeles, CA

Introduction: Older patients have been shown to have higher stroke rates with CAS than younger cohorts. Some studies have suggested that increased age is a surrogate for disadvantaged arch anatomy, though age-related morphologic arch changes have not been well characterized. We sought to analyze these arch changes using high-res MRA. Methods: GadMRA was performed on 105 patients (mean 60y, [19-89y]); blinded analysis of arch anomalies, arch type (I-III), vessel angles/diameters & arch radius of curvature (RC) was performed on Osirix image software.

Results: Advanced age correlated with increased incidence of Type II/III arch morphology (p=0.042 for age > 60y; Table 1). Arch branch vessel angle (vs aortic centerline) was increasingly acute with advanced age: innominate, L CCA, L SCA angles were 61°, 74°, 97°, respectively in pts <60y; 52°, 54°, 66°, respectively in patients >60y. These findings appeared to relate to arch elongation in older patients, as linear regression showed strong correlation between age and aortic arch radius of curvature (r=0.778, p<0.0001, Fig 1). Arch anomalies included: bovine 18%, right-sided 4%. Conclusions: Objectively quantification of morphologic changes occurring in the aortic arch with advanced age is feasible using robust MRA image data. Patients >60y have increased arch curvature and arch branch vessel angulation relative to younger patients. These factors may differentially affect endovascular outcomes.
METAL STAPLES FOR SKIN CLOSURE FOLLOWING OPEN FIXATION OF ACUTE TRAUMATIC ANKLE FRACTURES

Eva J. Lehtonen, Sierra Phillips, Harshadkumar Patel, Martim Pinto, Sameer Naranje, Ashish Shah, Department of Orthopaedics, University of Alabama at Birmingham, Birmingham, AL

Introduction: Recent comparisons of suture versus metal staple skin closure on the rates of wound complications in orthopaedic surgeries have yielded conflicting results. Several studies have since started to approach this question based on anatomic location, comparing suture versus staple closure in total hip and knee arthroplasty and acetabulum fracture surgery. Ankle fractures are one of the most commonly treated fractures by orthopaedic surgeons with unique challenges to skin closure due to the lack of subcutaneous support. However, to date there are no studies comparing superficial skin closure methods specifically in ankle surgery. The objective of this study was to evaluate the safety of staple versus suture closure for open fixation of acute traumatic ankle fractures. Methods: The medical records of patients treated at one institution by a single surgeon with open surgical fixation of an acute traumatic ankle fracture between 2011 and 2017 were retrospectively reviewed. Patients with less than 6 months of follow-up, polytrauma patients, diabetic patients, and patients with more than 3 medical comorbidities were excluded. Skin closure technique was determined by the presence or absence of metallic staples on postoperative imaging. Demographic variables, surgical characteristics, and postoperative outcomes up to one year were compared between patients who received superficial skin closure using staple versus suture techniques. Statistical analysis was performed using chi-squared tests and Fisher’s exact tests, with p=0.05 used to denote statistical significance. Results: This study included 94 patients aged 18 to 75; two groups of 47 patients (Staple group and Suture group) that were demographically similar at baseline. Overweight and obese patients constituted the majority of the sample, 34% and 46% of patients, respectively. Current tobacco use was reported by 45% of patients. Fractures tended to be right-sided (63%), low energy (64%), and closed (98%), and the most common fracture types were bimalleolar (30%), lateral malleolar (24%), and pilon (19%) fractures. Ten patients (10.6%) developed local wound related complications within 4 months postoperatively, including five incidences of wound dehiscence, four superficial wound infections, and one deep infection. Eight patients (8.5%) required revision surgery due to wound related complications. There was no difference in the incidence of surgical site infections (p=0.361), local wound related complications (p=0.316), or revision surgeries (p=0.267) between wound closure techniques. Suture group patients required more staff in the operating room compared with staple group patients (p=0.001). Conclusion: These results suggest that staples are a safe alternative to sutures for superficial skin closure in healthy, non-diabetic patients following open surgical fixation of acute traumatic ankle fractures. However, this retrospective, single-institution study was limited by the low number of available patients relative to the rare outcomes of interest. Larger, prospective studies are needed to validate the accuracy and generalizability of these results.

TREATMENT OUTCOMES OF iBALANCE HIGH TIBIAL OSTEOTOMIES IMPLANT SYSTEM: THE EFFECT OF CORRECTION ANGLES

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Introduction: High tibial osteotomy (HTO) is an orthopaedic procedure clinically indicated in patients with varus knee alignment associated with medial compartment arthrosis, knee instability, or osteochondral lesions. Successful outcomes necessitate accurate correction angles be cut in the tibia to achieve stable fixation and bone healing. While studies have shown successful long-term results for HTO, the risk of postoperative complication requiring treatment is reported at 9%. Although precise correction angles are critical to positive outcomes, current literature fails to examine the potential effects of varying sizes of implant correction angles on postoperative complications. The purpose of this study was to determine the effects of correction angle on postoperative complications following HTO. Methods: A retrospective chart review was conducted for surgical patients who underwent an HTO procedure using the Arthrex iBalance system. Patients who underwent HTO between January 2014 and July 2017 and who had at least 5 months of follow-up were included. Fisher exact tests were used to determine predictors of postoperative complications. Results: Twenty-one patients were included in this study, with an average correction angle of 8.2 degrees (SD = 2.6). At postoperative follow-up, 14.2% (n=3) of patients presented with lateral cortex fracture (LCF). The incidence of LCF was significantly greater (p=0.02) among patients with a correction angle ≥10 degrees as
compared with correction angles <10 degrees. Two patients underwent additional surgeries (correction angles = 6 and 10 degrees) and two patients presented with deep vein thrombosis (correction angles = 9 and 11 degrees). No patients presented with nonunion, stiffness, or clinical infection. The overall complication incidence was significantly higher (p=0.01) among patients with correction angles ≥10 degrees than correction angles <10 degrees. **Conclusion:** Larger iBalance implant correction angles are associated with higher overall complication and fracture incidence compared with smaller correction angles. However, most complications do not require further intervention. To the best of our knowledge, this is the first study to analyze postoperative complications by correction angle for HTO, though it is not without limitations. The inclusion of patients with a follow-up time as early as five months limits the ability to analyze potential postoperative complications. Furthermore, procedural performance by a single surgeon introduces potential for recall bias. Future studies should focus on larger cohorts with more time to follow-up.

**TO LOW VELOCITY GUNSHOTS: DOES OPERATIVE DEBRIDEMENT INCREASE INFECTION RATES?**

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**Introduction:** While gunshot induced extremity fractures are typically not considered “open fractures”, there is controversy regarding wound management in the setting of operative fixation to limit infection complications. Previous studies have evaluated the need for a formal irrigation & debridement (I&D) prior to intramedullary nailing (IMN) of gunshot induced femur fractures but none have specifically evaluated tibias. By comparing primary IMN for tibial shaft fractures caused by low velocity firearms additionally treated with a formal operative I&D compared to those without an I&D, we sought to identify if there are: 1- differences in treatment group infection rates, 2- particular fracture patterns more prone to infection, and 3- patient characteristics more prone to infections. **Materials and Methods:** Retrospective cohort study at a single Level 1 trauma center of gunshot induced tibial shaft fractures managed primarily with IMN. The following were studied: demographics, follow-up, fracture characteristics, injury management, and patient outcome. Fractures were categorized based on the Orthopaedic Trauma Association (OTA) classification system for diaphyseal tibia/fibula fractures. All patients had IV antibiotics at presentation, and received 3 days of post-operative IV antibiotics per institutional protocol. **Results:** In Group I, 6/23 patients (26.1%) developed superficial infections and 4/23 patients (17.4%) developed deep infections. In Group II, 0/16 patients (0%) developed superficial infections and 1 patient (6.25%) a deep infection, making the total infection rate 28.2% (11/39). Superficial infections were associated with intervention type while deep infections were not. Tobacco users and type 42-A fractures had significantly higher infection rates when treated with a formal I&D. **Conclusion:** A formal debridement, followed by primary IMN in tibia fractures caused by low velocity firearms is associated with an increased risk of superficial infection that is well managed with antibiotics, but the incorporation of a debridement does not affect rate of deep infection. A formal I&D during IMN fixation should be avoided in patients that are smokers and have type 42-A tibia fractures as these are factors associated with increased infection rates.

**SCOLIOSIS SEVERITY IN CEREBRAL PALSY PATIENTS IS ASSOCIATED WITH INCREASED NEED FOR RESPIRATORY ASSISTIVE AIDS**

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**Introduction:** Respiratory comorbidities are a leading cause of death among patients with Cerebral Palsy (CP). Many undergo spine surgery to slow the progression of pulmonary decline; however, no consensus has been reached regarding respiratory benefits of spine deformity surgery in this population. The purpose of this study is to examine the association between scoliosis severity and pulmonary dysfunction in patients with CP. We hypothesize that patients with large spinal curves will demonstrate increased use of respiratory aids compared to those with smaller curves. **Methods:** This single center retrospective cohort study collected patients diagnosed with CP and scoliosis seen between July 2005 and November 2016. Major coronal curve, surgical data, comorbidities, Gross Motor Function Classification Scale (GMFCS) and demographics were obtained by chart review. Major curves were measured using either the most recent x-ray or the x-ray taken after onset of respiratory aid use. A survey was utilized to obtain information about respiratory aid use, pulmonary comorbidities and medications, food modifications, and other respiratory risk factors. Respiratory aids included ventilation, tracheostomy, supplemental oxygen, cough assist,
or other. Patients who reported use of respiratory aids were compared to those who denied use using chi-square and independent sample t-tests. **Results:** 94 of 344 potential survey responses were received. 24 (25%) reported use of respiratory aids, of which 70.8% used aids every day. Average major coronal curve for patients who rely on respiratory aids was 48.4 ± 28° compared to 33.4 ± 18.3° in patients who don’t (p=0.031). Patients classified as GMFCS 1-3 relied on respiratory aids significantly less than GMFCS 4-5 patients (8.3% vs. 31.4%, p=0.025). Significant associations were found between major coronal curve and pulmonary medication use and tube fed patients (p=0.027 and p<0.001, respectively), and age and respiratory aid use (p=0.026). No association was found between major curve and asthma. **Conclusion/Discussion:** 1 of 4 patients with CP and scoliosis rely on respiratory aids, and the majority of these patients require them daily. A significant difference was found between major coronal curve of CP patients with scoliosis who use respiratory aids and those who do not, indicating an association between scoliosis severity and pulmonary dysfunction in CP patients. This study highlights the need for longitudinal examination of the association of increasing scoliosis and decreasing pulmonary function in patients with CP to optimize treatment protocols for this complex population. Surgical intervention may be beneficial for patients with more severe curvature to prevent pulmonary decline.

**DOES TYPE OF INSURANCE IMPACT OUTCOMES FOLLOWING TOTAL KNEE ARTHROPLASTY?**

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**Introduction:** Of the three categories that develop a quality score created by the Comprehensive Care for Joint Replacement (CJR) model for Medicare beneficiaries, Patient-Reported Outcomes (PROs) are not publicly available. Therefore, a retrospective chart review was performed to determine if patients undergoing total knee arthroplasty (TKA) covered under different insurance plans differed in PROs following surgery since the quality score determines the financial responsibility of hospitals that perform this procedure. **Methods:** A review of TKAs from 2013 to 2016 at a university-based orthopedic practice was completed. Data derived from patient medical records included demographics (age, gender, race, year of surgery, and type of insurance) and clinical data (body mass index [BMI], length of stay [LOS], and PROs). Two PRO measures were the Knee injury and Osteoarthritis Outcome Score (KOOS) and Patient-Reported Outcomes Measurement Information System (PROMIS-29 Profile V10). PRO data were collected prospectively pre-operatively and at scheduled post-operative follow-up visits (week 2 and 6 month 3, 6, and 12). Patients insured by commercial health plans, Medicare Advantage (MedAdv), or Medicare were analyzed. **Results:** 219 patients (51 commercial, 90 MedAdv, and 78 Medicare) were eligible for analysis. Medicare and MedAdv patients were significantly older than commercial patients (p<0.0001 for both comparisons). Without adjusting for patient demographics, commercial patients had a significantly shorter mean LOS (0.6 days) compared to Medicare (1.3 days, p=0.0074) and MedAdv (1.2 days, p=0.0017) patients. Pre-operatively, Medicare patients reported significantly more severe PROMIS-29 depression than MedAdv patients (p=0.0476) and a non-significant trend towards more severe depression compared with commercial patients (p=0.0725). A significant interaction of insurance type by time existed in post-operative KOOS Activities in Daily Living (ADL) scores (p=0.0094) with Medicare patients reporting significantly worse physical function than commercial patients at Day 180 (64.64 vs. 78.74, p=0.0069). Similarly, a significant time interaction by insurance type existed for KOOS knee-related Quality of Life (QOL; p=0.0272) with Medicare patients reporting lower QOL at Day 180 (46.27 vs. 62.30, p=0.0084) and Day 365 (47.31 vs. 62.13, p=0.0414) compared with commercial patients. A significant time interaction by insurance type existed for the PROMIS-29 pain interference (PAI) scores (p=0.0272) with MedAdv patients reporting significantly greater PAI at Day 365 than commercial patients (60.45 vs. 53.04, p=0.0384) and a similar non-significant trend for worse PAI among Medicare versus commercial patients at Day 180 (58.26 vs. 52.43, p=0.0540). **Conclusion:** Medicare patients have worse outcomes following TKA at the 6 and 12 month post-operative visits, as indicated by lower physical functionality (ADL) and QOL and more severe PAI, than patients with commercial or MedAdv insurance. Therefore, correlating the increased baseline risks of Medicare patients to poorer outcomes is imperative due to the difficulty in determining the healthcare costs a hospital incurs to offset those risks.
UNCORRECTED RETROVERSION RISKS GLENOID COMPONENT RADIOLUCENCY AFTER TOTAL SHOULDER ARTHROPLASTY

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Introduction: Glenoid retroversion has been shown in biomechanical, finite element analysis, and clinical studies to be related to the development of radiolucent lines and component loosening, one of the most common causes of failure after total shoulder arthroplasty (TSA). We present an analysis of version correction after TSA and the associated risk of glenoid component radiolucent line development at minimum 2-year follow-up. A novel method was utilized to measure post-operative version using routine post-operative X-rays and pre-operative CT scan along with computer software. Methodology: A retrospective analysis of TSA patients identified 15 with complete imaging and adequate length of follow-up to meet inclusion criteria. Standard true AP X-rays taken at least 2 years post-operatively were graded for glenoid radiolucent lines (average follow-up length 39.6 months). Pre-operative glenoid version was measured both using 3D-corrected CT scans and with Glenosys software (Imascap, Plouzane, France). Post-operative glenoid version was measured utilizing a novel method utilizing Mimics software (Materialise, Leuven, Belgium), performed by aligning post-operative radiographs with a 3D scapula model generated from the pre-operative CT. The position of the glenoid component was then aligned to the radiographs and measured relative to the scapula, giving version. Radiolucent line scores of 0-2 were defined as low-grade and those of 3-5 as high-grade. Patients were grouped based on their radiolucent line score, and unpaired two-sample t-tests were run to assess level of significance in differences in pre-operative version, post-operative version, and version correction. Results: Post-operative glenoid component retroversion >9 degrees had an 83% chance of high-grade radiolucent line score at 40-month follow up while only 33% of patients with post-operative retroversion <9 degrees had a high-grade radiolucent line score. There were statistically significant differences between the post-operative versions of patients with low-grade and high-grade radiolucent line scores (1.86 vs. 11.30 degrees, p=0.0061). There were also statistically significant differences between those groups' pre-operative versions as measured with both 3D-corrected CT (5.91 degrees vs. 14.94 degrees, p = 0.0257) and Glenosys software (8.80 degrees vs. 20.17 degrees, p = 0.0036). A 3D-corrected CT pre-operative version >15 degrees measured with Glenosys software increased it 5-fold. Conclusions: There is a significantly increased risk of developing glenoid component radiolucent lines after TSA in patients with poorly corrected retroversion to >9 degrees at 3.4-year follow-up. Significant pre-operative glenoid retroversion >15 degrees is also a risk for increased glenoid component radiolucency. Post-operative glenoid component retroversion can be calculated from standard post-operative X-rays and a preoperative CT scan using a novel image analysis method.
ORAL PRESENTATIONS II
FEBRUARY 21, 2018
1:45 PM – 4:30 PM
MICROPATTERNED MICROSPHERE SCAFFOLDS: OPTIMIZING THE PERFORMANCE OF ENGINEERED DERMAL SUBSTITUTES

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Introduction: Current dermal replacement products perform sub-optimally in complex wound beds, such as those that have been irradiated or those with exposed hardware, mostly as a result of insufficient cell invasion and vascularization. We have previously observed more robust endothelial cell invasion of scaffolds containing a micropatterned matrix of differential collagen stiffness in a murine model when compared to collagen controls. Herein we compare the performance of our micropatterned microsphere hydrogels (MSS) to a widely utilized commercially available dermal replacement product in vitro and in vivo. Methods: Microspheres composed of 1% type I collagen 50-150μm in diameter were created and encased in a 0.3% type I collagen bulk. For our in vitro study, polydimethylsiloxane (PDMS) wells of 4mm diameter and 2mm height were filled with the microsphere scaffolds. 3mm Integra® disks were placed inside PDMS wells. Non-microsphere containing 1% and 0.3% collagen scaffolds served as controls. A monolayer of endothelial cells was seeded onto this three-dimensional platform, activated for invasion with 1μM sphingosine-1-phosphate, and cultured for 3 days. The collagen hydrogels were then analyzed using confocal microscopy to quantify cell invasion. For our in vivo study, 8x2mm MSS disks were created, along with 1% and 0.3% collagen controls. 8mm Integra® disks were created, and the unilateral silicone layer was removed. A disk of each type was then implanted subcutaneously in the dorsum of 8-week old wild-type mice. The scaffolds were removed at 7 and 14 days, imaged, and analyzed with ImageJ. Results: Cells formed a confluent monolayer on the surface of the collagen disks, and migrated at a significantly higher rate into the MSS scaffold during 3 days of culture compared to control cultures as well as Integra® (142μm MSS vs 45μm Integra®, p<0.0001). Furthermore, in our in vivo study, MSS and Integra® both demonstrated robust cellular invasion spanning the depth of the scaffold at 7 and 14 days. Integra® had a lower cell density within the bulk at all depths with 705 cells per mm² compared to 1,454 cells per mm² in MSS at 14 days. Control collagen disks demonstrated low cell invasion and contraction. Conclusion: Micropatterned differential stiffness microsphere hydrogels (MSS) promote significantly more cellular invasion both in vitro and in vivo when compared to a widely available dermal substitute. This enhanced cellular invasion and accelerated neovascularization, which results solely from the unique architecture of the scaffolds, indicates superior efficacy in the rate of integration into the host wound bed and may result in decreased length of time between its application and definitive wound closure. Further, the significantly more robust cellular invasion and integration of these scaffolds indicates their applicability in the treatment of suboptimal wound beds, which is beyond the capability of currently available dermal substitutes.

SCAFFOLDING THE SCAFFOLD: 3D-PRINTED CONTOUR-MATCHED CAGES MITIGATE LOSS OF VOLUME AND TOPOGRAPHY OF ENGINEERED AURICULAR CARTILAGE

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Introduction: Autologous reconstruction of the ear, whether for microtia or acquired deformity, is a complex procedure with substantial donor site morbidity and suboptimal aesthetic outcomes. An engineered auricular scaffold would obviate donor morbidity and provide improved aesthetic outcomes. A major obstacle to clinical translation of tissue-engineered auricles is the significant contraction and loss of topography that occurs during maturation of the soft collagen/chondrocyte matrix into elastic cartilage. Previously, we demonstrated that a 3D-printed biodegradable cage significantly mitigated contraction of simple disc-shaped collagen hydrogels seeded with human auricular chondrocytes (HAuCs) in vivo without impeding the development of elastic cartilage. Herein we fabricate cages to invest chondrocyte-collagen hydrogels with more intricate "anatomic" topographic features. Methods: Custom external cages were designed with a geometric element representative of the helical rim using SolidWorks, then 3D-printed using polylactic acid (PLA) on a MakerBot printer. Using auricular cartilage from discarded otoplasty specimens, HAuCs were harvested and expanded to passage 2. The chondrocytes were encapsulated into type I collagen hydrogels at a density of 25million cells/ml with high fidelity contour matching to the cages. The hydrogels, protected or unprotected by the PLA cages, were implanted into nude rats and explanted after 3 months. Results: After
3 months \textit{in vivo}, all constructs developed a glossy white cartilaginous appearance, similar to native auricular cartilage. Histologic analysis demonstrated development of an organized perichondrium composed of collagen, a rich proteoglycan matrix, cellular lacunae, and a dense elastin fibrin network by safranin-O and Verhoeff’s stain. Biochemical analysis confirmed similar amounts of proteoglycan and hydroxyproline content in the constructs when compared to native auricular cartilage. Cage-protected constructs contracted significantly less than unprotected constructs on base area comparison (14.33\% vs. 56\% contraction, \(p=0.0023\)), retained volume (76.2\% vs. 41.9\% retention, \(p=0.0290\)), and maintenance of the topographic "helical rim" feature compared to unprotected constructs. \textbf{Conclusion:} We have shown that custom contour-matched 3D-printed biocompatible/biodegradable external cages significantly mitigate contraction and maintain the complex topography of HAuC constructs. Furthermore, cages do not impede formation of mature elastic cartilage. This technique can be used to create custom cages that contour to any form, enabling the fabrication of engineered autologous cartilage tailored to individual patient anatomy, without the contraction and loss of topography that has thus far impeded translation to the clinic.

\textbf{MATURE ADIPOCYTES MAY FUEL BREAST CANCER: STUDIES IN A PATIENT-DERIVED, TISSUE ENGINEERED BIOMIMETIC BREAST MODEL}

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\textbf{Introduction:} Obesity is a known risk factor for the development and prognosis of breast cancer (BC). Obesity is associated with less response to BC therapy and more aggressive disease. Adipocytes have been identified as a source of exogenous lipids in many cancer cell types, including breast, and provide energy to fuel malignant survival and growth in BC. Autologous fat transfer is an increasingly ubiquitous adjunct procedure for breast reconstruction after mastectomy, but the oncologic safety is largely unknown. There is a compelling need to better understand the biology behind the obesity-BC link. We have developed a 3D, patient-derived tissue engineered platform to directly assess the metabolic interactions among cells of the BC tumor microenvironment. \textbf{Methods:} Breast tissue from breast reduction cases were collected from the operating room and enzymatically digested to retrieve mature adipocytes and adipose derived stromal cells. Polydimethylsiloxane wells were filled with 0.6\% (w/v) type I collagen encapsulated with stromal cells (2 million cells/mL) and adipocytes (10\% v/v) labeled with the fluorescent lipid dye boron-dipyrromethene (BODIPY) 493/503. RFP-labeled MDA-MB-231 BC cells were subsequently cultured on the surface of the collagen disk at 250 cells/mm$^2$. Cultures of MDA-MB-231 in non-adipocyte containing collagen matrices as well as adipocyte-containing collagen without BC cells served as controls. Samples were fixed in 4\% formalin and subsequently stained with DAPI. Lipid transfer was analyzed using laser scanning confocal microscopy and image analysis. \textbf{Results:} After 24 hrs of co-culture, the 3D collagen culture platform demonstrated BODIPY-stained mature adipocytes neighbored by stromal cells, akin to the native architecture in human breast tissue. At the interface of the cancer cells with the stroma lipid transfer was observed—BC cells which were close in proximity to the lipid-filled adipocytes filled centrally with green fluorescent lipid droplets and the cytosol pushed to the periphery. \textbf{Conclusion:} We have established a novel 3D tissue engineered platform to study BC microenvironment, including metabolic interactions between primary human breast adipocytes and BC cells. Transfer of fluorescently-labeled lipids directly from adipocytes to BC cells may induce aberrant metabolism to fuel malignant growth and adaptive survival which may have implications in the setting of autologous fat transfer after oncologic resection.

\textbf{COMBINATION OF PROTEIN PHOSPHATASE 2A INHIBITION AND PD-1 BLOCKADE SYNERGISTICALLY INDUCES REGRESSION OF MURINE INTRACRANIAL GLIOBLASTOMA}

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\textbf{Introduction:} Checkpoint inhibition using monoclonal antibodies against programmed cell death protein 1 (PD-1) is currently under evaluation for treatment of glioblastoma (GBM). Inhibition of protein phosphatase 2A (PP2a) was recently identified as a novel strategy to enhance cancer immunity. We hypothesized that pharmacologic inhibition of PP2a utilizing the small-molecule inhibitor, LB-100, could enhance the therapeutic effect of anti-PD-1 checkpoint inhibition in a syngeneic murine GBM model. \textbf{Methods:} C57BL/6 mice were inoculated with 130,000 GL261-Luc$^+$ cells in their right striatum. When the bioluminescent intensity (BLI) reached 1.3-2.6 million photon/sec*mm$^2$ in the
region of interest (ROI) on bioluminescent imaging, mice were randomized into four treatment groups: control (PBS), anti-PD-1, LB100, and combination. For in-vitro studies, CD8 cells isolated from mouse splenocytes were co-cultured with GL-261 cells separated through transwell cell culture inserts. FACS analysis was performed to determine the lymphocyte proliferation index and PDL1 tumor cell expression. IFN-g supernatant levels were determined by ELISA bead-based immunoassay. **Results:** Mice treated with the combination therapy demonstrated a significant increase in survival compared to monotherapy (p<0.005) or control (p<0.001). Tumors in the combination therapy group displayed a significant decrease in tumor burden as measured by BLI after the first treatment compared to control (p<0.005). Complete regression (CR) occurred in 25% of combination treated mice. No CR was seen in any other group. FACS analysis demonstrated an increased proliferation index of activated CD8 cells after exposure to LB-100. LB-100-treated CD8 cells also induced a higher expression of PDL-1 in co-cultured GL261 cells. IFN-g supernatant levels were reduced to baseline with concomitant administration of anti-IFN-g. **Conclusion:** This data suggests that PP2a inhibition and PD-1 monoclonal antibody checkpoint inhibition act synergistically against intracranial GBM. This finding appears to be at least partly attributed to LB100-induced upregulation of PDL1. This report supports further clinical investigation of combining LB-100 with checkpoint immunotherapy.

**NEURONAL AUTOPHAGY WITH CPLA2 ACTIVATION FOLLOWING SPINAL CORD INJURY**

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**Introduction:** Autophagy is a homeostatic cellular process required for the recycling of proteins and damaged organelles. Under normal physiological conditions, autophagy is believed to promote cell survival. However, there is accumulating evidence that under certain pathological situations, autophagy can also trigger and mediate Type II programmed cell death (autophagic cell death). Recently, autophagy dysregulation has been implicated as a cause of autophagic cell death following spinal cord injury (SCI). Autophagic flux has been shown to be necessary for normal neuronal homeostasis, and its dysfunction contributes to neuronal cell death in several neurodegenerative diseases. Elevated autophagy has been reported after SCI; however, its mechanism and role in SCI remain unclear. The objective of this study was to investigate whether autophagy increases after SCI, and whether such an increase confers a neuroprotective or pathological effect on neurons in the context of spinal cord injury. We hypothesize that the autophagy marker LC3B increases, and autophagic flux is disrupted, after SCI. **Methods:** A contusive SCI in mice was performed at the T9 level using an Infinite Horizon Impactor (Infinite Horizons, Lexington, KY) at an impact force of 60 kdyne according to our lab standard protocol. A 10-mm spinal cord segment containing the injury epicenter was dissected at the designed time after SCI. Western blot and immunohistochemistry were used to investigate whether autophagy and cPLA2 activation were upregulated following contusive SCI. **Results:** Western blot analysis shows a significantly elevated proportion of LC3B-II to LC3B-I at 1 day post-SCI. Cell quantification following immunohistochemistry indicates a significantly greater proportion of LC3B puncta-positive neurons in the SCI cohort, compared to neurons in the Sham cohort. Western blot analysis also revealed expression of the cPLA2 activation marker, p-cPLA2, increases after SCI. Activated cPLA2 was localized mainly in neurons. **Conclusion:** Autophagy is elevated in neurons following SCI in mice and may be the result of disrupted autophagic flux, due to cPLA2 activation. Activated cPLA2 may hydrolyze the lysosome’s membrane and induce lysosomal dysfunction. Whether autophagy’s role is neuroprotective or pathological, and to what extent, remains to be seen.

**AUTONOMIC SENSORY INNERVATION OF THE PANCREATIC ISLET**

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**Introduction:** The brain receives and processes stimuli from the viscera to adjust autonomic output and regulate glucose metabolism as part of body homeostasis. Visceral stimuli are detected by free nerve endings of the vagus nerve and are transmitted to the hindbrain via sensory neurons. However, the signals that activate vagal sensory neurons in the periphery are not known. We are specifically interested in the sensory innervation of the pancreatic islet of Langerhans, the major regulator of glucose metabolism. The long-term goal of this research project is to understand the contribution of sensory innervation to islet function and glucose metabolism. The hypothesis is that vagal sensory neurons innervating the pancreatic islet (1) transmit chemosensory inflammatory information from the
islet to autonomic centers in the brain and (2) release the neuropeptides substance P and CGRP to impact inflammatory processes in the islet. We propose that excessive activation of the vagus nerve promotes islet inflammation and leads to dysregulation of glucose metabolism. **Methods:** We have developed tools that allow us to characterize molecular and functional profile of islet-specific vagal sensory neurons. *In-vivo* Ca²⁺ imaging of mouse nodose ganglion, a sensory ganglion that contains cell bodies of vagal sensory fibers, allows us to identify specific subpopulations of vagal neurons that innervate different organs. **Results:** We are focused on establishing a response profile of neurons that respond to pancreatic islet-derived substances. To this end, we have identified two distinct populations of pancreatic sensory neurons that respond to serotonin (5HT) and cholecystokinin (CCK). The observed response profile suggests that these neuronal populations are tuned to sense differentially endocrine and exocrine pancreas. While endocrine sensory neurons are sensing local 5HT that is co-released with insulin, exocrine neurons sense CCK a hormone that stimulates release of digestive enzymes. **Conclusions:** Our data suggest that pancreatic sensory neurons are important regulators of pancreatic physiology. By taking a snapshot of endocrine and exocrine pancreatic microenvironments and sending this information to the brain, sensory neurons might trigger feedback loops and help the organ to be tuned to physiological needs. Altogether, we have a model where we can characterize islet-specific neural circuits, we expect this study to provide insight into pancreatic sensory innervation and its contribution to glucose metabolism.

**ROLE OF HISTONE DEACETYLASE 3 (HDAC3) IN MODULATING ALZHEIMER'S DISEASE PATHOLOGIES**

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**Introduction:** Alzheimer’s disease (AD) is the sixth leading cause of age-related dementia and it is characterized by extracellular amyloid-β (Aβ) plaque deposition, and intracellular hyperphosphorylated and acetylated tau accumulation. A growing body of evidence indicates that epigenetics plays an important role in AD pathophysiology. Members of the histone deacetylase (HDAC) family of epigenetic eraser proteins remove acetyl group from lysine residues on histones and serve as a scaffold for the recruitment of macromolecular complexes to modify chromatin accessibility and transcriptional activity. Although these changes can be inherited, they are also subject to dynamic regulation in response to environmental stimuli, and the epigenetic regulatory pathways upstream of these changes remain largely unexplored. We propose that HDAC3 inhibition has a favorable anti-AD profile, and thus has the potential to have meaningful benefits as a treatment for AD in patients. **Methods:** In this study two cellular (HEK/APPsw cell line and two IPS cell lines obtained from APOEε4-carrying AD patients) and one animal model (triple transgenic APP/PS1/tau mice, 3xTg-AD) was used. HDAC3 activity was measured by fluorescent HDAC3 activity assay, followed by Western blot and ELISA analysis for detection of Aβ and phosphorylated and acetylated tau. Behavioral effects of RGFP966 on 3xTg-AD mice were assessed using novel object recognition, Barnes’s maze, Y-maze spontaneous alteration and open field tests. One-way ANOVA or repeated measures two-way ANOVA with appropriate post hoc analyses were used for multiple comparisons. **Results:** Consistent with the role as an HDAC3 inhibitor, RGFP966 increases histone H3 and H4 acetylation on three lysine (K) residues (H3K4, H3K27 and H4K16), previously associated with memory and cognition *in vitro*. We found that chronic treatment with low dose of RGFP966 improves memory and cognition in 3xTg-AD mice. No adverse effect on motor activity was observed. RGFP966 reverses hyperphosphorylation of pathological tau protein at Thr181, Ser202, Ser396 and decreases Aβ protein levels in the hippocampi, prefrontal cortex and entorhinal cortex of 3x-Tg AD mice, with no effect on total tau and Aβ in the cerebellum. Analysis of AD derived neurons showed that RGFP966 significantly decreased extracellular Aβ accumulation, tau phosphorylation and acetylation at disease-relevant residues with no effect on total tau protein. Having observed differential gene expression of BDNF, NRG1 and CLU using RNA-seq analysis from four AD patients, we are currently investigating the regulatory role of HDAC3 and its association with promoters of these genes using chromatin immunoprecipitation *in vitro*. **Conclusion:** These data suggest that HDAC3 plays an important regulatory role in the expression and regulation of AD related pathogenic proteins, and provides support for the idea that HDAC3 may be a disease modifying therapeutic target, and thus using a single epigenetic compound to simultaneously address several aspects of AD would have meaningful clinical outcomes.
**Introduction:** Smoking is a preventable risk factor for stroke and smoking-ingested nicotine exacerbates post-ischemic damage via inhibiting estrogen receptor beta (ER-β) signaling in the brain of female rats. ER-β regulates the innate immune component—inflammasome—activation in the brain. Therefore, we hypothesized that chronic nicotine exposure activates inflammasomes in the brain thus exacerbating ischemic brain damage in female rats.

**Methods:** Adult female Sprague-Dawley rats (6-7 months old) were exposed to nicotine (4.5 mg/kg/day for 16 days) or saline and divided into two cohorts. One cohort of rats were used for brain tissue collection for Western blot analysis. Rats belonging to another cohort were exposed to transient middle cerebral artery occlusion (tMCAo; 90 min) and sacrificed one month later for histopathological analysis. We tested the hypothesis that inhibition of nicotine-induced inflammasome activation improves post-ischemic neuronal survival. This proof of principle experiment was conducted using an in vitro—organotypic slice culture—model of ischemia. Slices were exposed to nicotine (100ng/ml; 14-16 days) or saline then exposed to the inflammasome inhibitor isoliquiritigenin at different concentrations (1µM/10µM/40 µM; 24 h) or vehicle prior to oxygen-glucose deprivation (45 min).

**Results:** The histopathological analysis revealed a significant increase in infarct volume in the nicotine-treated group (64.24 ± 7.3 mm³; Mean ± SEM; n=6) compared to the saline-treated group (37.12 ± 7.37 mm³; n=7, p<0.05). Immunoblot analysis demonstrated significantly high inflammasome proteins caspase-1, adaptor protein and interlukein-1β by 88%, 48% and 149% (n=8; p < 0.05) respectively, in the cortex of nicotine exposed rats as compared to the saline. Inhibition of nicotine-induced inflammasomes activation significantly decreased post-ischemic neuronal death.

**Conclusion:** Overall, this study shows that nicotine exposure exacerbates ischemic brain damage via activation of inflammasomes in the brain of female rats.

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**DISCOVERING NOVEL THERAPEUTICS FOR CARM1-OVEREXPRESSING ACUTE MYELOID LEUKEMIA**

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**Introduction:** Whereas a fraction of leukemia are due to specific driving mutations or fusion proteins that can be specifically targeted for treatment (e.g. t(8;21), t(9;11), etc.), a significant population of AML patients display no attributable chromosomal anomaly. The Nimer laboratory previously identified, coactivator-associated arginine methyltransferase 1 (CARM1) as an epigenetic regulator that is aberrantly overexpressed in acute myeloid leukemia (AML) and unexpressed in healthy cells. CARM1 interacts with transcription factors and pro-expression regulators to increase cell proliferation and repress cellular differentiation. In AML, CARM1 overexpression results in the rapid proliferation of immature myeloid cells characteristic of leukemia. Silencing CARM decreases proliferation of patient-derived AML cells, induces differentiation and increases cell death. Thus, chemical inhibition of CARM1 may be an important step towards treating AML. **Aim:** I aim to design a therapeutic strategy for inhibiting CARM1 in AML that can be implemented for other epigenetic drivers in cancer; using a systematic computational-based approach: (1) developing a novel CARM1 inhibitor series using machine learning and computational models and (2) using perturbation response gene expression data amassed from the NIH Library of Integrated Network-based Cellular Signatures (LINCS) Program to predict for combination treatment strategies for treating CARM1-overexpressing AML. There is no FDA approved drug targeting CARM1 and there is currently only one promising pre-clinical candidate. Diversity in drug structure, and subsequently drug binding, lends to broadened applicability and affect. Multiple types of CARM1 inhibitors are beneficial towards treating the various types of CARM1-overexpressing AML. **Methods:** To develop a novel CARM1 inhibitor series (drug type) that can be further optimized to create a novel pre-clinical/clinical CARM1 inhibitor, I characterized binding interactions, activity and structure types of known CARM1 inhibitors from relevant literature and confirmed these findings by docking known inhibitors in computational models of CARM1. I aggregated docking results across models and compared interacting protein residues. Next, I developed a machine learning model to predict for CARM1 inhibitor activity from known inhibitors from a commercially available compound database. I selected for the top 10,000 predicted CARM1 active compounds.
and docked them in CARM1 docking models. **Results:** After clustering compounds by structure type, I averaged docking scores and analyzed relevant binding interactions by cluster. I filtered for clusters with docking scores greater than 6.5, which revealed roughly 27 prospective inhibitor types. **Conclusion:** If selected inhibitor-types display activity against CARM1 in biological assays, a novel preclinical CARM1 can be optimized from the predicted active inhibitor types. The Schürer laboratory has previous employed this systematic approach on kinases to success. Optimizing this pipeline towards targeting epigenetic proteins provides a new pathway for drug discovery for other protein target classes.

**ARGINYLTTRANSFERASE ATE1 REDUCTION DRIVES PROSTATE CANCER METASTASIS**

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**Introduction:** While prostate cancer affects a large population of men, it is usually a dormant disease and is only lethal in the small subpopulation in which distal metastasis occurs. Unfortunately, distal metastasis is currently difficult to predict and treat. Understanding what provokes metastasis in prostate cancer is therefore clinically important. Ate1 is the enzyme solely responsible for mediating post-translational protein arginylation in most eukaryotic cells, including mammalian cells. Previous studies show that a complete loss of Ate1 in yeast and mammalian cells increases resistance to stress-induced cell death and promotes genomic instability. Furthermore, a lower level of Ate1 appears to correlate with shorter survival in patients with several types of cancer, including prostate cancer. However, the role of Ate1 in progression and metastasis of prostate cancer (or any cancer) remained unknown. Here we demonstrate in prostate-relevant models that a reduction of Ate1 drives prostate cancer progression and metastasis. **Methods:** We used PC-3 and LNCaP prostate cancer cells with Ate1 stably knocked down (compared to nontargeting control) to analyze stress response, mutagenesis, and cancer-relevant phenotypes such as anoikis and invasion using well-established assays such as soft agar and Boyden chamber assay. PC-3 Ate1-KD cells alongside controls were then injected into prostates of immune-compromised mice to observe their ability to metastasize to distal sites. Finally, histology and data mining was performed on protein and mRNA of Ate1 to observe trends of Ate1 expression in prostate cancer. **Results:** Consistent with our hypothesis, Ate1 knockdown resulted in less cell death during stress, and elevated spontaneous and stress-induced mutagenesis. Interestingly, while a reduction of Ate1 in these cell lines does not affect proliferation, it does cause an increase in anchorage-independent growth in LNCaP cells via the soft agar assay, and an increase in PC-3 cell invasion through Matrigel. Additional analysis of prostate cancer cell lines of varying metastatic potential showed a distinct and significant relationship between increased malignancy and decreased Ate1 expression. Ate1-knockdown in orthotopic mouse model was found to drive PC-3 metastasis compared to nonmetastatic control. As further support for Ate1’s role in prostate cancer progression, results from data mining and immune-histological examination of human tissue samples revealed a consistent downregulation of Ate1 protein and mRNA during prostate cancer progression and metastasis, offering promising value of predicting metastatic events before they occur. **Conclusion:** Ate1 reduction may be a potent indicator of prostate cancer progression, and provide insight into the molecular mechanism of prostate cancer metastasis.

**OSTEOPONTIN DEFICIENCY AMELIORATES HFpEF BY UPREGULATING MITOCHONDRIAL OGDHL IN A RENAL DISEASE MOUSE MODEL**

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**Introduction:** Osteopontin (OPN) is a pro-fibrotic cytokine that is increased in the circulation of patients with Heart Failure with Preserved Ejection Fraction (HFpEF). Using the chronic kidney disease model Col4a3−/− mouse which also shows elevated circulating OPN levels, we evaluated the role of OPN in regulating myocardial energetics in renal-induced HFpEF. **Methods and Results.** In the Col4a3−/− mouse, a model of chronic kidney disease, we found a HFpEF-like cardiac phenotype including hypertension, had diastolic dysfunction, cardiac hypertrophy and fibrosis as well as
Elevated levels of OPN in plasma (FC=2.1, n=6; p<.01). In addition, Col4a3⁻/⁻ hearts had dysmorphic mitochondria, lowered antioxidant capacity, higher lipid peroxidation, and lower protein levels of mitochondrial respiratory complexes I, II and IV (p<.05). Extracellular flux assay in adult cardiomyocytes confirmed impaired mitochondrial respiration in Col4a3⁻/⁻ hearts as shown by reduced basal and maximal oxygen consumption rates, spare respiratory capacity, ATP-linked respiration and proton leak (n=9; p<.001). Moreover, found that genetic deletion of OPN in Col4a3⁻/⁻ mice (Col4a3⁻/⁻OPN⁻/⁻) resulted in significant improvement in survival, cardiac diastolic dysfunction, hypertrophy and fibrosis. Microarray data (validated by mitochondrial blot) showed OGDHL, a Krebs cycle protein, was decreased in Col4a3⁻/⁻ mice hearts but increased in OPN deficient Col4a3⁻/⁻OPN⁻/⁻ hearts, implicating OGDHL upregulation as the mechanism underlying cardioprotective effects conferred by OPN deficiency. We also confirmed that treating neonatal cardiomyocytes with OPN recombinant protein impairs ATP production and reduces OGDHL expression, reflecting the negative regulation of OGDHL and myocardial energetics by OPN. In Col4a3⁻/⁻ mice, heart-specific AAV9-mediated overexpression of OGDHL, similar to genetic OPN deletion, extended survival by ~50-100% (p<.0001). Furthermore, isovolumetric relaxation time which is prolonged in Col4a3⁻/⁻ mice (26.17 vs 15.30±1 ms in WT, n=26; p<.001), a sign of diastolic dysfunction, was decreased in Col4a3⁻/⁻OPN⁻/⁻ mice (18.1±1 ms, n=37; p<.01) as well as in AAV9-cTnT-OGDHL-treated Col4a3⁻/⁻ mice (16.7±2.5 ms, n=8; p<.05). Myocardial energetics was also improved in adult cardiomyocytes of AAV9-cTnT-OGDHL-treated Col4a3⁻/⁻ mice. In cardiac biopsies of patients with heart failure, we found that the level of OGDHL mRNA was markedly increased in both HFpEF (FC=5.1; p=0.002) and HFrEF (FC=4.0; p=0.003) clinical samples compared to healthy controls (n=12 per group).

Conclusion. In conclusion, we present the Col4a3⁻/⁻ mouse as a new and useful HFpEF-relevant model that despite its limitations can be used to identify molecular targets relevant to clinical HFpEF. We report that OPN deletion or cardiac-specific OGDHL gene therapy in Col4a3⁻/⁻ mouse improved lifespan, diastolic function and myocardial energetics. We found that OGDHL gene expression is dysregulated in both HFpEF and HFrEF human hearts compared to healthy controls. Our results elucidate for the first time the pivotal roles of circulating OPN and cardiac OGDHL in HFpEF pathophysiology and present two related potential therapeutic targets for HFpEF.
ORAL PRESENTATIONS III
FEBRUARY 22, 2018
9:15 AM – 11:30 AM
THE IMPACT OF OBESITY ON ESTIMATED BLOOD LOSS DURING THE SURGICAL MANAGEMENT OF A MORBIDLY ADHERENT PLACENTA (MAP)

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Introduction: MAP is a condition in which the placenta implants in an abnormal and invasive fashion. This leads to difficulty separating the placenta from the uterus at the time of delivery, which can have catastrophic consequences if not recognized or correctly managed. MAP is one of the leading causes of intrapartum hemorrhage and often requires cesarean hysterectomy. The purpose of this study is to determine if there is a correlation between body mass index (BMI) and estimated blood loss (EBL) in surgically managed cases with confirmed MAP. Methods: This is a retrospective study of patients with pathology confirmed MAP who delivered at CUMC between 2011 and 2017. Delivery was planned in the main operating room with availability of massive transfusion products and a multidisciplinary team. We compared EBL at the time of delivery between two groups of patients, BMI ≤ 29.9 versus BMI ≥ 30. Statistical analysis was preformed using the Statistical Analysis System (SAS). Women with percretas were excluded. Results: We included 73 patients with MAP with a median maternal age of 35 years old and a median gestational age of 34 weeks. Among them, 36 women had BMI ≤ 29.9 (group 1) with a range of 19.7 to 29.9 and median of 27.6, and 37 women had BMI ≥ 30.0 (group 2) with a range of 30.0-46.4 and median of 33.7. In group 1 88.9% had a scheduled delivery while 11.1% were delivered emergently, and in group 2, 91.9% had a scheduled delivery while 8.1% were delivered emergently. In group 1, 41.2% had one prior C-Section (CS), 35.3% had 2 prior CS, 14.7% had 3 prior CS and 8.8% had ≥ 4 prior CS. In group 2, 30.6% had 1 prior CS, 33.3% had 2 prior CS, 25.0% had 3 prior CS, and 11.1% had ≥ 4 prior CS. Group 1 had a median EBL 2,500 ml (range 400-6,000 ml) and group 2 had a median EBL of 3,000 ml (range 500-12,000 ml), p value =.78. Conclusion: The purpose of this study is to determine if increasing BMI impacts EBL at the time of delivery for women with MAP. We found that in women with a BMI >30.0, there is a trend towards greater blood loss at time of delivery than for BMI<29.9. As the obesity epidemic continues to expand and rates of MAP increase, recognition of the impact of BMI on blood loss can be useful with regards to surgical planning for these high risk patients.

REPRODUCTIVE HEALTH ADVOCACY PROGRAM: A STUDENT-LED TEACHING PROGRAM THAT EMPOWERS MEDICAL STUDENTS TO CONNECT PATIENTS TO REPRODUCTIVE HEALTH CARE

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Introduction: Although the Association of Professors of Gynecology and Obstetrics and American College of Obstetricians and Gynecologists recommend that medical students graduate with the knowledge and skills to counsel patients on the full range of reproductive health options, including long acting reversible contraceptives (LARC) and abortion, many do not. LARC is used by 7.2% of all women ages 15-44 in the United States (Branum and Jones, 2015), however, access is limited for underserved women. In this study, medical students under faculty mentorship sought to improve medical education on these topics through a student-to-student teaching model and patient advocacy program for women with barriers to accessing LARC and abortions. Here, we report on results of the training program and on student-reported outcomes of patient advocacy. Methods: Senior medical students designed an 8-hour training program to educate first-year Student Reproductive Health Advocates in contraception, patient counseling, pregnancy options, and legal-financial concerns. Pre- and post-training surveys assessed students’ knowledge and attitudes regarding reproductive healthcare. Patients were then referred to advocates for connection to LARC and abortions. Advocates reported progress with patients biweekly. One year of data was collected for training program outcomes and three years of data were collected for advocacy outcomes. Results: Seventeen students completed pre-and post-training surveys, 15 were female, 2 were male, and the average age was 23.9 years. Our program resulted in improved knowledge of reproductive healthcare, from a pre-training score of 61.18% to a post-training score of 81.18% (p <0.01). The training was associated with a change in attitudes regarding reproductive health, with 58.8% students strongly agreeing that abortion is safe pre-training and 76.5% post-training. Similarly, 52.9% strongly agreed that abortion access was significantly restricted in their community before training and 82.4% post-training. Over three years, 48 students advocated for a total of 196 patients, and students reported outcomes for 174 patients. Out of the 71% of patients that students successfully contacted, 37% were lost to follow up after counseling. Advocates made appointments for the remaining 34% of patients, out of which 58% received the service they requested (LARC or
abortion). Students cited insurance restrictions, patient loss of interest in LARC, and LARC availability as barriers in 36% of the patients. Patients who had any of these barriers were less likely to receive LARC (p < 0.05). 

Conclusions: Our student-lead program increased knowledge of contraception, abortion options and barriers to healthcare. Student-reported patient outcomes revealed aspects of success and areas of improvement for the program. Expansion of our model into medical curricula would improve student training and benefit patients.

9:45 am

IMPACT OF HAITIAN RESIDENCY TRAINING PROGRAM ON CHILD MORTALITY IN TWO HOSPITALS IN PORT-AU-PRINCE, HAITI: A RETROSPECTIVE ANALYSIS

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Introduction: Haiti has an under-five mortality rate of 69/1,000—the highest in the Western Hemisphere. One contributing factor to this high mortality rate could be the lack of trained Haitian physicians—there are approximately 400 pediatricians to care for 4 million children. In September 2013, two hospitals in Port-au-Prince, Haiti, Hospitals St Damien (SD) and Bernard Mevs (BM), established a new pediatric residency program in order to address this disparity. This study aims to evaluate the relationship between the implementation of the residency program and pediatric mortality rates at both hospitals. 

Methods: This was a retrospective study of patients (0-18 years) who were admitted to SD and BM between January 2011 and May 2017. Data from a total of 27,798 admissions were gathered from the registries at SD and BM. Mortality rates were calculated for each age group: neonates, 1 month–5 years, and >5 years. Regression models were fitted to mortality rates by age-group, hospital, and residency program implementation. Statistical analyses were performed with SASv9.4. 

Results: There was no significant decrease in mortality at SD (p=0.6665) or BM (p=0.213) before September 2013. SD exhibited significantly decreased mortality from October 2013–May 2017 (p=0.0001). BM showed a slight increase from October 2013–September 2016 (p=0.0407). BM had suffered several nosocomial outbreaks in their neonatal unit during this time frame. When the data was reanalyzed without the neonatal data, there was no significant change in mortality (p=0.6086). 

Conclusions: Mortality rates at SD but not BM decreased significantly after 2013. BM functioned on a robust international volunteer program, which provided increased human resources, whereas SD was completely Haitian-staffed. Replacing volunteers with Haitian residents helped phase out dependence on foreign volunteers for pediatrics and also had no influence on the mortality rate, suggesting that local human resources are just as good as foreign volunteers. Our study demonstrates that increasing in-country training of Haitian health professionals may improve outcomes, especially in settings void of foreign volunteer-physicians as seen in HSD, and can be a mechanism to phase out dependence on foreign health professionals as seen in HBM.

10:00 am

THE DEBBIE PROJECT: A SERVICE LEARNING PROGRAM AIMED AT REDUCING BIAS AMONG MEDICAL STUDENTS TOWARDS INDIVIDUALS WITH INTELLECTUAL AND DEVELOPMENTAL DISABILITIES

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Introduction: Studies endorse the idea that exposure to developmentally different patients helps reduce bias and discomfort among physicians. However, few medical schools offer structured experiences for learning about patients with special needs. The Debbie Project (DP) was established to provide medical students a structured, longitudinal exposure to children with developmental disabilities, with the goal of increasing comfort and willingness to provide care to this patient population. The Debbie School (DS), where volunteering takes place, is a preschool for children with developmental disabilities. We hypothesize that active, longitudinal engagement with persons with disabilities improves attitudes of medical students toward this population. 

Methodology: Participating medical students attended the DS for one hour weekly during the 2016-17 school year. Volunteer attitudes were measured before and after participation using the Multidimensional Attitude Scale Toward Persons with Disabilities (MAS). The MAS consists of a written scenario pertaining to an individual in a wheelchair with questions designed to assess the responder’s affect, behavior, and cognition. Subjects respond using a 5-point scale, ranging from 1 (not at all) to 5 (very much). In addition, demographic data of volunteers was collected, and a short qualitative survey was administered. Surveys were administered in an anonymous online format. Descriptive statistics, paired and independent sample t-tests were
performed using SPSS software. Results: In all, 19 students completed surveys. Attendance ranged from 8-16 weeks. All students reported subjective improvements in comfort treating patients with disabilities and would recommend that other students have this experience. Interestingly, volunteers with family members with disabilities had less stress (p =0.026) and depression (p =0.001) at baseline. Paired post-survey data revealed that attitudes evolved in multiple areas. MAS results showed significant improvements in relaxation (p = 0.004, MD 0.889 +/- 0.267), serenity (p =0.003, MD 0.889 +/-0.254), calmness (p=0.001, MD 0.994 +/-0.249), pity (p=0.024, MD 0.667 +/-0.268), alertness (p=0.001, MD 1.444/-0.372), and desire to leave (p= 0.002, MD 0.667+/-0.181). There was no category on the MAS in which attitudes worsened. Notably, volunteers with disabilities in their family, who displayed better attitudes at baseline, also had improvements. Finally, the change in MAS score following the program was significant (p=0.017, MD=-10.31+/-3.84). Conclusion: This is the first prospective cohort study to evaluate a service learning based medical education initiative related to persons with disabilities. Our data demonstrates that structured, longitudinal volunteering substantially improves medical student attitudes towards this population. Though the study was limited by a small cohort, the results are promising and warrant further investigation.

STIMULATING ENDOGENOUS REPAIR MECHANISMS IN MAMMALIAN RETINAS THROUGH SMALL MOLECULE INDUCTION OF PRO-NEURAL PIONEER FACTORS

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Introduction: Damage to the retina in mammals results in gliosis and irreversible loss of retinal neuronal phenotypes. Unlike mammals, many non-mammalian vertebrates are able to regenerate these retinal neurons by activating genes encoding pro-neural pioneer factors, like Ascl1 and Sox2, upon injury. Initially quiescent glial cells are then able to de-differentiate into a multipotent retinal progenitor cell (RPC) phenotype that, in turn, give rise to new retinal neurons and restore vision. Mammals lack this self-repairing ability since these pioneer factors are tightly repressed in heterochromatin. Thus, our project aimed to use epigenetic modifying compounds to reactivate these pro-neural factors and re-establish an RPC program in terminally differentiated mammalian glial cells. Methods: To quantify the expression of Ascl1 and Sox2 throughout development, time course DNase-seq was performed on whole mouse retinas. Confocal imaging of Ascl1-cre/ERT2 x Brainbow mouse retinas was carried out to visualize the progressive silencing of Ascl1 in different retinal phenotypes. Epigenomic modifications were initially screened with selected small molecules in neural crest-derived glial cells, treated over 7 days in vitro. Drugs tested include various methyltransferase inhibitors [3-deazaneplanocin A (DZNep), chaetocin, azacitidine (5-Aza)] and a histone deacetylase inhibitor [valproic acid (VA)], both individually and in combination. Real-time PCR, IHC imaging, and histone extraction were completed to assess histone mark modulation and expression level of pro-neural genes. Results: DNase-seq showed progressive silencing of Ascl1 and Sox2 with trace levels of sequencing counts by week 1 post-partum and absent by week 8. Ascl1-cre/ERT2 x Brainbow imaging of mouse retina demonstrated a similar silencing pattern, showing Mueller glia cells as the last retinal cells to lose Ascl1 expression around postnatal day 15 in mice. Following in vitro drug treatment of neural crest-derived cells, mRNA expression of pioneer factor genes (Ascl1 and Sox2) and neural progenitor markers (Oct4, Nanog, and Nestin) were significantly upregulated in multiple treatment groups, with the 5-Aza/chaetocin combination group showing the greatest upregulation among all 5 genes (p<0.03). The drugs differentially regulated key repressing and activating histone markers. Conclusion: Collectively, these results demonstrate that epigenetic modification with small molecules can effectively activate early progenitor programs to regenerate retinal neural progenitors in vitro. A combination of 5-Aza (DNMT-1 inhibitor) and chaetocin (H3K9-locus specific methyltransferase inhibitor) showed the greatest upregulation of pro-neural pioneer factors and neural markers. Thus, drugs with similar targets may provide analogous or improved results. Further refinement for retinal multipotency and in vivo studies are needed, but the results of our study offer promise for stimulating retinal regeneration from within diseased eyes.
WHOLE EXOME SEQUENCING IDENTIFIES NOVEL PATHOGENIC VARIANTS FOR ANTERIOR SEGMENT DYSGENESIS

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Introduction: Anterior segment dysgenesis (ASD) comprises a wide spectrum of ocular anomalies of the cornea, iris, and lens. ASD may involve only the eye or may be part of a systemic syndrome. Causative variants in eight genes have been identified in isolated ASD. Over 40 syndromes comprise ASD as a finding. Methods: In our ongoing study to identify causative DNA variants in patients with isolated or syndromic ASD, we performed whole exome sequencing in 24 unrelated probands recruited through the Bascom Palmer Eye Institute in Miami. We used Sanger sequencing to confirm and evaluate segregation of the candidate variants in available family members. Results: Overall, we identified 11 causative variants (6 novel) in 9 of the families (38%). Each variant was observed only in one family. Single nucleotide variants in isolated ASD genes include those in FOXC1 (2 families heterozygous; 1 novel), PAXD (1 family compound heterozygous; 2 novel), CYP1B1 (1 family homozygous), and FOXE3 (1 family homozygous; novel). In addition, a child with bilateral aniridia and glaucoma is heterozygous for a large deletion including PAX6. Syndromic ASD genes with causative variants are BMP4 (syndromic microphthalmia 6; 1 family heterozygous; novel), B3GLCT (Peters plus syndrome; 1 family compound heterozygous; 1 novel) and GJA1 (1 family heterozygous). One patient with Peters anomaly is compound heterozygous for two PXDN variants; causative variants in PXDN have not previously been reported in this condition. Further analysis for variants in novel genes is ongoing. Conclusion: Comprehensive analysis of DNA variants via whole exome sequencing allows us to search for causative variants in both known and novel genes. We can explain the cause of ASD to more families and provide better genetic counseling with this information.

EPIGENETIC SUPPRESSION OF VEGF IN RETINAL PIGMENT EPITHELIAL CELLS BY ASCORBATE

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INTRODUCTION: Age-related macular degeneration (AMD) is the leading cause of vision loss in adults in the developed world and advanced stages (wet-AMD) are characterized by choroidal neovascularization (CNV). Vascular endothelial growth factor (VEGF) signaling is crucial for the rich vasculature in the retina, but in excess it plays a critical role in pathological angiogenesis in the eye. By depriving the availability of VEGF, intraocular anti-VEGF therapies are highly effective for many cases of wet AMD. Using either antibodies (such as Lucentis, Avastin) or soluble decoy receptors (such as Eylea), current anti-VEGF therapies target the interaction between VEGF and its receptors, but not endogenous VEGF expression. Reduced intake of vitamin C (ascorbate) has been associated with AMD, but the reason for this association has previously been unknown. Here we explore the epigenetic effects of vitamin C on the retinal pigment epithelium (RPE) to investigate the link between vitamin C and AMD. METHODS. Dot-blot was used to measure 5-hydroxymethylcytosine (5hmC) in cultured ARPE-19 cells treated with or without ascorbate (50 µM). Whole transcriptome sequencing (RNA-seq) and hydroxymethylated DNA immunoprecipitation sequencing (hMeDIP-seq) were applied to evaluate the impact of ascorbate on the transcriptome and DNA hydroxymethylome. Quantitative RT-PCR, immunoblot and ELISA were conducted to examine the transcription, translation and secretion of VEGF. Primary human retinal pigment epithelial cells (hRPE) and Rodent RPE-J cells were used to verify the impact of ascorbate on VEGF in vitro and Gulo−/− mice were used to verify the impact of ascorbate on VEGF in vivo. RESULTS. In cultured ARPE-19 cells, treatment with ascorbate (50 µM) induced 5hmC generation and led to differential 5hmC levels throughout the genome, as revealed by hMeDIP-seq. This shift in the hydroxymethylome was accompanied by differential expression of 3,186 genes, as revealed by RNA-seq. One of the most downregulated genes was VEGFA, the gene encoding VEGF protein. Consequently, the translation and secretion of VEGF are decreased by ascorbate treatment. The suppression of VEGF is independent of HIF-1α and of antioxidant effects, but corroborates with increased 5hmC in the gene body. The downregulation of VEGF expression by ascorbate was further validated in both RPE-J cells and primary human fetal RPE (hRPE). Furthermore, we found that supplementation of ascorbate in Gulo−/− mice, which are dependent on exogenous ascorbate, also downregulated VEGF levels in the vitreous. CONCLUSIONS. These results support the notion that ascorbate suppresses VEGF through a
5hmC-mediated epigenetic pathway. Our findings provide experimental basis for using ascorbate to treat or prevent wet AMD.

**ELUCIDATING THE GENETIC UNDERPINNINGS OF MULTIPLE SCLEROSIS IN U.S. MINORITY POPULATIONS**

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*Introduction:* Multiple Sclerosis (MS) exhibits variable prevalence across populations, with European populations having a higher prevalence than either Hispanic or African. In addition to environmental influences, this observation could be partly due to a greater genetic risk in European populations. Genetic association studies in individuals of European descent have identified 200 established MS risk variants in 153 loci outside of the Major Histocompatibility Complex. Our goal was both to replicate these loci in genetically admixed samples from Hispanic and African American populations as well as to use local ancestry to identify novel loci which may be related to MS.

*Methodology:* Genotype data from the custom Illumina ‘MS Chip’ were available on Hispanic (1398 cases, 1386 controls) and African American (1305 cases, 1155 controls) samples, and on the fine-mapping Illumina ImmunoChip for a subset (Hispanics: 187 cases, 47 controls; African Americans: 973 cases, 1354 controls). The ‘MS Chip’ was used for replication and the ImmunoChip to assess novel loci, due to the design of the arrays. Local ancestry was computed with RFMix, after first phasing the haplotypes using Beagle. Global ancestry was computed by averaging local ancestry estimates across the genome. Reference data for African and European populations were taken from the 1000 Genomes and for the Native American population from the Human Genome Diversity Project. Separately in Hispanic and African American samples, logistic regression was used to test for the association of each of the established variants with MS risk after adjustment for global ancestry. Likewise, using the ImmunoChip, the association of MS risk with the number of European and Asian haplotypes observed at each position was assessed, after controlling for global ancestry.

*Results:* In Hispanics, 62 of 153 established loci replicated (41%) and in African Americans, 23 of 153 loci replicated (15%) with one-sided p < 0.05. In both the Hispanic (6.35E-02) and African American (p = 3.69E-04) samples we find evidence of a decreased number of European haplotypes in cases at the NOD2 locus (a well-known Crohn’s disease locus; novel to MS), indicating NOD2 as a potential loci for MS with an African specific risk haplotype.

*Conclusions:* These results highlight the utility of previously established MS risk loci in U.S. minority populations and establish the value of local ancestry evaluation in admixed populations to potentially identify novel MS loci.

**GENE-BASED BURDEN ANALYSIS DECIPHERS GENETIC ARCHITECTURE OF INHERITED PERIPHERAL NEUROPATHIES**

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*Introduction:* Inherited peripheral neuropathies, also known as Charcot-Marie-Tooth (CMT) disease, are rare, clinically and genetically heterogeneous diseases that lead to distal muscular atrophy and sensory loss. Mendelian high-penetrance alleles in one over hundred different genes have been shown to cause CMT; yet, more than 50% of patients with the axonal type of CMT do not receive a genetic diagnosis. A more comprehensive spectrum of genes and alleles is warranted, including causative and risk alleles. Exome studies in the international Inherited Neuropathy Consortium are beginning to be sufficiently powered to perform gene-based rare variant burden analysis.

*Methods:* Our approach compared the frequency of damaging alleles at the gene unit in exomes of 343 CMT cases and 935 controls. We tested 17,637 protein coding loci for association using the C-alpha test. *Results:* After filtering results by the PLINK/SEQ i-statistic and applying Bonferroni multiple-testing correction, three genes, KDM5A (p-value= 9.9x10^{-7}, OR=3.6), EXOC4 (p-value= 6.9x10^{-6}, OR=2.1), and CEP78 (p-value=...
2.3x10^{-5}, OR=4.4), reached experiment-wide significance ($p$-value=$2.3x10^{-5}$, $\alpha=0.05$). Interestingly, several known CMT genes achieved nominal $p$-values <0.05, serving as a ‘positive control’ for the ability of this approach to identify both risk and causative genes. We are currently performing molecular genetics and cell biology follow up studies and also working towards enlarging our sample size. **Conclusions:** In summary, statistical methods, traditionally reserved for more ‘common’ phenotypes, are becoming increasingly available for rare disease genetics such as CMT and will help to comprehensively define the genetic architecture of complex rare neurodegenerative disorders.
ORAL PRESENTATIONS IV
FEBRUARY 22, 2018
3:00 PM – 5:45 PM
MODULATION OF BDNF-TRKB INTERACTIONS ON SCHWANN CELL-INDUCED ORAL SQUAMOUS CELL CARCINOMA DISPERSION IN VITRO

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Introduction: Perineural invasion (PNI) is a significant pathological feature in head and neck cancer. The molecular mechanisms of PNI are poorly understood. Contrary to previous belief that cancer cells invade nerves, recent studies have shown that Schwann cells (SC) can dedifferentiate, intercalate between cancer cells, and promote cancer dispersion. Communication between cells through brain-derived neurotrophic factor (BDNF) activation of TrkB-receptor may contribute to these cellular events. Our study aimed to determine direction of cell migration and degree of SC-induced cancer dispersion in vitro, and to determine the effect of TrkB-receptor inhibitor (ANA-12) on SC migration, intercalation into cancer clusters, and dispersion of cancer. Methods: Levels of BDNF and TrkB-receptor in both Schwann and cancer cell-lines were determined using a Western Blot. An in vitro model of Schwann cell and cancer cell interaction was created by performing a spheroid-migration cell invasion assay with mouse oral squamous cell carcinoma (B4B8 cell-line) and rat SCs (infected with lentiviral green fluorescent protein vectors). There were four internal controls (SC only, B4B8 only, SC+ANA-12, and B4B8+ANA-12) and two experimental groups (SC+B4B8 and SC+B4B8+ANA-12). After four days in co-culture, the number of SC-induced cancer cell dispersion and direction of cell dispersion were measured. Mann Whitney U and Kruskal Wallis test with multiple pairwise comparisons were performed. Results: Cancer cells expressed higher levels of BDNF and TrkB-receptor compared to SCs. When cultured independently, there was random migration of cancer cells and SCs. When cultured together, SCs preferentially migrated towards cancer; however, there was minimal SC-induced cancer dispersion. In the presence of TrkB-receptor inhibitor (ANA-12), there was less migration of cancer cells. When there was contact of cells, more SC-induced cancer dispersion was seen (p<0.05). Conclusions: These results demonstrated that SCs are motile, migrate towards cancer cells, and have the unique ability to intercalate between and disperse cancer cells. BDNF and TrkB interactions can modulate SC response to cancer cells. Understanding the role of SCs and neurotrophic factors in promoting PNI has important implications for therapeutic intervention.

PHARMACOKINETICS OF HUMAN RED BLOOD CELL MICROPARTICLES INTENDED FOR USE AS A HEMOSTATIC AGENT

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Introduction: Red cell derived microparticles (RMPs) have been investigated to identify their efficacy as a hemostatic agent. Their capacity to accelerate fibrin formation and reduce bleeding time without expressing tissue factor makes them an ideal conduit to elicit controlled clotting at the site of endothelial injury. These cumulative effects suggest that RMPs would be suitable to treat various bleeding disorders including hemorrhagic stroke and brain trauma. Thorough preclinical evaluation is necessary prior to assessing this treatment in a clinical setting. Methods: Size, purity, stability, and pharmacokinetic activity of RMPs were assessed in vitro and in a rat model. High-pressure extrusion was used to isolate RMPs from Type O+ human red blood cells. Purity of RMPs was determined by comparing CD235a-positive cells to markers for leukocyte and platelet microparticles using flow cytometry. Annexin V-positive particles were quantified as a surrogate marker for phosphatidylserine to indicate procoagulant activity. Size was evaluated using two methods including flow cytometry and the Doppler electrophoretic light scattering analysis (DELSA) method. Particle stability (size, RMP counts, and procoagulant activity) was assessed for five storage conditions of varying temperature and relative humidity. Procoagulant activity was assayed in vitro by thromboelastography. Male rats were used for in vivo assessment of pharmacokinetic activity; RMPs were administered into the femoral vein in various dosing regimens, and blood samples were taken at several intervals to determine pharmacokinetic parameters. Results: Purity assessment showed that 99.98±0.002% of particles were RMPs and a miniscule percent were leukocyte or platelet microparticles. The ratio of CD235a-positive/annexin V-positive particles was 1.6, indicating robust procoagulant activity. DELSA revealed roughly 75% of particles to have a diameter between 0.05 and 1.18µm, signifying that RMPs will not obstruct blood flow through capillaries. RMPs were observed to accelerate fibrin formation in vitro with increasing concentrations of particles. The stability of RMPs remained around 70% of baseline activity for 12 months at -20°C, and above 80% of baseline for 9 months when stored at 5°C; the activity of all other storage conditions declined after 3 months. Blood plasma concentrations of RMPs >25% of the
target therapeutic concentration (ED80 = 6×10^7 particles/mL) was attained in every treatment regimen. In vivo evaluation showed the half-life to be brief, averaging <90 seconds. **Conclusion:** These results collectively indicate that RMPs remain stable and retain procoagulant properties over a prolonged period. Their short half-life and ability to accelerate fibrin formation makes them an ideal agent to briefly elicit hemostasis at the site of tissue injury without undesirable prolonged thrombosis. These results build on earlier research identifying RMPs as a promising hemostatic agent and propose a potential benefit for treating bleeding disorders.

**CHARACTERIZING PTGER4 AS A TARGET GENE OF AUTISM PROTEIN E6AP**

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**Introduction:** ASD has been found to be associated with duplication or triplication of the UBE3A gene, which encodes for E6-associated protein (E6AP, an E3 ubiquitin ligase and transcriptional coactivator). However, the few E6AP ubiquitination substrates found do not explain ASD pathology. This study tests the hypothesis that deregulation of E6AP-mediated steroid hormone receptor transcriptional signaling in the brain leads to the development of ASD. The project aims are to identify steroid hormone-dependent E6AP target genes in neurons and to study the role of these target genes in the pathogenesis of ASD. **Methods:** Potential E6AP target genes were identified by microarray of MCF-7 breast cancer cells. Cells from the mouse neuroblastoma Neuro2a cell line were cultured. Cells were transfected with E6AP or had E6AP knocked down by siRNA and then were treated with physiologically relevant doses of estrogen, the estrogen receptor antagonist tamoxifen, or vehicle. Assays included western blot, co-immunoprecipitation, qRT-PCR, and microscopy. **Results:** The learning and memory gene for prostaglandin E receptor 4, PTGER4, is an E6AP-dependent target gene that is downregulated in the presence of E6AP or estrogen. **Conclusion:** We have identified a memory and learning gene that is regulated by E6AP and E2-dependent: PTGER4. This is evidence that PTGER4 may be altered in ASD, leading to learning and memory symptoms. PTGER4 allows phosphorylation of glycogen synthase kinase 3 (GSK3). GSK3 has a large role in apoptosis and has been implicated in neuropsychiatric disorders such as Alzheimer's disease and bipolar disorder. Given that GSK3 is amyloidogenic and ASD patients exhibit increased beta amyloid deposition, increased E6AP leading to decreased PTGER4 may lead to decreased inhibitory phosphorylation of GSK3. In a case study, the GSK3 inhibitor ketamine actually improved an adult ASD patient's symptoms, supporting this theory. Further experiments will be necessary to confirm these promising findings.

**THE PROLINE-ARGININE DIPEPTIDE REPEAT PROTEIN BINDS TO NUCLEOPHOSMIN AND IMPEDES DNA DAMAGE REPAIR IN C9ORF72-RELATED ALS/FTD**

**Nadja Andrade**, Rustam Esanov, Wenjun Liu, Samuel Del’Olio, Michael Benatar; Yan Bin Zhang, Claes Wahlestedt, Zane Zeier; The Center for Therapeutic Innovation and Department of Psychiatry & Behavioral Sciences, University of Miami Miller School of Medicine, Miami FL, 33136, Department of Biochemistry and Molecular Biology, University of Miami Miller School of Medicine, Miami FL, Department of Neurology, University of Miami Miller School of Medicine, Miami FL

**Introduction:** The C9ORF72 hexanucleotide repeat expansion (HRE) mutation is the most common known genetic cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Translation of HRE sense and antisense RNAs produces several dipeptide repeat (DPR) proteins. The proline-arginine (PR) DPR co-localizes with nucleophosmin (NPM1), a multifunctional nucleolar protein that binds ribosomal RNA, facilitates DNA damage repair, and has been implicated in C9ORF72 ALS. In this study, we sought to determine whether PR toxicity results from its interaction with NPM1. **Methods:** To determine which NPM1 domain might be responsible for binding to PR, we generated NPM1 mutants fused to GFP. The degree of PR-NPM1 co-localization was assessed by fluorescent microscopy and immunoblotting of subcellular fractions. To determine whether PR impedes NPM1-mediated DNA repair, the efficiency of specific double strand break repair pathways in the presence of PR was assessed by cell sorting using site-specific endonuclease-induced DNA break repair assays. Induced pluripotent stem cells (iPSC) motor neurons were subjected to genomic editing to excise the HRE mutation in order to determine its effects on DNA damage in patient derived motor neurons. Finally, we used an automated high content imaging based screen to identify epigenetic small molecules that might reduce DNA damage in cells expressing PR. **Results:** We found that PR binds
directly to the acidic loop of NPM1 and that ectopic expression of PR increases DNA damage which enhanced when nucleophosmin is depleted. More specifically, we found that PR significantly impedes single strand annealing DNA repair. Finally, we found that AK-7, a neuroprotective Sirtuin-2 inhibitor ameliorates PR induced DNA damage.

**Conclusion:** We found that PR binds directly to NPM1, increases DNA damage and decreases DNA damage repair. Activation of apoptotic signaling resulting from DNA damage likely contributes to neurodegeneration in C9ALS, which may be mitigated by AK-7.

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**4:00 pm  FOXA2 PROMOTES PROSTATE CANCER BONE COLONIZATION**

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**Introduction:** It is estimated that 26,000 men will die from prostate cancer (PCa) in 2017. Androgen deprivation therapy (ADT) is the gold standard treatment for advanced PCa. Initially, patients respond to treatment, however, these tumors almost invariably progress to castrate-resistant PCa, for which there is no cure. Most PCa patients who fail ADT develop metastasis and preferentially relocate to the bones. Bone metastasis results in significant morbidity and mortality as the average time to death is approximately 3-5 years with no treatment available. Understanding the mechanisms by which PCa grow in the bone is critical for the development of novel therapeutics to treat and decrease tumor-mediated bone destruction.

**Methods:** Gene expression profiling studies have found that FOXA2, a forkhead transcription factor that is expressed in embryonic prostate and neuroendocrine PCa, is present in a subset of metastatic PCa specimens. Our preliminary study found FOXA2 expression in a sample set of human PCa bone metastases, suggesting an involvement of FOXA2 in human PCa bone metastases. Also, we found high levels of FOXA2 in aggressive PCa PC3 cells, but not in PCa LNCaP cells. PC3 cells generate osteolytic lesions in bone, whereas LNCaP cells minimally grow following bone inoculation. To establish FOXA2’s role in promoting PCa metastasis, FOXA2 was stably knocked down in PC3 cells and overexpressed in LNCaP cells. **Results:** We found that FOXA2 knockdown in PC3 cells resulted in a significant decrease in PC3 mediated *in vivo* bone destruction following intra-tibial injection. To understand how FOXA2 is facilitating these changes, we examined the expression of integrins and observed that FOXA2 knockdown decreased the expression of collagen-binding integrins α1 and αv in PC3 cells. Furthermore, we found FOXA2 knockdown decreased PC3 cells’ adhesion and spreading on collagen I (a major component of bone ECM) coated surfaces. The Foxa2-controlled expression of integrins α1 and αv and the resulting changes in the adherence and spreading would provide a mechanism for PCa cells colonize bone and initiate the bone-destruction cycle. Additionally, FOXA2 knockdown in PC3 cells resulted in a significant decrease in expression of parathyroid hormone-related protein (PTHrP), a bone remodeling-associated protein. We observed that PTHrP mRNA was decreased in FOXA2 knockdown cells and protein in FOXA2 knockdown subcutaneous grafts. When PC3 FOXA2 knockdown cells were co-cultured with osteoblast and osteoclast, osteoclast markers were decreased. **Conclusions:** Taken together, FOXA2 plays a major role in facilitating PCa’s ability to colonize bone, and further, promote osteoclast activation.

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**4:15 pm  A NOVEL ZEBRAFISH MODEL OF PEDIATRIC HEART FAILURE**

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**Introduction:** Dilated Cardiomyopathy (DCM) is the most common cause of heart failure and reason for cardiac transplantation in children. DCM is characterized by adverse remodeling of the left ventricle (LV), leading to decreased LV function and eventually end-stage heart disease. LV function recovery correlates with improved quality of life and long-term survival. However, the mechanisms of cardiac recovery are poorly understood, and novel pediatric heart failure therapeutics remain elusive despite decades of research. **Methods:** To identify causative mechanisms underlying pediatric heart failure, we developed a zebrafish (*D. rerio*) model of heart failure (*corazoncito*) that was generated through an N-ethyl-N-nitrosourea (ENU) mutagenesis screen. We phenotypically characterized *corazoncito* using standard markers of heart failure, and we used next-generation sequencing to identify the *corazoncito* mutation, which was verified through recapitulation of the mutant. Student’s t test or ANOVA was used for comparisons between groups, with P-values of less than 0.05 considered significant. **Results:** Morphologic and histological examination of heart failure mutants revealed marked reduction in cardiac hyperplasia, increased cardiomyocyte hypertrophy and normal patterning of the atrium, ventricle and outflow tract. Next-generation sequencing mapped the *corazoncito* nonsense mutation to exon 3 of *taf5*, an evolutionarily conserved and poorly
understood regulatory subunit of TFIID. CRISPR-Cas9-generated taf5 knockout (taf5) fish were not only phenotypically identical to corazoncito fish, but also they failed to complement when crossed with corazoncito fish. Gene expression patterns of both corazoncito and taf5 fish paralleled expression patterns seen in established heart failure models. **Conclusion/Discussion:** Together, these data suggest a role for taf5 in pediatric heart development and function. The specific nature and mechanism of taf5’s role in heart development and function remains unclear and hence, additional inquiry is necessary. Furthermore, the conservation of heart developmental pathways – and heart pathology – between zebrafish and humans provides the opportunity to use zebrafish models like corazoncito as discovery systems for identifying novel players and therapies for pediatric heart failure.

4:30 pm  
**NUCLEOLAR ELECTRIC SWITCH ACTIVATES AN AMYLOIDOGENIC PROGRAM OF PHYSIOLOGICAL PHASE TRANSITION**

**Miling Wang,** Xianzun Tao, Mathieu D. Jacob, Clayton A. Bennett, Mark L. Gonzalgo, Timothy E. Audas and Stephen Lee, Department of Biochemistry and Molecular Biology, Sylvester Comprehensive Cancer Center, Department of Urology at Miller School of Medicine, University of Miami, FL, Department of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada, Department of Molecular Biology and Biochemistry, Simon Fraser University, Burnaby, Canada

**Introduction:** The concept of phase transition in biology between gas, liquid and solid states of matter has recently been suggested to drive formation of cellular membrane-less compartments. Cellular liquid bodies include the nucleolus, nuclear speckles and cytoplasmic stress granules. Amyloid-bodies (A-bodies) are membrane-less nuclear compartments composed of immobilized proteins that exhibit solid or amyloid-like properties. Physiological amyloidogenesis enables cells to store large quantities of different proteins and enter a dormant state in response to stressors. The molecular mechanisms that target and convert native-fold proteins into A-bodies are currently under investigation. **Methods:** We used live cell microscopy techniques to follow changes in GFP-tagged protein dynamics and mobility on stress such as heat shock and acidosis. We performed RNA-sequencing and silencing experiments to interrogate the RNA and protein interactions involved in A-bodies formation. **Results:** Here, we show that cells manipulate nucleolar electric potential to activate a physiological amyloidogenesis program that transitions proteins across phase boundaries. On stimulus, clusters of chromatin-associated ribosomal intergenic spacer RNA (rIGSRNA) act as electric scaffolds that initiate liquid phase condensation and denaturation of proteins in nucleoli. The denatured proteins capable of forming strong amyloidogenic bonds undergo liquid-to-solid transition to form nascent A-bodies. Once seeded, A-bodies expand or dissolve by amyloidogenic propagation or chaperone-assisted disaggregation, respectively. The Amyloid-Converting Motif (ACM) is a β-amyloid-like motif that senses electric intensity to transition proteins between gas-like, liquid and solid states. Exogenous polyanions prevent phase transition in nucleoli and elicit the formation of aberrant cytoplasmic amyloid aggregates. **Conclusion:** We suggest that cells have evolved rIGSRNA/ACM as a physiological multi-phasic system that switches molecules between different states of matter. The next step will consist of understanding if alterations in rIGSRNA/ACM-assisted cellular phase transition programs can explain amyloid diseases.

4:45 pm  
**WFA INHIBITS EMT IN RENAL TUBULAR EPITHELIAL CELLS BY INHIBITING PROPER VIMENTIN ASSEMBLY**

**Tigran Divanyan,** Zhen Wang, Reynold Lopez-Soler Dept. Of Cellular and Molecular Physiology, Division of Surgery, Section of Transplantation, Albany Medical College, Albany, NY, 12208

**Introduction:** Around 20-30% of renal allografts fail ten years post-transplant, a number unchanged since 1989. Most renal transplants fail secondary to interstitial fibrosis and tubular atrophy (IFTA). Epithelial to mesenchymal transition (EMT) is a precursor to IFTA in renal transplants. Vimentin, an intermediate filament family protein, is a characteristic marker of EMT. However, it is unknown whether the development of a vimentin-based cytoskeleton or whether vimentin signaling alone is required for the progression EMT in renal epithelial tubular cells. Withaferin A (WFA) is a steroidal lactone concentrated in the *Withania somnifera* plant, and has been shown in previous studies to bind to and alter the assembly and distribution of vimentin intermediate filaments. Therefore, this study is aimed to elucidate whether WFA will prevent EMT and subsequent IFTA in renal tubular epithelial cells by prohibiting proper vimentin assembly. **Methods:** Cultured human proximal renal tubular (HK-2) cells were treated with TGF-B in order to induce EMT, and were then treated with 5 uM of WFA. Western blot analyses and wound-healing assays were used to track the development of EMT and changes in EMT related protein expression. In addition, vimentin knockout and wildtype
mice underwent a Unilateral Ureter Obstruction (UUO) to induce fibrosis. Mice were sacrificed at one, two, and four-week timepoints and their kidneys were subject to immunofluorescence staining for EMT related proteins as well as immunohistochemistry and Masson’s Trichrome staining for Collagen Type I. Statistical significance was assessed through t-tests, with a p-value less than 0.05 being considered statistically significant. **Results:** Immunofluorescence showed a substantial increase in vimentin expression in wildtype mice, as well as differential translocation of EMT-related protein B-catenin in vimentin knockout mice two weeks post UUO. Immunohistochemistry demonstrated significantly less collagen deposition in vimentin knockout mice compared to wildtype mice. WFA treatment resulted in a decrease of assembled vimentin filaments as well as increased retention of the epithelial marker, E-cadherin. Wound-healing assays revealed decreased cell motility and increased retention of epithelial morphology in WFA treated cells. **Conclusions:** Increased vimentin expression and mesenchymal differentiation propagates collagen deposition and IFTA in vivo. Also, WFA administration decreases vimentin filament assembly and aids in retention of epithelial morphology in vitro. These results provide insight into the possible therapeutic role of WFA in slowing the progression of IFTA. Future experiments will further define the mechanism of WFA inhibition of EMT. The use of WFA as a therapeutic modality will be tested in a mouse renal fibrosis model and rat renal transplant model.

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**CHARACTERIZATION AND OPTOGENETIC MANIPULATION OF THE AFFECTIVE ITCH CIRCUIT IN MOUSE MODELS OF ITCH**

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**Introduction:** Chronic itch is a common symptom that is often accompanied by negative emotional states like anxiety. These emotions greatly impair quality of life for chronic itch patients and may worsen itch severity as well. However, there is currently a poor understanding of itch-related emotions and their central mechanisms. Using mouse models, we aimed to 1) establish the effects of acute itch on anxiety-like behavior, 2) assess activation of a potential affective itch circuit in the brain, and 3) selectively stimulate itch-responsive amygdala neurons and observe effects on itch- and anxiety-related behavior. **Methods:** Intradermal injection of histamine, chloroquine, or serotonin provokes robust scratching (itch-related behavior) in mice through different signaling pathways in the skin and spinal cord. We tested whether injection of these chemicals induces anxiety-like behavior in mice using the elevated plus maze (EPM) and the open field test (OFT). Next, we assessed whether injection of histamine, chloroquine, or serotonin alters activity in key anxiety-related brain areas. Immunohistochemistry was used to label c-Fos, a marker of neuronal activation, in the amygdala, lateral parabrachial nucleus, and medial prefrontal cortex. Finally, we used the Targeted Recombination in Active Populations (TRAP) system to specifically induce Cre recombinase in histamine-responsive neurons. TRAPping of PBS-responsive neurons was used as a control. By bilaterally injecting AAV-FLEX-CHRONOS-GFP to the amygdala in these mice, we induced expression of Chronos, a fast opsin that causes neuronal activation under blue light, in the TRAPped cells. We assessed anxiety-like behavior (EPM and OFT) and itch-related behavior (scratch response to histamine and chloroquine injection) with and without optic stimulation of TRAPped amygdala neurons. **Results:** Histamine, chloroquine, and serotonin injections induced anxiety-like behavior as indicated by reduced open arm time on the EPM and increased percent center entries on the OFT (p<0.05, t-test chemical vs. vehicle). These chemicals also induced substantial activation of the amygdala as measured by increased number of c-Fos+ cells. Moderate changes were observed in other brain areas. Optic stimulation of itch-responsive neurons increased anxiety-like behavior in the EPM and OFT and enhanced the scratch response to histamine and chloroquine injection (p<0.05, ANOVA followed by Bonferroni). Stimulation of PBS-responsive neurons had no significant effect on behavior. **Conclusion:** Our research is the first to identify key brain regions of the affective itch circuit. Our results suggest that itch-signaling cells in the amygdala are key regulators of the emotional component of itch and can influence itch-related anxiety and scratching. Further research could uncover new pathways of central itch processing and potentially provide new targets to break the itch-anxiety cycle and thereby treat chronic itch and its related affective symptoms.
SCREENING OF T CELL ANTIGENS IN THE SKIN OF C3H/HEJ MOUSE MODEL OF ALOPECIA AREATA

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Introduction: Alopecia areata (AA) is a non-scarring cell mediated autoimmune inflammatory disease of the hair follicle (HF). In most AA patients, histopathological examination reveals dystrophic anagen stage hair follicles that are surrounded by a peri- and intra-follicular inflammatory cell infiltrates, consisting primarily of CD4+ and CD8+ T cells. Due to this AA is believed to be a disease that primarily targets anagen HFs, though this has not been confirmed. We hypothesize that anagen HFs are preferentially targeted, leading to the destruction of active growing hair follicles. As such anagen HFs may contain a reservoir of specific autoantigen epitopes that can induce the activation of T cells.

Methods: Here, we present an unbiased screening approach to assess whether anagen HFs are being targeted and to identify the autoantigen epitopes in the AA mouse model. We isolated skin-draining lymph node cells (LNCs) from AA-unaffected and AA-affected C3H/HeJ mice (induced via adoptive transfer of cultured cells) and extracted protein homogenate from anagen and telogen skin. LNCs were cultured with protein homogenate and assessed for T cell activation via IFNg ELISpot assays. Individual fractions of proteins separated by column chromatography are being analyzed individually. Protein identities from fractions with positive responses will be identified with mass spectrometry and epitope peptides will be predicted with publicly available MHC binding algorithms.

Results: Our initial results show that anagen skin protein homogenates were able to induce a higher frequency of T cell activation in both AA and unaffected mice, showing that T cells are more activated by anagen HFs than telogen HFs. This also further emphasizes that epitopes derived from anagen-specific proteins are targeted by T cells. We are testing more mice to be able to validate this result further.

Conclusion: We have identified that anagen skin/HFs are able to induce greater frequency of T cell activation, confirming that this is an anagen stage disease and indicating the presence of autoantigens in the anagen hair phase compared to the telogen phase. Specifically, when fractionated by column chromatography we found that anagen fraction 3, which contains molecules with larger molecular weight, is more likely to induce an immune response. Potentially this is due to the fact that larger proteins have more possible configurations of peptides that are able to shown to the T cells. Further characterization of the protein contents will be done and this phase is still ongoing. Successful identification of autoantigen epitopes would facilitate rational development of better, more efficient, cell-specific therapies.
POSTER PRESENTATIONS
FEBRUARY 23, 2018
9:00 AM – NOON
1 CD9 AND CD9P-1 MEDIATE GROWTH AND RADIATION RESISTANCE IN Glioblastoma Multiforme

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Introduction: Glioblastoma multiforme (GBM) is the most malignant primary brain tumor with a median survival of approximately 14 months. Despite aggressive treatment of surgical resection, chemotherapy and radiation therapy, only 3-5% of GBM patients survive more than 3 years. Contributing to this poor therapeutic response, it is believed that GBM contains both intrinsic and acquired mechanisms of resistance, including resistance to radiation therapy. In order to define novel mediators of radiation resistance, we conducted a functional knockdown screen, and identified tetraspanin CD9 and its molecular partner, CD9P-1. Tetraspanins, a family of 4 transmembrane proteins, organize laterally with themselves and other membrane proteins to form enriched microdomains, where they can influence cell migration, invasion, cell-cell fusion, survival and signaling events. Therefore, we hypothesize that CD9 and CD9P-1 may be mediating resistance to radiation in GBM. Methods: In order to address the roles of CD9 and CD9P-1 in GBM radiation resistance, we performed several assays, including clonogenic survival assays, cell proliferation assays, and HR reporter assays, utilizing shRNA and siRNA to specifically target CD9 and CD9P-1. Results: In clonogenic survival assays, CD9 and CD9P-1 was found to provide protection from ionizing radiation in GBM cells. Additionally, altered DNA repair response in CD9 and CD9P-1 knockdown cells compared to shGFP control was determined. Furthermore, reducing CD9 and CD9P-1 expression potently decreased the rate of cell proliferation, as shown by cell proliferation assays, and tumor growth in vivo. CD9 has also been shown to regulate EGFR signaling, and in biochemical studies, it was observed that inhibition of CD9 or CD9P-1 results in significant reduction in basal phosphorylated Akt levels. Conclusion: These findings may suggest CD9 and CD9P-1 as potential mediators of growth and radioresistance in GBM cells via mitogenic signaling.

2 THE ROLE OF TWIN CX9C PROTEINS IN COPPER DELIVERY FOR COMPLEX IV IN HUMAN CELLS

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Introduction: The mitochondrial respiratory chain is composed of four respiratory complexes that generate a proton gradient later used to generate ATP. Complex IV, also called Cytochrome c Oxidase (COX), is the terminal enzyme of this respiratory chain. It is formed by 14 subunits of dual origin. Three catalytic subunits (COX1, COX2, and COX3) are encoded by mitochondrial DNA, and the other 11 are encoded by nuclear DNA. COX1 and COX2 contain metal centers, which accept electrons from Complex III and transfer them to oxygen. The COX1 subunit contains two metal centers, heme a and copper (CuB). The redox state of coordinating cysteines in proteins transporting copper is crucial for the function of these proteins. COX1 assembly factors COX19, PET191, COX23, and CMC1 belongs to a family of proteins with twin Cysteine-X9-Cysteine (CX9C) motifs. However, in mammalian cells, their role in copper transport is unclear. Therefore, our aim is to investigate the role of twin-CX9C motif proteins in copper transport and delivery to COX1. Methodology: Using mitochondria from HEK293T wild-type cells, the native redox state of cysteines in selected twin-CX9C motif proteins (PET191, COX23, CMC1 and COX19) will be used to repeat the above procedure, allowing for investigation of the entire COX1 copper insertion architecture. Results: The shift in molecular mass has been established in CMC1 protein of wild type cells. Now the treatment conditions for COX23 and PET191 are being determined. After conditions are optimized, the native cysteine state in these proteins will be established. Conclusion: It is likely that COX23, PET191, and COX19 are present in the mitochondria intermembrane space in a state in which their cysteines are protected from TCEP. This could be a protein complex, a binding state in which the cysteine is not accessible to TCEP. Once experimental conditions are optimized for COX19, COX23, and PET191, investigation will proceed into cysteine redox states in proteins of interest in knock out cell lines.
DEUBIQUITINATING ENZYME USP24 STABILIZES G2/M CHECKPOINT

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Introduction: DNA Damage Response (DDR), a network of pathways that integrates DNA integrity with cell division, is critical for proper genome maintenance and tumor suppression. Cell cycle checkpoints lie at the heart of DDR by pausing the cell cycle to scan for DNA damage and recruit necessary repairs, thereby preventing transmission of damaged DNA and mutagenesis. Previously we have shown that the novel enzyme USP24 deubiquitinates and stabilizes p53 protein levels, thereby leading to apoptosis resistance and an elevated mutation frequency. Our previous studies suggest that USP24 plays an important role as a tumor suppressor and this study seeks to further characterize the role of USP24 as a modulator of DDR by examining how it influences cell cycle checkpoint activity. Methods: DDR was induced by treatment with doxorubicin. This study quantified cell proliferation directly by cell counting, as well as indirectly by means of cell proliferation markers WST-1 and crystal violet staining. This study also examined rates of progression through cell cycle checkpoints via double thymidine block synchronizations and release. Additionally, regulation of G2-M transition proteins was investigated by Western Blotting. Results: In this study we identify that USP24 plays an additional role in DDR by regulating the G2/M checkpoint of the cell cycle, likely in part through its stabilizing effect on p53. We show that USP24 depletion causes increased cell proliferation, decreased percentage of cells residing in G2/M phase, as well as faster entry into G2/M phase and increased accumulation of cells in G2/M phase under DNA damaging conditions. Additionally, we report that phosphorylation of Tyrosine 15 on the classic G2 checkpoint regulator, CDK1, is downregulated when USP24 is depleted. Conclusion: USP24 represses overactive cell proliferation and is required for cell cycle arrest at the G2/M checkpoint. By modulating the G2/M cell cycle checkpoint which prevents propagation of damaged cells with compromised genomic integrity, our data further supports the role of USP24 as an important tumor suppressor.

BRANCH ANALYSIS 2D/3D: AN AUTOMATED ALGORITHM FOR MORPHOMETRY ANALYSES OF BRANCHING STRUCTURES

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Introduction: Morphometric analyses of biological features have become increasingly common in recent years with such being subject to a large degree of observer bias, variability, and time consumption. While commercial software packages exist to perform these analyses, they are expensive, require extensive user training, and are usually dependent on the observer tracing the morphology. Aim: To address these issues, we have developed a broadly applicable, easy-to-use, and a no-cost ImageJ plugin to perform morphometric analyses of structures with branching morphologies including neuronal dendritic spines, vascular morphology, and primary cilia. Methods: Observers analyzed sample images (from neuronal dendritic spines, retinal vasculature, and primary cilia) using already existing software packages (Neurolucida, AngioTool, and ImageJ respectively) as well as BranchAnalysis2D/3D. One observer performed the analysis on two days to account for intra-observer variability. The observer’s output (total spine density and spine distribution, blood vessel length and diameter, cilia length and number) and time taken for analysis were compared to the output and analysis time of BranchAnalysis2D/3D. Results: BranchAnalysis2D/3D allows for rapid quantification of the length and thickness of branching morphologies in both 2D and 3D data sets independent of user tracing. We validated the performance of our algorithm against trained human observers using pre-existing software packages in images from tissue, and find that our algorithm outputs similar results as available software, but allows for faster analysis times and unbiased quantification. Conclusion: As such, this algorithm allows inexperienced observers to output results similar to the output of more trained observers efficiently, thereby increasing the consistency, speed, and reliability of morphometric analyses.
THE EFFECTS OF PERIODONTAL LIGAMENT STEM CELL CONDITIONED MEDIUM ON INFLAMMATORY GENE EXPRESSION OF IL-1B TREATED CHONDROCYTES

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Introduction: Degeneration of cartilaginous tissues often results in major clinical problems, such as osteoarthritis, low back pain and temporomandibular disorder. These clinical issues afflict millions of people and represent a significant health and economic concern in the United States. For this reason, multiple avenues of research are exploring treatment options to prevent the degeneration of cartilaginous tissues. One such avenue to prevent degeneration may be through the introduction of growth factors, exosomes and other secretions of mesenchymal stem cells into diseased joints. Mesenchymal stem cells (MSCs) are immune-privileged adult stem cells which have a well-established capacity for mesodermal differentiation, including chondrogenesis. Accumulating evidence suggests that secreted factors and exosomes from MSCs stimulate cell survival by inducing anti-apoptotic effects, promoting cell proliferation and suppressing inflammatory responses during tissue injury, thus promoting repair of damaged tissues. Therefore, introducing MSC-secreted factors and exosomes into diseased cartilaginous joints could be a potential treatment to prevent tissue degradation by inhibiting apoptosis and inflammation and promoting tissue regeneration. This study aims to investigate these claims using human periodontal ligament stem cell conditioned medium which contains exosomes and observing the effects on inflamed chondrocytes. Methods: Chondrocytes were taken from porcine cartilaginous tissues and interleukin-1 beta (IL-1β), a well-known inducer of apoptosis and catabolic mediator, was used as an inflammatory cytokine. The chondrocytes were separated into four groups, a negative control using concentrated medium, a positive control using conditioned medium, another using IL-1β and concentrated medium, and the treatment group using IL-1β and conditioned medium. The RNA from these four groups of cells was then extracted and PCR was used to analyze the expression of the inflammatory genes: IL-1β and TNFα. All gene expression results were measured in relation to expression of 18S, a ribosomal RNA gene used in PCR analysis due to its invariant expression. Results: IL-1β was found to increase expression of the genes IL-1β and TNFα in relation to 18S. On the other hand, the conditioned medium tended to prevent this upregulation and reduce the inflammatory gene expression of IL-1β treated chondrocytes. Since differences in gene expression among the experimental groups did not reach a significant level due to a small sample size, future research is needed to confirm the findings. Conclusion: However, these results still suggest that MSC-derived medium may provide a means to decrease gene expression of inflammatory cytokines and prevent the degeneration of cartilaginous tissues. Since the conditioned medium contains exosomes, further isolation of exosomes from the conditioned medium is necessary to discover the specific mechanism at work. Through further isolation and experimentation, mesenchymal stem cells may hold the key to a new therapeutic approach in degenerative cartilage disorders.

GREM1 IMPROVES THE REGENERATIVE POTENTIAL OF CARDIAC PROGENITOR CELLS VIA THE UPREGULATION OF THE ERK/NRF2 SIGNAL PATHWAY

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Introduction: Ischemic heart disease is the leading cause of mortality in the United States. Autologous stem/progenitor cell therapy can restore myocardial structure and function. However, its efficacy is severely limited by cell aging and senescence. Gremlin-1 (GREM1), a member of the bone morphogenetic protein antagonist family, has been implicated in cell proliferation and cell survival. However, GREM1’s role in cell aging and cell senescence has never been investigated in human cardiac progenitor cells (hCPCs). Therefore, this study aimed to test whether overexpression of GREM1 rejuvenates the cardiac regenerative potential of aging hCPCs to a youthful stage and improves the effectiveness of cell therapy. Methods: hCPCs were sorted from right atrial appendage derived cells of patients with cardiomyopathy. Lentiviral particles were used to overexpress GREM1 in aging hCPCs. Protein and mRNA expression were assessed through Western Blot and RT-qPCR. FACS analysis for Annexin V/PI staining and lactate dehydrogenase release assay were used to assess cell survival. Cell proliferation was determined through FACS analysis with BrdU incorporation. Statistical significance was assessed through t-tests, with a p value less than 0.05 being considered statistically significant. Results: Cell aging and cell senescence led to a decrease in GREM1 expression. In addition, overexpression of GREM1 led to a decrease in senescent and quiescent gene expression.
GREM1 appeared to have a cytoprotective effect, with a decrease in cell apoptosis and cytotoxicity evident in GREM1-overexpressing hCPCs. Furthermore, hCPCs that overexpressed GREM1 had an increase in cell proliferation. Overexpressing GREM1 also induced cytoprotective properties by decreasing reactive oxidative species and mitochondrial membrane potential. This result was associated with the increased expression of antioxidant proteins such as SOD2 and catalase and the activation of the ERK/NRF2 survival signal pathway, as evidenced by the increased expression of phosphorylated ERK and NRF2. **Conclusions:** Taken altogether, these results indicated that overexpression of GREM1 can coerce aging hCPCs to adopt a more robust phenotype with increased proliferation, improved survival, and decreased senescence. Future work will include confirmation of the mechanism by inhibiting the ERK/NRF2 signal pathway and subsequently evaluating whether GREM1-mediated rejuvenation is diminished. Overall, this study established GREM1 as a promising target that can rejuvenate aging hCPCs and enhance the effectiveness of cardiac stem/progenitor cell therapy for ischemic heart disease.

7 **NOVEL MECHANISMS OF Wnt-INDUCED NEURITE GROWTH IN RETINAL GANGLION CELLS**

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**Introduction:** Wingless-type (Wnt) signaling plays important roles in regulating neuronal survival and axonal regeneration in the adult CNS after injury. Previous studies using axonal injury in various model systems showed that Wnt ligands activate signaling pathways in both non-neuronal cells and neurons during axonal growth. However, the cellular mediators of the regenerative effect of Wnt in the retina are unclear. Additionally, the molecular mechanisms of Wnt3a-mediated RGC axonal growth remain unknown. A commonly used model of axon regeneration is neurite growth in cultured RGCs. In this study, we tested the hypothesis that Wnt signaling induces RGC neurite growth through the activation of intrinsic signaling pathways. **Methods:** Mouse primary RGC cultures were obtained at PN12, and incubated with increasing concentrations of Wnt3a ligand to induce Wnt signaling. Additionally, RGCs were treated with Wnt inhibitor Dickkopf-related protein 1(Dkk1), Wnt3a+Dkk1, PBS (vehicle control) or the receptor-interacting serine/threonine-protein kinase 1 (Ripk1) inhibitor Necrostatin-1. RGC neurite growth was quantified by measuring length and number of the beta-tubulin-positive neurites. Ripk1 and Ripk3 expression was measured using qPCR. **Results:** Wnt3a induced significant dose-dependent increases in average neurite length (up to 134.8 um ± 5.8) compared to controls (35.5 um ± 12.6) and increased the number of neurites per cell (up to 5.1± 0.45) compared to controls (1.9 ± 0.73, n=3-6, p<0.05). Dkk1 blocked Wnt3a-induced neurite growth (n=3, p<0.05). Furthermore, significant reductions of Ripk1 and Ripk3 transcripts were associated with Wnt-dependent neurite growth (n=4, p<0.05), and inhibiting Ripk1 signaling lead to increased neurite numbers per cell (50% increase, n=4 p<0.05), but not increased neurite length. **Conclusions:** Wnt3a induced neurite growth within RGCs in a dose-dependent manner by activating the canonical Wnt signaling pathway, indicating that RGCs are direct targets of Wnt-induced axonal growth. Furthermore, we demonstrated a novel association between Wnt signaling and Rip kinases in neurite formation.

8 **THE EFFICACY AND SAFETY OF TOFACITINIB IN THE TREATMENT OF ALOPECIA PATIENTS**

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**Introduction:** Treatments for Alopecia Areata (AA) have limited efficacy, reliability, and safety. Recently, oral immunomodulators, such as the JAK 1/3 inhibitor tofacitinib, have demonstrated potential in AA treatment. To ascertain whether they should be included in routine AA management, further studies are required to determine appropriate dosing, safety, and side effect profile in AA patients. **Methods:** In order to further comprehend the role of tofacitinib in AA management, we reviewed the records of alopecia areata patients over age 18 who had been treated with tofacitinib at CUMC. **Results:** Efficacy endpoints included change in Severity of Alopecia Tool (SALT) scores, change in percentage of hair loss, change in bloodwork, as well as side effect types and frequency. Additionally, we hope to better characterize dose response. In particular, we have found preliminary results that in certain populations, benefit may arise from induction dosing or double dosing with subsequent dose decrease after an undetermined time period. **Conclusion:** With the results of this study, we aim to ascertain the percent of hair regrowth and to optimize the tofacitinib dose and administration regimen for Alopecia Areata(AA), Alopecia Totalis (AT), and
Alopecia Universalis (AU) patients. Preliminary results have demonstrated that tofacitinib is a promising therapy for AA patients with limited adverse effects.

TARGETING DRUG RESISTANCE IN BRAF MUTANT HUMAN MELANOMA CELLS

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Introduction: Melanoma accounts for the greatest mortality rate among skin cancers in the United States. Genetic analysis has determined that 50% of melanoma patients have a common mutation in the BRAF gene. The B-Raf protein is a key mediator of the mitogen-activated protein kinase pathway (MAPK) and mutated BRAF leads to constitutive proliferation. Therapeutic agents, such as Vemurafenib, were formulated to target the BRAFV600E mutation, but recent studies have indicated that patients developed drug resistance to this treatment. This project focused on exploring alternative mechanisms that reactivate the classical MAPK pathway. One such proposed mechanism is via the p38 MAPK pathway. We hypothesize that a novel CoREST inhibitor, Corin2, can potentially combat drug resistance by downregulating the expression of p38. Methods: Vemurafenib-sensitive (A375P) and Vemurafenib-resistant (A375R) lines of A375 human melanoma cells with BRAFV600E mutations were cultured in DMSO. The A375P and A375R cells were treated overnight with experimental conditions including DMSO as negative control, Vemurafenib as the BRAF inhibitor, and Corin2 as the potential therapeutic. Subsequently, protein was extracted from the cells and western blots were performed to probe for the expression levels of total p-38 and phosphorylated-p38 (P-p38). Results: The results from the western blot experiments indicated that there was not a significant difference in the expression of the P-p38 level in the A375R cells treated with Corin2 versus that of those treated with Vemurafenib. This suggests that the p38 MAPK pathway might not be the primary pathway mediating
the alternative mechanism enabling the drug resistance phenomenon to occur in BRAFV600E mutant cells. **Conclusion:** We tested the hypothesis that the CoREST inhibitor Corin2 may overcome targeted-therapy resistance by inhibiting the p38-mediated MAPK pathway in human melanoma cells. The results of the western blot experiments suggested that p38 may not be involved in the acquired resistance in melanoma and hence may not be a therapeutic target of Corin2. Future studies can further explore alternative mechanisms to effectively target drug resistance.

**USE OF DUPILUMAB TO TREAT SEVERE ATOPIC DERMATITIS IN A PATIENT WITH MELANOMA**

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**Introduction:** Novel biologic therapies have revolutionized treatment of atopic dermatitis. Despite increasingly focused targets within the immune system, there remains concern regarding the use of drugs that target the immune system in patients with cancer. It has been theorized that the use of biologic therapies in patients with active malignancy may lessen the bodies’ ability to detect and to eliminate cancer cells. Moreover, a frequent side effect of many immunotherapies used to treat cancer is the induction or worsening of atopic dermatitis. For these patients, associated skin changes and pruritus can significantly reduce quality of life. Those with atopic dermatitis and cancer may be forced to face an unfortunate paradox: choose chemotherapy that may worsen atopic dermatitis or less effective treatments. The novel biologic agent, dupilumab, is a monoclonal antibody that modulates IL-4 and IL-13 signaling. Dupilumab is indicated in the treatment of moderate to severe atopic dermatitis. Dupilumab has not been reported to cause immunosuppression, however, there is no data on the use of dupilumab in patients with melanoma. **Method:** In this report, we present a patient with a diagnosis of amelanotic melanoma stage IIIb and severe atopic dermatitis with extensive involvement (forearms, arms, neck, chest, and legs) and significant pruritus (numerical rating scale [NRS] of 8 out of 10). Following resection of the melanoma and after discussion with her oncologist, the patient opted not to receive the immunotherapy protocol for melanoma, SWOG-S1404, given that the reported adverse effects include a worsening of atopic dermatitis. Instead the patient opted for regular follow-ups and periodic imaging until her atopic dermatitis could be better controlled. The patient’s atopic dermatitis had failed to significantly improve with standard therapies, which included topical corticosteroids and wet dressings, as well as oral corticosteroids. The patient began dupilumab, a targeted therapy for atopic dermatitis, with the goal of better controlling her atopic dermatitis and eventually beginning the SWOG-1404 immunotherapy regimen. **Results:** In a follow-up twelve weeks after beginning dupilumab, the patient presented with significant improvement in her atopic dermatitis (see figure 1) with only scattered lesions and a dramatic reduction in pruritus (NRS 3 of 10). Examination for new lesions suspicious for reoccurrence of melanoma has been negative and surveillance imaging has since been unremarkable. Future follow-ups in the coming weeks will seek to monitor the patient’s atopic dermatitis and confirm these observations. **Conclusion:** This case report suggests that, in patients suffering from severe atopic dermatitis, the short-term use of dupilumab may be safe in those with melanoma, and could allow for earlier initiation of potentially aggravating immunotherapy regimens for melanoma.

**OPTICAL COHERENCE TOMOGRAPHY IMAGE PROCESSING FOR IN VIVO 3-DIMENSIONAL VISUALIZATION OF BASAL CELL CARCINOMA**

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**Introduction:** The use of optical coherence tomography (OCT) imaging of basal cell carcinoma (BCC) has been widely studied leading to the description of multiple defining features with the conclusion that this imaging modality may assist in diagnosing, subtyping, and managing BCCs. However, the clinical applicability of this technology remains to be fully explored. The aim of this study was to determine whether an algorithm can be created for and applied to automated feature detection of BCC features visualized under OCT and displayed to the clinician in a valuable manner. **Methods:** This study developed an image processing algorithm within Matrix Laboratory (MATLAB) and applied it to OCT images and rendered the new images in 3D within Medical Image Processing, Analysis and Visualization (MIPAV) software. Patients were imaged using a multi-beam dermatologic OCT scanner prior to diagnostic biopsy confirming BCC. Image processing was developed using one BCC image and subsequently applied to one other BCC image. Highlighted BCC features were visually compared to unprocessed images to verify accurate localization. **Results:** Using OCT followed by image analysis, our algorithm was able to identify and
highlight a characteristic feature of BCCs in vivo and render the image for 3D visualization and handling. The algorithm was successfully applied to the second BCC image, detecting and displaying the BCC in a comparable fashion. **Conclusion:** Image processing using a computer algorithm for feature detection enabled us to detect BCCs within a 3-dimensional model of in vivo tissue based on OCT images. This technique builds upon the resolution and depth acquisition capabilities of OCT for tissue visualization. We believe further characterization and detection of BCC features can develop a more detailed and inclusive representation of the entire lesion allowing for greater applicability that may be used for diagnosis, precise biopsy and surgical localization, and noninvasive monitoring of therapy as the development of noninvasive treatments progresses.

**CELL–SPECIFIC EXPRESSION OF ANTIMICROBIAL PROTEIN PERFORIN-2 IN RESPONSE TO INFECTION**

**Lulu Wong,** Andrea Ferreira, Cheyanne Head, Laura Romero Natasa Strbo, Andrew Sawaya, Robert Kirsner, Irena Pastar, Marjana Tomic-Canic

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**Introduction:** Bacterial infection often impedes wound-healing process and contributes to chronicity of non-healing ulcers. Perforin-2 (P-2) is a membrane-attack-complex-perforin (MACPF) domain containing functional proteins involved with killing intracellular bacteria. **Methods:** Using novel, Prime-Flow RNA assay, P-2 expression in human skin and diabetic foot ulcer tissues were analyzed. This study achieved simultaneous detection of P-2 RNA and cell surface proteins by using fluorochrome-conjugated antibodies that allow for further discrimination of specific cell subpopulations. This approach identified P-2 transcript in both CD45+ and CD45- cell populations, confirming P-2 expression in both professional and non-professional phagocytes in skin. Using PrimeFlow analyses and qPCR corroboration, single cell suspensions derived from DFU tissues were compared with suspensions obtained from healthy tissue. **Results:** Results indicate that DFU tissues have a decrease in total number of CD45- cells expressing P-2 and also a decreased overall expression of P-2 in CD45+ cells. These findings suggest that CD45+ cells found in DFUs are unable to respond to intracellular pathogens. Using human ex vivo wound models, we further investigated P-2 importance in skin barrier restoration. Using RNA isolated from ex vivo wounds, P-2 levels were evaluated immediately after wounding and daily thereafter for up to seven days. P-2 levels remain increased in ex vivo wounds up to 7 days post-wounding, with a peak on post-wounding day 2 in CD45+ cells. P-2 mediated-response in the presence of pathological versus commensal bacterial was also evaluated by infection of human ex vivo wounds with *S. aureus* and *S. epidermis*. *S. aureus* infection resulted in delayed healing and decreased P-2 expression in CD45+ cells, whereas *S. epidermis* did not mediate significant change. **Conclusion:** Our data suggests that cell specific expression of P-2 plays an important role as an innate immunity effector during barrier restoration, and its suppression in non-healing DFUs contributes to chronicity of infection.

**UNDERSTANDING THE ROLE OF *Kdm6a* IN BETA CELL DIFFERENTIATION, MATURATION, AND FUNCTION**

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**Introduction:** Diabetes is caused by insulin deficiency resulting from dysfunction of beta cells. Beta cell dysfunction is also seen in Kabuki syndrome, a rare, x-linked disease that is characterized by multiple system disorders including facial abnormalities, growth delays, and intellectual disabilities, among others. In some cases, Kabuki syndrome has also been linked to congenital hyperinsulinism, which occurs when beta cells release insulin, regardless of glucose stimulation, leading to dangerously low blood glucose levels. Lysine-specific demethylase 6A (*KDM6A*; also called *UTX*) is mutated in the subset of patients with Kabuki syndrome who have hyperinsulinism, suggesting that ineffective demethylase activity may cause beta cell dysfunction. *Kdm6a* is involved in removal of the transcriptional repressive mark, H3K27me3, and thus is potentially involved in activation of gene transcription in beta cells. Additionally, *Kdm6a* mutations have also been noted in insulinomas, which have increased beta cell proliferation. We hypothesize that *Kdm6a* is necessary for beta cell differentiation, maturation, and function. **Methods:** We generated *Kdm6a* knock-out mice using a Cre-loxP recombination system. We bred Ngn3-Cre mice with *Kdm6a* flox mice to study beta cell differentiation; we bred Ins1-Cre mice with *Kdm6a* flox mice to study beta cell maturation and function. We used Cre- littermates as controls. Intraperitoneal glucose tolerance tests were performed on mice at 2 months of age. Plasma
insulin levels were measured using ELISA. Beta cell proliferation was measured using immunofluorescence on paraffin pancreatic sections labeled with anti-Ki67, anti-PDX1, and anti-Insulin antibodies with Dapi nuclear stain. Immunofluorescence was also performed with anti-KDM6A antibodies. Results: We did not note any effect of Kdm6a deletion on mortality or early growth. Glucose and insulin levels during the glucose tolerance test were very similar between control and knock-out mice. No significant difference was seen in beta cell proliferation between the groups. We confirmed that KDM6A was present in the beta cells of controls but not in the knockout mice. Conclusion: We found no difference with regard to the glucose tolerance, insulin secretion, or beta cell proliferation between control and knockout mice. However, because we know that Kdm6a had in fact been deleted in the Ngn3-Cre and Ins1-Cre mouse lines, we think that KDM6B might be compensating for the loss of KDM6A. In the future, we plan to knock out both genes in order to test the role of H3K27me3 demethylation in beta cell differentiation, maturation, and function. This research could have important implications for understanding beta cell dysfunction in patients with Kabuki syndrome, congenital hyperinsulinism, and diabetes.

SCREENING AND IDENTIFICATION OF NOVEL VARIANTS AND GENES IN HEREDITARY NON-SYNDROMIC DEAFNESS

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Introduction: Hearing loss (HL) is one of the most common, sensory deficit, among the human population presenting itself at the rate of 1 in 500 births. Studies thus far project at least 70% of HL cases is non-syndromic (NSHL) where HL is the only observed phenotype and 30% is syndromic (SHL), where HL is a symptom of another disease or disorder. More than 90 genes have been identified and approximately140 loci have been associated with HL, making it one of the most genetically heterogeneous traits. Although we have identified some key genes in hearing loss, there is not a complete picture of their role in the mechanotransduction process that allows the detection and processing of sounds of varying frequencies. Methods: Screening and detection of potential causal variants is done using the MiamiOtoGenes panel, a compendium of 180 (80 non-syndromic and 100 syndromic) known and candidate deafness causing genes. The target size is approximately 1.327 MB and covers all the exons, 5’ UTRs and 3’ UTRs with at least 95% coverage of all targeted regions. Bioinformatics tools, to filter variants based on read depth, minor allele frequency (MAF) and pathogenicity prediction are used to analyze the sequence data. Families negative for mutations on known genes are analyzed by whole exome sequencing (WES). Results: This study utilizes patient samples from Iran and South Florida. So far, bioinformatics analysis shows pathogenic and likely pathogenic variants across these families, with an estimate of 27% (9/33) among the South Floridian and 50% (5/10) Iranian origin families. The next steps involve the confirmation of variant in the affected patients by Sanger sequencing and check if the variant segregates within the family. Further functional studies would help relate the genotype and the phenotype. Conclusions: This study has utilized Next Generation Sequencing strategies for variant detection in a multi-ethnic cohort and resulted in the identification of sequence variants in 28 known genes. They are multiplex families with more than one affected member, hence, validation of the variant and segregation analysis would help in the identification of the causal variant. Further computational and functional analysis will be performed to validate the impact of the mutation and their role in deafness. Families without a known cause after panel screen would be classified as unsolved, and will be further analyzed by WES.

CIRCADIAN RHYTHM AND EXERCISE CONTROL INFLAMMATION

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Introduction: Sepsis is a systemic inflammatory response to infection, with no preventative strategies. The beneficial effects of exercise on brain function were demonstrated in animal models and in a growing number of clinical studies on humans. Dopamine (DA), noradrenaline (NE), and adrenaline (E) are the three major catecholamine neurotransmitters that are known to be modulated by exercise. This study focuses on how exercise affecting these three neurotransmitters and how it can work against sepsis. The suprachiasmatic nucleus of the brain regulates the circadian through several mechanisms including autonomic innervations. As sympathetic and parasympathetic activity fluctuates throughout the day, we hypothesized that the inflammatory reflex arc may behave differently at different times. Methods: In this study blood is collected by cardiac puncture from anesthetized control and exercised mice.
Blood is collected from exercised mice after 1 hour of swimming. We use an LPS (endotoxin) as a sepsis model. TNF and catecholamine are measured by ELISA. **Results**: TNF, INF-gamma, HMGB1 are pro-inflammatory and IL-10, TGFβ1 are anti-inflammatory cytokines. Blood TNF in morning is higher than evening (AM: 0.865 vs. PM: 0.667 ng/ml). TNF is increases in sepsis but we found that exercises decreases blood TNF in sepsis (Ex: 0.646 vs. C: 0.940 ng/ml). Also Exercise increases blood dopamine levels (Ex: 1.912 Vs C: 1.217). **Conclusion**: We conclude that inflammatory responses in sepsis are more severe in the morning as compared to evening and exercise decrease inflammation. Our result signifies that exercise has beneficial effects against inflammation.

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**THE BEYOND THE BOOKS PROGRAM: IMPROVING MEDICAL STUDENT ATTITUDES TOWARD THE UNDERSERVED**

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Introduction: The Beyond the Books (BTB) program is an 8-month first year elective at Geisel School of Medicine designed to better prepare medical students to serve underserved communities. Medical school negatively impacts student attitudes toward the underserved, and despite recommendations from the Association of American Medical Colleges (AAMC) and the Liaison Committee on Medical Education (LCME), medical schools in the United States have continued to graduate students lacking the knowledge and empathy necessary to effectively intervene on behalf of underserved communities.1-5 **Methods**: BTB utilizes a combined didactic and experiential curriculum to provide medical students with a better understanding of health disparity and the systemic racism, social determinants of health (SDH) and barriers to health that drive it while simultaneously fostering an empathy for the communities it impacts. The effect of the curriculum on attitudes toward the underserved was evaluated via a longitudinal prospective cohort study. The Medical Student Attitudes Toward the Underserved (MSATU) questionnaire was administered to BTB participants (n = 13) and non-participant first year medical student controls (n = 29) at the initiation and conclusion of the program. The BTB cohort was comprised of a larger percentage of women than the control cohort (84% vs. 71%). Data regarding ethnicity was limited because some students chose not to specify ethnic identity. However, among students who provided ethnic data, the BTB and control cohorts appear to have similar ethnic composition (64% Caucasian vs. 68% Caucasian). BTB’s effect on understanding of SDH, health disparity, personal bias and empathy was assessed via a qualitative, 5-point Likert scale (strongly disagree to strongly agree) questionnaire distributed to participants at the end of the program. **Results**: Students acknowledged that BTB had helped them: 1. learn more about SDH and health inequity (4.27) in addition to the barriers to health associated with socioeconomic disadvantage (4.1), 2. identify and correct false stereotypes and preconceptions (4.18), and 3. increase their empathy for underserved communities (4.4). Additionally, while there was no significant difference between participant and non-participant MSATU score at the start of the program, at BTB’s conclusion participant MSATU scores were observed to be significantly higher than scores of non-participant controls (P<0.001). **Conclusion**: Our preliminary MSATU data support the capability of short-term, pre-clinical interventions to significantly impact student attitudes toward underserved communities during formative years of medical education.

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**PrEP PREFERENCES OF TRANSGENDER INDIVIDUALS SEEKING GENDER AFFIRMATION SURGERY**

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Introduction: Transgender individuals represent a population disproportionally affected by HIV. Pre-exposure prophylaxis (PrEP) with daily oral tenofovir/emtricitabine has been proven to significantly decrease the transmission of HIV to at-risk individuals. This study aims to investigate PrEP knowledge and preferences among transgender individuals in the process of gender affirmation surgery. Transgender individuals face discrimination, stigma, and rejection within our society, leading to inadequate healthcare use. Those undergoing gender transition surgery, however, are actively engaged in medical care, providing a unique opportunity to evaluate PrEP within this population. Information and insights gathered from this study will be used to form a strategy for PrEP implementation during the gender affirmation process. **Methods**: An electronic survey was designed and distributed to adult transgender patients seen for gender affirmation surgery consultation at a University of Miami LGBTQ clinic. Participating individuals completed the survey on a tablet device and subsequently received PrEP counseling after completing the survey.
Demographic data were collected along with questions to assess knowledge of PrEP, self-perceived risk of HIV, and interest in using PrEP. **Results:** Sixteen participants completed the survey, ranging from age 23 to 63 (mean 36). Their self-identified gender included six transgender females (38%), six transgender males (38%), three (19%) females, and one male (6%). Fourteen (88%) had a primary care provider and health insurance coverage. Before this study, nine (56%) subjects had heard about PrEP. The majority (88%) had not ever discussed taking PrEP with a medical provider, yet 54% were interested in taking PrEP as a method to prevent HIV infection. When asked if they would like to receive preventive sexual health resources such as PrEP through our clinic, 38% reported they would. Of these individuals, 100% were interested in PrEP, 80% interested in HIV screening, and 80% interested in STI screening and treatment services. **Discussion:** Our objective in this study was to assess PrEP awareness and attitudes among transgender individuals being seen in a clinic for surgical gender affirmation with the goal of developing a strategy for implementation of preventative sexual health resources to this at-risk population. While over half of subjects were aware of PrEP prior to the study, the vast majority had not the opportunity to discuss it with a medical provider. Furthermore, a notable portion of participants were receptive to receiving PrEP care in our unique clinical setting. These preliminary results support the implementation of PrEP counseling during the gender affirmation consultation process.

**BIOGENETIC FEATURES AND FUNCTION OF THE MITOCHONDRIAL RIBOSOME**

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**Introduction:** The mitochondrial DNA encodes for thirteen highly hydrophobic protein components of the oxidative phosphorylation system (OXPHOS) which is responsible for the majority of cellular ATP production. Disturbances in the expression or regulation of these thirteen proteins impairs OXPHOS functionality and can produce debilitating disorders, known as mitochondrial diseases, which often present with neurological symptoms. The mitochondrial ribosome is an intricate and highly specialized molecular machine dedicated solely to the translation of these thirteen mtDNA encoded proteins. Consequently, the appropriate biogenesis and functional regulation of the mitoribosome is critical to maintain OXPHOS system activity. A critical step in the translation of the mitochondria encoded genome is the co-translational insertion of nascent polypeptides into the inner mitochondrial membrane (IMM). Though a few proteins involved in co-translational insertion have been identified in yeast, no mechanism for how these proteins contribute to this function has yet been proposed. Additionally, no proteins facilitating co-translational insertion in eukaryotes have been identified. mL45 is the homologue of the yeast protein MBA1 which is known to be involved in mitoribosome co-translational insertion. Structural studies show that mL45 localizes to the polypeptide exit tunnel of the mitoribosome and interacts with the IMM, suggesting a role for mL45 in co-translational insertion that has yet to be evidenced biochemically. Structural studies of the IMM associated mitoribosome indicate that mL45 may also be responsible for mitoribosome to IMM attachment, a key step in mitoribosome biogenesis. Full appreciation of the role of the mitoribosome in mitochondrial disorders will require comprehensive investigation of mL45’s contribution to mitoribosome form and function. **Methods:** To characterize the role of mL45 in mitoribosome biogenesis and mL45’s structure-function relationship this project employs mL45 knock-out (KO) and knock-down (KD) cells generated from the U87 glioblastoma derived cell line. mL45 KO and KD cellular phenotype has been assessed in terms of mitoribosomal protein steady-state levels, assembly status, translational competence, and OXPHOS complex activity. We plan to investigate the mL45 structure-function relationship by re-introduction of mL45 constructs into the KO cell line that are modified in domains that may be responsible for IMM association, guidance of nascent polypeptides into the IMM, and binding to the mitoribosome. **Results:** Early results show cellular growth and translational deficits in cells lacking mL45 that evidences a role for mL45 in mitoribosomal assembly or translational activity. **Conclusion:** mL45 is necessary for translation of mitochondria encoded genes and normal mitochondrial function. Pending work on mL45 structure-function relationships will reveal mL45’s specific contributions to these essential cellular functions.
POST-STROKE ESTROGEN RECEPTOR BETA AGONIST TREATMENT REDUCES INFARCT VOLUME IN THE BRAIN OF REPRODUCTIVELY SENESCENT FEMALE RATS

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Introduction: Stroke is the fourth leading cause of death, and its rate of occurrence and mortality is influenced by gender. Women have a higher lifetime risk of stroke, higher mortality rates from stroke, and a higher tendency for recurrent strokes than men. Women’s risk for ischemic stroke climbs rapidly after menopause, which is demarcated by low production of ovarian hormones; i.e., progesterone and estrogen. Estrogen has been suggested to confer natural protection to premenopausal women from ischemic stroke and some of its debilitating consequences. A recent study from our laboratory demonstrated that periodic 17β-estradiol pretreatment protects neurons from ischemic injury through the activation of estrogen receptor subtype beta (ER-β). Apart from neuroprotection, periodic activation of ER-β in ovariectomized rats significantly improves hippocampus-dependent learning and memory. In the current study, we tested the hypothesis that post-stroke ER-β agonist treatment reduces ischemic brain damage and improves cognition in reproductively senescent female rats. Methods: We tested the proposed hypothesis using 9-11 month old retired breeder female Sprague-Dawley rats. Retired breeder rats that remained in constant diestrous were considered reproductively senescent and were exposed to transient middle cerebral artery occlusion (tMCAO; 90 min). After tMCAO, rats were randomly assigned to one of two treatment groups: Group 1– ER-β agonist (beta 2, 3-bis(4-hydroxyphenyl) propionitrile; DPN; 1 mg/kg; s.c.; at 4.5h after tMCAO) or a Group 2–vehicle control (dimethyl sulfoxide (DMSO)/saline mixture). Rats were either sacrificed a day later to study alteration in infarct volume or allowed to survive for a month so hippocampal-dependent cognitive test could be performed to investigate alteration in cognitive abilities. The infarct volume was stained using TTC (2,3,5-triphenylte-trazolium chloride) technique and areas of infarct were measured using ImageJ software. Results: Post-tMCAO ER-β agonist treatment significantly (p < 0.05) reduced infarct volume and improved cognition in female rats as compared to the vehicle treated group. Conclusion: Post-stroke ER-β agonist treatment protects the brain from ischemic damage. This study provides a basis for future targeted interventions to enhance recovery and ameliorate cognitive deficits after stroke in women.

GENETIC KNOCKDOWN AND KNOCKOUT PHENOTYPIC COMPARISON IN A ZEBRAFISH MODEL OF COMPLEX NEUROLOGICAL DISORDER CAUSED BY MUTATIONS IN SLC25A46 GENE

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Introduction: Both knockdown and knockout approaches are widely used in deciphering gene function in a model organism. Yet, there have been reports about the occurring discrepancies between the observed phenotypes, which affect the interpretation of the gene function. Those reports indicate the existence of a genetic buffering mechanism, which is a poorly understood phenomenon, presenting itself in compensatory gene expression to buffer against deleterious mutations in stable knockout models. In our study we decided to compare the phenotypes between the previously reported morpholino knockdown and the biallelic knockout of a mitochondrial carrier protein slc25a46, generated by us with CRISPR. In humans, recessive mutations in this protein cause moderate to severe complex neurological disorder, which includes ataxia, cerebellar hypoplasia, optic atrophy and peripheral neuropathy. Previous studies in zebrafish were conducted with a morpholino translational knockdown approach, which yielded phenotypes of early motor neuron deformities, optic nerve degeneration and a decreased brain size. Methods: For the generation of our stable knockout model we designed multiple guides against a conserved exon of slc25a46 and injected Cas9 protein along with guide RNAs into single cell stage zebrafish embryos, confirmed mutagenesis by fragment analysis of the targeted region, and outcrossed the adult founders twice to segregate for the germline transmission of the frameshift mutations. Once the compound heterozygous knockout mutants were obtained, we analyzed the larvae at early stages of development by performing motor neuron and cerebellar cells immunostaining and behavioral swimming assays (visual motor response assay, optokinetic response assay) Results: Although expected to be more drastic, the second generation (F2) of CRISPR targeted zebrafish selected for compound heterozygous frameshift mutations showed mild phenotypes. The motoneuron immunostaining at 48 hours post fertilization in a stable mutant showed an expected decrease in axon length but no truncated or disrupted axons as observed in previous findings using morpholino. Previously reported gap between midbrain and hindbrain boundary
in a morphant was not replicated in the mutant phenotype. Expected to have an optic atrophy, a cerebellar deficiency and a peripheral neuropathy, slc25a46 mutants did not show any significant difference in swimming performance or in response to light-dark stimuli. **Significance:** Our study serves as an important checkpoint for discrepancies between two major methodologies for functional gene studies and as a ground for further optimization of disease modeling approaches.

**SPINAL CORD INJURY AND THE GUT MICROBIOME: MECHANISMS FOR SCI-INDUCED BOWEL DYSFUNCTION**

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**Introduction:** There are currently over 250,000 people in the US living with a Spinal Cord Injury (SCI). These patients experience common secondary complications that can severely compromise health and quality of life. Gastrointestinal dysfunction (eg. Constipation), affects up to 60% of the SCI population and may trigger autonomic dysreflexia, a severe and potentially life-threatening disease. Despite attention to the pathophysiology of SCI with the goal of protection and repair, the relationship of the gut microbiome with SCI and SCI-induced GI dysfunction is just now being explored. We sought to characterize the effects of chronic SCI on the GI tract in a rat model of T9 (impactor) moderately severe SCI, by looking at microbiome composition, bacterial quorum sensing molecules, and intestinal inflammation. **Methods:** To determine changes in microbiota composition we conducted 16s rRNA sequencing, to determine inflammation we measured changes in pro-inflammatory cytokine by ELISA, and whole-cell biosensors were used to determine changes in bacterial communication by quorum sensing molecules. **Results:** After 16s rRNA sequencing we found changes in bacterial diversity on a phyla, family, and species level. Interestingly, there was a significant increase in the relative abundance of species of *Bifidobacteriaceae* and *Clostridiaceae* which are both present in the healthy gut and are of interest in GI function. We also measured changes in Quorum Sensing Molecules (QSMs) via whole-cell sensors, and found AI-2 to be drastically increased in the SCI model compared to the control group at 8 weeks post-injury. To investigate inflammation, we looked at IL1-β, IL-12, MIP-2, and TNF-α in the intestinal tissue. Not only did we find all of these cytokines to be altered at 8-weeks post injury, indicating long-term inflammation, but we also saw significant directional correlations between cytokines and certain species of bacteria. **Discussion:** These results hint at a potentially mechanistic relationship between cytokines and specific bacteria and encourages further research into bacterial changes, as inflammation is a huge player in both GI dysfunction and pathology of SCI. This study provides new information regarding the injury-dependent changes on the gut microbiome and begins to reveal microbiome-host interactions that may contribute to the long-term effects of SCI on GI function. Identifying mechanisms behind these changes will aid in the development of new therapeutic and prevention strategies that can be clinically evaluated to vastly improve health quality of life for people living with SCI.

**PTEN KNOCKDOWN VIA CRISPR/CAS9 INDUCES AXON REGENERATION IN VIVO**

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**Introduction:** CRISPR/Cas9 is a primitive bacterial endonuclease immune system that has evolved the amazing capacity to use a short RNA sequence called a guide RNA to target and selectively remove portions of DNA from an organisms genome. Recently, this system was used to knockdown gene expression *in vivo* in mouse brain, using a virally delivered guide RNA sequence. The aim of this study was to determine if CRISPR/Cas9 can be used to knockdown PTEN, a tumor suppressor gene, in Retinal Ganglion Cells (RGCs; the principle sensory neurons in the retina) *in vivo* and induce axon regeneration. **Methods:** This study used a Cre-lox inducible Cas9 knock-in mouse line, adeno-associated viral (AAV) vectors produced in house, the Optic Nerve Crush (ONC) injury paradigm, a model of CNS nerve injury, and confocal light microscopy to determine the effect that a candidate guide RNA sequence against PTEN has on axon regeneration. **Results:** the guide RNA sequence targeting Cas9 to the PTEN gene effectively knocked down PTEN protein expression in both mouse and human primary cell lines *in vitro*. This guide RNA was also capable of reducing gene expression *in vivo* using the Cas9 knock in mouse line. Finally, this guide RNA was used to effectively promote RGC survival and axon regeneration after ONC *in vivo*. **Conclusion:** These results demonstrate that the CRISPR/Cas9 system can be used to produce functional gene knockdown *in vivo*, thus providing an incredibly powerful tool to explore the function of potentially any gene via knockdown in axon regeneration in the future.
PERMEABILITY OF NANOPARTICLES TO THE INNER EAR FOLLOWING TRANSTYMMPANIC ADMINISTRATION IN A RAT MODEL

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Introduction: Intratympanic injection is becoming an easy and common procedure in otolaryngology for delivery of drugs to the inner ear. Targeted drug delivery to the inner ear however remains a challenge due to the difficulty of anatomic accessibility, the blood labyrinth barrier and the permeability through round window membrane resulting in a low level of drugs within the cochlea after locally administered drug. Nanoparticles are nanoscale carriers that can deliver localized drug doses to a site of interest. We investigated the permeability of the biocompatible polyester nanoparticle poly-lactic-co-glycolic acid (PLGA), which has been FDA approved for treatment of diseases in other organ systems but not the inner ear. Our aim is to determine whether transtympanic administration of PLGA leads to penetration of the nanoparticles through the middle ear to the inner ear, and to determine their localization and biodistribution in the various cochlear compartments including auditory hair cells, sensory epithelium, round window membrane (RWM), spiral ganglions, stria vascularis and spiral ligament.

Methods: Fluorescent PLGA nanoparticles were injected intratympanically in rats using a 28 gauge transtympanic needle. Rats that received no injection served as the control group. The cochleae from treated and control groups were then resected, snap-frozen, and cryosectioned for immunohistological examination under confocal microscope. Fluorescent intensity was quantified in nanoparticles injected rats and control cochleae and compared using t-test and Mann-Whitney U test. Results: Preliminary data shows that transtympanic administration leads to permeability of nanoparticles all the way into the inner ear. There was strong fluorescent signal in auditory hair cells, sensory epithelium, and stria vascularis but faint to no signal in spiral ganglion neurons. Cochleae of control rats showed no fluorescence. The fluorescent intensity calculated using ImageJ software showed more nanoparticle accumulation in auditory hair cells followed by stria vascularis. Conclusion: The results of this study suggests that transtympanic administration of PLGA nanoparticles lead to their in vivo permeability all the way to the inner ear and this delivery method appear to be promising for future use in clinical otology. Experiments are in progress in our laboratory to determine the bio-distribution of these nanoparticles into cochlea. The results of this study will lay the foundation for developing nanoparticle based novel treatment modalities for auditory disorders.

A CASE REPORT OF PRURITIC URTICARIAL PAPULES AND PLAQUES IN EARLY PREGNANCY

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Introduction: Pruritic urticarial papules and plaques of pregnancy (PUPPP) is a benign, self-limiting pruritic inflammatory disorder that typically affects women in the last few weeks of their first pregnancy or immediately postpartum. PUPPP occurs in 1 in every 160-300 pregnancies and arises from striae on the abdomen. The rash can spread to the thighs and buttock, but the exact pathogenesis of the condition is unknown. Methods: A rare presentation of PUPPP occurred in a 40-year-old G5P2204 woman at 25.3 weeks gestation. The patient was clinically followed in the hospital and the literature was used as reference for the typical presentation and risk factors for this dermatologic condition in pregnancy. Results: The main risk factors for PUPPP include first pregnancy, multiple gestations, white ethnicity, young age, maternal hypertension, and rapid weight gain. The rash presents late in the third trimester around the abdomen and spares the face, palms, and soles. The patient studied lacked most of the risk factors and typical presentation for PUPPP. The patient was of advanced maternal age, had a singleton pregnancy, was Hispanic, and had no history of maternal hypertension. The rash also erupted in the second trimester, which deviates from the mean onset of 35 weeks set by the American Academy of Dermatology. Additionally, in a case study by the American Journal of Dermatopathology, 73% of patients presented with PUPPP in the third trimester, the other 23% presented postpartum, but none presented in early pregnancy. In terms of etiology, the patient in this case was obese; suggesting striae may cause damage to the connective tissue and lead to exposure of dermal antigens that trigger an inflammatory response and the subsequent rash. Conclusion: The diagnosis of PUPPP in this patient was clinical based on rash appearance, distribution, and the response to treatment with mild to high dose topical corticosteroids. The importance of recognition of PUPPP in early pregnancy is to differentiate it from a more serious, similar-looking rash called pemphigoid gestationis (PG) using direct immunofluorescence. PG has increased morbidity for mom and baby, including increased rash recurrence rates for mom, small for gestational age babies, and premature babies. PUPPP, on the other hand, poses no risk of fetal or maternal morbidity and recurrence is rare. Early
determination of the rash in pregnancy as PUPPP rather than PG can reduce morbidity for both mom and baby and lead to quick treatment and rash resolution.

26 THE EXPERIENCES AND POSTPARTUM DRUG USE OF PREGNANT WOMEN WITH ADDICTION

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**Introduction:** It is estimated that 5.0% of pregnant women use one or more addictive substances. Drug use during pregnancy significantly increases the risk of adverse maternal and fetal outcomes. The Prenatal Recovery Clinic (PRC) is a specialty clinic at Jackson Memorial Hospital that provides care for pregnant women with addiction. The two objectives of this pilot study are to 1) gain a greater understanding of the patient-health care provider relationship in the PRC compared to the hospital and 2) to compare drug use at different stages of pregnancy to evaluate the effect of the clinic. **Methods:** Pregnant women between 18-50 years old that used substances and were patients at the PRC between March 2016 and April 2017 were eligible to participate in the study. A survey was administered at two different times; the first at a PRC prenatal visit and another postpartum. The surveys asked patients seven questions via a Likert scale about whether they felt their health care provider showed them trust, respect, and judgment. The PRC ratings were compared to their hospital delivery staff ratings by unpaired t tests. The surveys also asked patients questions regarding the frequency and timing of their drug use. **Results:** Twelve participants completed the prenatal survey, and six participants competed the postpartum surveys. Participants rated the PRC clinic experience overall more favorably than their experience at the hospital for delivery. Specifically, patients felt more judged (p=0.14), that they had less opportunity to say what their health care team needed to know (p=0.14), and did not feel they could share information without repercussion (p=0.13) in the hospital setting compared to the PRC setting. Of the women who completed both surveys, the percentage reporting drug use in the past 30 days (33%) did not increase in the postpartum survey. **Conclusions:** This pilot study reveals challenges that will need to be addressed in a future full investigation. First, twelve patients completed the prenatal survey, and only six went on to complete the postpartum survey revealing large losses to follow up. Second, a control group of pregnant patients that does not have addiction investigation. First, twelve patients completed the prenatal survey, and only six went on to complete the postpartum survey.

27 MOLECULAR TARGETS IN GYNECOLOGICAL CANCERS: ARE WE MISSING OPPORTUNITIES?

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**Introduction:** With the growing understanding of the molecular and genetic profiles of cancers, targeted treatments, such as hormone therapies and immunotherapies, are being increasingly utilized in personalized cancer care. The objective of this study was to study how these advances have translated into practice by examining how frequently molecular profiling of recurrent gynecological tumors lead to changes in treatment. **Methods:** We identified women at our institution from Nov 2014 to June 2017 who had molecular tumor testing performed. Data extracted from electronic medical records included demographics, molecular testing results (next generation sequencing and protein expression with immunohistochemistry), and treatment histories. We determined (1) if molecular profiling identified actionable targets for which therapy is available (FDA approved treatments and investigational therapeutics) and (2) whether the patient’s treatment course changed as a result of molecular profiling results. Fisher’s exact test was used with a p value of <0.05 considered significant. **Results:** We identified 152 patients with gynecological cancers who underwent molecular profiling of recurrent tumors. These patients included 78 ovarian cancers (51.3%), 46 endometrial cancers (30.3%), 15 cervical cancers (9.8%), 6 uterine sarcomas (3.9%), 5 vulvar cancers (3.3%), and 2 gestational trophoblastic disease (GTD) (1.3%). Median age was 57. Of the 152 patients, 116 (76.3%) had actionable mutations identified, and 41 (35.3%) of the patients with actionable mutations received a subsequent change in treatment. When stratified by type of cancer, molecular profiling most frequently found an actionable target in patients with cervical and vulvar cancers; identifying 12 (80%) and 4 (80%) patients with actionable mutations, respectively. In patients with endometrial cancer 36 (78%) actionable mutations were identified, and in ovarian cancer, 56 (72%) actionable mutations were identified. Changes in treatment occurred more frequently in patients with endometrial
cancer, 19 (53%), and ovarian cancers, 17 (30%), as compared to patients with cervical and vulvar cancer (p=0.03). There was no difference in the utilization of test results in type I versus type II endometrial cancers (p=0.55). In ovarian cancer, the most frequent actionable targets identified were ER, BRCA 1/2, and PD1, whereas in endometrial cancer, ER, PTEN, and CTNNB1 were more common. In cervical cancer, PIK3CA, EGFR, and PD1 were most common, whereas PD1 was most common among vulvar cancers. **Conclusion:** Molecular profiling in recurrent gynecologic cancers often identified at least one actionable mutation; however, only in a minority of these cases was the course of treatment changed. Changes in treatment occurred most frequently in patients with endometrial cancer. Further studies with higher power are needed to determine if specific mutations are more actionable than others, and to identify the frequency of actionable mutations and therapy changes in those specific gynecological cancers less represented in this sample. Finally, additional investigation is needed to determine why molecular profiling often does not lead to changes in treatment.

**ANALYSIS OF PERIOPERATIVE OUTCOMES OF HYSTERECTOMY AND EVALUATION OF A CLINICAL DECISION TREE ALGORITHM**

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**Introduction:** Despite the advent of minimally invasive procedures, an abdominal hysterectomy remains the most commonly performed gynecologic procedure. The aim of this study was to evaluate differences in perioperative outcomes between minimally invasive surgery and abdominal surgery within the hospital setting. **Methods:** A retrospective chart review was conducted of 607 women out of which 413 were included in our analysis. Patients included in our analysis underwent either a benign abdominal hysterectomy (AH) (n=273), a laparoscopic hysterectomy (LH) (n=129), or a vaginal hysterectomy (VH) (n=11) from 1/1/2015 and 12/31/2016. Patients who underwent a robotic hysterectomy or a hysterectomy for pelvic organ prolapse were excluded from this study. Statistical analysis was performed using SPSS 22, and categorical data was analyzed with Chi-square and Fisher’s exact tests. Logistic regression was used to calculate adjusted p-values. T-test and ANOVA were used to obtain p-values for continuous data, and a general linear model was used for the adjusted p-values. **Results:** There was no statistical difference in operating times, adjusted for uterine size, between an AH and a LH (p=0.6). There was no significant difference in the BMI of patients who had an AH vs. a LH, but the BMI of patients who underwent a VH was significantly lower than the other 2 groups. Interestingly, there was no significant difference in the number of comorbidities (p=0.063) or previous abdominal surgeries (p=0.846) between the groups. As we expected, a LH had the least amount of blood loss (mean of 144 ml, p<0.001). The length of stay was also significantly less (p<0.001) for a patient undergoing a LH (mean stay of 1.36 days) compared to an AH (mean stay of 2.88 days). The mode of hysterectomy depends on multiple factors, not only uterine size and comorbidities, and we believe that a number of AHs could have been avoided. Using criteria gleaned from the patients converted to a laparotomy, we created an algorithm (Figure 1) to select the most appropriate type of hysterectomy. **Conclusion:** The retrospective clinical decision tree algorithm was applied to all AHs to discern whether an AH was a necessity. The algorithm showed that 51 AHs could have been avoided. This is intended for cases of benign disease with the intent of minimizing the amount of abdominal hysterectomies performed.

**RETROSPECTIVE ANALYSIS OF WHETHER MATERNAL AGE IMPACTS DEVELOPMENT OF RISK FACTORS FOR STROKE FOLLOWING PREECLAMPSIA**

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**Introduction:** Preeclampsia (PE) is a significant cause of maternal fatalities. 75% of these fatalities are attributable to acute cerebral complications, including intracranial hemorrhage, ischemic stroke, and cerebral edema. Patients with PE consequently have an increased lifetime risk for heart disease and stroke. It is therefore essential to monitor the development of risk factors and comorbidities of cerebrovascular and cardiovascular diseases. The aim of this retrospective study was to evaluate the risk women diagnosed with preeclampsia have of developing cerebrovascular disease comorbidities and to detect a possible correlation between age of pregnancy and development of comorbid conditions post-preeclampsia. **Methods:** 183 female patients diagnosed with PE were retrospectively identified at Jackson Memorial Hospital between January 2012 and December 2013. Inclusion criteria for the study was adult females ages over 18 years old, races, and socioeconomic status diagnosed with PE during pregnancy who were
followed up within the Jackson Health System one to 10 years after the index pregnancy. Patients under 18 years old and/or were unable to give consent were excluded from the study. Electronic Health Records (EHRs) of these patients were re-assessed for development of hypertension, dyslipidemia, migraines, obesity and diabetes mellitus from January 2014 to December 2016. The information gathered for post-PE was compared to whether there was presence of the mentioned comorbidities before the diagnosis of PE. T test was applied for comparison of means and a generalized linear model was used to evaluate the effect of pregnancy age to development of the previously mentioned comorbidities. **Results:** Mean age of patients diagnosed with PE was 32.3 years old. Controlling for preexisting conditions, between pre-preeclampsia and post-preeclampsia, patients had a 1.7 times the risk for developing hypertension ($p = 0.0018$), 3 times the risk for developing dyslipidemia ($p = 0.03$), 2.4 times the risk for migraines ($p = 0.04$), 2 times the risk for diabetes ($p = 0.036$), and no increased risk for obesity ($p > 0.05$). There was no significant association between age of pregnancy and subsequent disease occurrence. **Conclusion:** Our findings demonstrate that regardless of age of pregnancy, patients with previous preeclampsia had up to a three-fold risk of developing hypertension, dyslipidemia, and migraines. This underscores the importance of surveillance and treatment of vascular risk factors after a PE diagnosis, irrespective of the woman’s age.

**CASE REPORT: DABRAFENIB AND TRAMETINIB TREATMENT FOR ERDHEIM-CHESTER DISEASE WITH BRAINSTEM INVOLVEMENT**

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**Introduction:** Erdheim–Chester disease (ECD) is a rare form of non-Langerhans cell histiocytosis characterized by infiltration of multiple organs by CD68+ and CD1a− lipid-laden histiocytes, including the central nervous system in more than one-third of patients. Genetic analysis of ECD samples has demonstrated a high prevalence of BRAF$^{V600E}$ mutations as high as 54%. Experience-based management of ECD involves the use of immunotherapy, steroids, surgery, chemotherapy, and radiation. On November 5th, 2017, vemurafenib became the only FDA approved treatment for ECD patients with specific indication for patients who carry the BRAF$^{V600E}$ mutation. Compared to vemurafenib, the BRAF inhibitor dabrafenib has been shown to have greater brain distribution. The MEK inhibitor trametinib is indicated for secondary prevention of the cutaneous side effects of dabrafenib. **Methods:** We describe a 44-year-old female patient who initially presented to with 2-year history of lightheadedness, fatigue and vertigo. On exam, the patient was moderately dysmetric, diffusely hyperreflexic and dysarthric in the bilateral upper and lower extremities. Her gait was wide-based. She also had clear dysarthria of speech and nystagmus on horizontal gaze bilaterally. MRI showed an extensive area of increased T2/FLAIR signal in the brainstem, enhancement in the pons, thickening of the pituitary stalk and an enhancing lesion in the midbrain. PET/CT showed intense symmetrical increased radiotracer uptake involving the distal femur and tibia bilaterally, which was biopsied. Immunohistochemical staining was negative for BRAF$^{V600E}$, but genomic sequencing revealed the presence of the mutation. Involvement of long bones was redemonstrated using whole-body $^{99m}$Tc-bone scintigraphy. **Results:** 2 years after initial presentation, the patient was formally diagnosed with ECD and placed on combination therapy with dabrafenib and trametinib. Following some dose adjustments, her final regimen was dabrafenib at 75 mg twice-daily p.o. and trametinib at 1 mg every evening. Her dysarthria, dysmetria and gate improved remarkably. Her speech pattern is back to normal. She continues to have mild nystagmus on horizontal gaze bilaterally. PET/CT and MRI 9 and 16 months after initiation of treatment showed complete resolution of all radiographic evidence of the disease. **Conclusion:** The presence of BRAF$^{V600E}$ mutation presents unique opportunities for targeted treatment. In this case report, we demonstrate the success of a combination therapy with the BRAF inhibitor dabrafenib, and MEK inhibitor to treat ECD trametinib.

**CHARACTERIZING THE TUMOR MICROENVIRONMENT IN MELANOMA BEFORE AND AFTER TREATMENT WITH T-VEC USING QUANTITATIVE MULTIPLEX IMMUNOFLUORESCENCE**

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**Introduction:** In 2015 Talimogene laherparepvec (T-Vec) became the first oncolytic virus to gain FDA approval for the treatment of cancer, specifically advanced melanoma. T-Vec is an injectable live herpes virus type 1 engineered...
to selectively infect tumor cells and expresses granulocyte-macrophage colony-stimulating factor. Viral replication within tumor cells is thought to stimulate a local and distant antitumor immunity and to alter the composition of the tumor microenvironment (TME) as evidenced by the reduction of immunosuppressive cell types such as CD4+ FoxP3+ regulatory T cells, CD8+ FoxP3+ T cells, and myeloid-derived suppressor cells observed after treatment with T-Vec. The effects of T-Vec however, have not yet been fully characterized. Quantitative multiplex immunofluorescence (qmIF) is a novel and powerful technique, which allows for automated cell phenotyping, tumor and stromal identification, cell density assessment, and precise quantitative spatial analysis to evaluate the distance between immune cells to each other as well as to tumor cells. In this study, qmIF is used to analyze the TME in pre and post T-Vec treated melanoma lesions with the goal of shedding additional light on T-Vec’s anti-tumoral mechanisms. Methods: Pre and post-treatment biopsies from a patient with metastatic melanoma, previously treated with T-VEC, were obtained. Slides cut from formalin-fixed paraffin-embedded (FFPE) tissues were stained for DAPI, CD3, CD4, CD8, CD68, SOX10, and FOXP3. H&E slides were reviewed by a dermatopathologist to confirm the presence of tumor in pre-treatment lesions, and to histologically characterize post-treatment lesions. Multispectral images at 20x magnification were acquired with Vectra™ (Perkin Elmer) and images were analyzed using inForm™ (Perker Elmer) software. Image analysis consists of four steps: tissue segmentation, cell segmentation, cell phenotyping, and marker scoring. During each step, the computer algorithm is ‘taught’ how to analyze a representative image, and is then able to apply the analysis to all multispectral images. Results: A total of 5 biopsies from cutaneous melanoma lesions (2 pre-treatment and 3 post-treatment with T-Vec) were obtained. Multiplex staining was performed using the antibody panel described above. Multispectral images were obtained using Vectra™ and are currently undergoing spatial and quantitative analysis. Conclusion: The application of quantitative multiplex immunofluorescence to pre and post melanoma lesions treated with T-Vec allows for further characterization of the TME and T-Vec’s oncolytic activity. New data that cannot be obtained from conventional immunohistochemistry, such as quantitative spatial analysis of immune and tumor cells pre and post treatment, will be presented. In addition to a better mechanistic understanding, such findings may lead to new strategies to augment the efficacy of T-Vec’s oncolytic and immune priming activity, which would have important implications in the future treatment of metastatic melanoma and potentially other cancers.
clinicians’ capacity to prevent SO-mediated ocular damage. As more surgical techniques adopt OCT imaging technology, we foresee the applications of this theory to extend beyond strictly retinal detachment repairs.

COMBINATION RRV-MEDIATED PRODRUG ACTIVATED SUICIDE GENE THERAPY FOR THE TREATMENT OF OVARIAN CANCER

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Introduction: Replicating retroviral vectors (RRVs) provide a unique platform of gene therapy targeting cancer cells. By arming RRVs with prodrug activated suicide genes, these RRVs become potent vehicles for causing cancer cell death. Once cancer cells are transduced with RRVs, a prodrug (either 5-Fluorocytosine (5-FC) or CB1954) can be administered leading to cell death. The aim of this project is to demonstrate efficacy of combination RRV therapy using two RRVs for the treatment of ovarian cancer. Methods: Four ovarian cancer cell lines (OCI-C5x, OCI-P5x, SKOV3, and Nutu-19) were used to carry out this aim. Each cell line was tested for viral spread over the course of 27 or more days using each RRV alone and in combination at various multiplicities of infection (MOIs). Each therapeutic RRV was tested for viral stability and its ability to cause cell death upon administration of prodrug. Genomic DNA was extracted from the cells followed by PCR using RRV specific primers to determine viral integration and stability and qRT-PCR was performed to determine viral copy number per cell. MTS assay was used to provide viability data. Flow cytometry assessing for emerald GFP, mStrawberry, and Gag viral protein were used to determine transduction and expression levels of RRVs. Results: All four ovarian cancer cell lines can be transduced by RRVs with varying degrees of transduction efficiency. For example, The OCI-C5x, OCI-P5x, and SKOV3 cell lines reach >80% transduction with each RRV alone and in combination by the end of the spread assay with the highest MOI of 1 whereas Nutu-19 cells reach only >10% transduction. Cytotoxicity assay by MTS demonstrated that RRV-mediated prodrug activated suicide gene therapy is an effective approach at least in vitro for killing ovarian cancer cells. At 1mM of 5-FC and 10µM CB1954 prodrugs used as monotherapy, all cell lines showed ≥50 reduction in viability. Combination therapy using varying concentrations of prodrugs (from 10mM to 1µM of 5-FC combined with 100µM-10nM of CB1954) resulted in greater cell death than single agent. Conclusion: Collectively, these results raise the possibility that RRV-mediated prodrug activated suicide gene therapy may be an effective strategy for patients with ovarian cancer. The data presented supports the further development of this strategy in vivo and eventually in the clinic.

TIMING OF ADJUVANT CHEMOTHERAPY AND SURVIVAL FOLLOWING RADICAL CYSTECTOMY

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Introduction: Radical cystectomy (RC) is the standard of care for surgical management of patients with muscle-invasive bladder cancer (MIBC). The use of perioperative chemotherapy is also important for achieving optimal outcomes. We investigated the impact of timing of adjuvant chemotherapy (AC) on survival following radical cystectomy. Methods: Patients with newly diagnosed pT2-T4, N0, M0 urothelial cell carcinoma who received no chemotherapy prior to RC were identified in the National Cancer Data Base (NCDB). Patients who underwent RC and received no AC or patients who received AC > 45 days following RC were propensity matched to patients receiving AC ≤ 45 days following RC. Median survival was calculated using Kaplan-Meier analysis. Adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI) were calculated from a multivariable Cox regression model to examine factors affecting overall survival (OS). Results: A total of 284 patients with MIBC treated with AC within 45 days of RC were identified from 2004-2014. Patients who received AC ≤ 45 days following RC had better 5 year OS (47.0%, 95% CI: 40.6%-53.2%) compared to patients who received AC > 45 days following RC (37.5%, 95% CI: 31.4%-43.7%) or no AC (41.2%, 95% CI: 35.0%-47.2%). There was no significant difference in OS between patients who received AC > 45 days and no AC (1.11, 0.89-1.38, p=0.348). AC > 45 days and no AC were significant predictors of worse OS compared to AC ≤ 45 days (1.27, 1.02-1.59, p=0.033 and 1.41, 1.12-1.78, p=0.003). Conclusions: Patients who received AC ≤ 45 days following RC had better overall survival compared to patients who received AC > 45 days or no AC following RC. These data highlight the importance of appropriate timing of AC following RC.
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35  **AFPep FOR THE TREATMENT AND PREVENTION OF BREAST CANCER**

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**Introduction:** Breast cancer is a leading cause of morbidity in the US, affecting more than 200,000 women each year. About 80% of these cancers are estrogen receptor (ER) positive. There are several therapeutic options available for ER positive patients, including SERMs such as tamoxifen. However, since these agents have serious side effects, they have not been acceptable for prevention. This project aims to develop a non-toxic agent with therapeutic and preventative efficacy for ER positive breast cancer. AFPep is a synthetic peptide derived from alpha fetoprotein, a protein naturally found during fetal development. It is known that AFPep retains the anti-estrogenic and anti-breast cancer activity of its parent molecule. The hypothesis of this study is that AFPep is safe and effective for the treatment and prevention of breast cancer. **Methods:** Therapeutic efficacy of AFPep was assessed using human breast cancer xenografts growing in a mouse model. Solid MCF-7 breast cancer tumors were introduced orthotopically in immunodeficient SCID adult female mice. Animals were exposed to estrogen and were treated with either saline or 100 µg AFPep/day for 14 days. Tumor volume was monitored during the 14-day treatment period. Preventative efficacy of AFPep was assessed in ACI rats, a strain that develops breast cancer when exposed to high but physiological levels of estrogen. Female rats were exposed to estrogen for 24 weeks. Rats were treated once daily with saline or 25 µg AFPep for either 4 weeks, 8 weeks, or 12 weeks to mimic multiple pregnancy cycles. Rats were weighed weekly and palpated twice weekly for 24 weeks. Tolerability was assessed in rats treated with AFPep using animal weight, behavioral parameters, and organ weights at necropsy. **Results:** In therapeutic assessment, AFPep stopped the growth of established human breast cancer xenografts. In preventative assessments, AFPep significantly decreased formation of mammary tumors under estrogen exposure. AFPep showed no signs of adverse effects. **Conclusion:** AFPep is effective for the treatment and prevention of ER positive breast cancer, and engenders no evidence of adverse side effects. Efficacy without toxicity suggests that AFPep should be developed for breast cancer treatment and prevention.

36  **EFFECT OF S-NITROSYLATION ON CASTRATE RESISTANT PROSTATE CANCER**

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**Introduction:** The androgen receptor (AR) is a vital driver of progression of prostate cancer. Although enzalutamide and abiraterone represent breakthroughs in the treatment of metastatic castration-resistant prostate cancer (CRPC), approximately 20 to 40% of patients have no response to these drugs. A variety of mechanisms for progression to CRPC are being studied but recent evidence implicates AR not only in the initiation but progression to CRPC. Nitrosative stress via S-nitrosylation was found to interfere with AR DNA binding and effect CRPC. GSNO, a nitrogen donor, is known to induce nitrosative stress by modulating covalent attachment of nitric oxide to AR. We hypothesized that inducing S-nitrosylation with exogenous GSNO could suppress downstream targets of AR and suppress tumor growth. **Methods:** A total of 7 (4 experimental and 3 control) NOD-SCID adult mice were castrated. One week after orchietomy, 22Rv1 (5x10^6 suspended in 1:1 Matrigel) cells were mixed and xenografted subcutaneously. After the tumor volume reached an average of 150mm^3, we treated 4 mice with GSNO (10 mg/kg/day) intraperitoneally or PBS (500 µL/kg/day) for two weeks. The tumor volumes were checked every alternate day. After two weeks the animals were sacrificed the grafts were harvested and evaluated for weights. qRT-PCR was used to evaluate TMPRSS2 and PSA expression in grafts and western blot was used for 3-nitrotyrosine (3-NT) levels. **Results:** Proper effective drug concentration of GSNO was determined in vitro using a proliferation assay. Growth of 22Rv1 cells was limited and expression of PSA and TMPRSS2 were decreased by GSNO treatment in vitro. In animal models, GSNO decreased tumor volume (mean fold-change, 4.025 vs 7.634, p = 0.04) in 3/4 (75%) and tumor weight (mean, 0.79 vs 1.04, p=0.018) in 2/4 (50%) of mice compared to vehicle. Analysis of downstream targets from excised grafts also showed a decrease in PSA and TMPRSS2 expression in 2/4 (50%) of treated mice. Western blot showed decreased 3-NT levels in proteins of 25-45 kDa in GSNO treated mice. ERK protein, with a molecular weight of 43 kDa, has been shown to be an important part of the signaling pathway responsible for cancer progression in CRPC. Western blot results confirmed that pERK, activated ERK, was suppressed as a result of GSNO treatment. **Conclusions:** S-Nitrosylation imbalance appears to affect castration resistant prostate cancer through androgen receptor signaling. Further analysis into possible mechanisms and role of GSNO and GSNOR inhibitor in in vivo models is needed.
MLH1 DEFICIENCY INCREASES THE RISK OF HEMATOPOIETIC MALIGNANCIES POST LOW-AND HIGH-LET RADIATION EXPOSURE

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Introduction: Natural sources of radiation in space include galactic cosmic rays (GCR), solar energetic particles and trapped energetic particles in a planetary magnetic field. These sources are difficult to shield because of their high energies and dense ionization patterns, thus posing significant health risks to astronauts on long-term inter-planetary missions. During space travel, genomic instability is a major concern where astronauts are exposed to potent sources of ionizing radiation, namely GCR consisting of high energy and charged atomic nuclei. In particular, hematopoietic stem cells (HSCs) are susceptible to internal and external stresses that threaten the integrity of the cell, and accumulation of damage can lead to HSCs dysfunction and oncogenesis. Recent data from our group has demonstrated that middle-aged individuals show frequent defects in DNA mismatch repair (MMR) in HSCs. Therefore, we hypothesized that high-LET (linear energy transfer) radiation characteristic of the GCR that will confront astronauts on space missions will damage HSCs and contribute to induction and progression of hematopoietic malignancies.

Methods: To study this hypothesis, we employed a DNA mismatch repair deficient mouse model (Mlh1 +/-) to study the effects of low-LET γ-ray vs high-LET 56Fe ion radiation on HSCs of potential astronaut population. In vitro colony forming unit assays and in vivo complete blood count (CBC) plus competitive repopulation assay were carried out to understand harmful impact of radiation and Mlh1 deficiency on HSCs functions. In addition, mice were followed up to 18 months post irradiation to observe HSC malignancies in Mlh1+/- and Mlh1+/- mice. Results: HSC short- and long-term functional assays showed defects in HSCs/HPCs function caused by irradiation, but not depending on Mlh1 status. CBC 5 and 9 months post irradiation demonstrated no impact of irradiation or Mlh1 status on HSC differentiation. However, 56Fe-ion irradiated Mlh1+/- mice showed a significant higher incidence of lymphomagenesis compared to γ-rays irradiated and sham-irradiated Mlh1+/- mice. In addition, immunohistochemistry analysis of lymphomas displayed significant higher incidence of T-cell rich B-cell lymphoma in 56Fe ion irradiated Mlh1+/- mice compared to γ-rays or sham-irradiated Mlh1+/- mice. Conclusion: Thus, the data show that MMR defects in HSCs leads to sensitization to radiation induced hematopoietic malignancy, and that radiation quality effects exacerbate the sensitivity. The findings could have profound effects on astronaut screening and designing better mitigators for space missions.

VALIDATION OF A NOVEL METHOD TO ACCURATELY MEASURE POST-OPERATIVE GLENOID COMPONENT VERSION UTILIZING ROUTINE POST-OPERATIVE RADIOGRAPHS

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Introduction: Significant glenoid component retroversion has been associated with implant loosening and failure after total shoulder arthroplasty (TSA). Current post-operative version measurement methods are either unreliable or require the additional radiation and cost of a post-operative CT scan. Using imaging software integrated with routine clinical imaging, glenoid component version was accurately measured with validation against gold-standard post-operative CT scans in a cadaver model. Methodology: Fourteen pre- and post-operative CT scans and AP/axillary radiographs were performed on cadaveric shoulders that had undergone implantation of a glenoid component used in TSA. Glenoid component version was determined via our novel protocol using Mimics software (Materialise, Leuven, Belgium), performed by aligning post-operative radiographs with a 3D scapula model generated from the pre-operative CT. The position of the glenoid component was then aligned to the radiographs and measured relative to the scapula, giving version. Secondly, as the gold-standard, the post-operative CT was evaluated as a 3D model, and the glenoid component version was measured directly. We further compared various clinically utilized version measurement methods, using 3D-corrected, mid-glenoid, and inferior-to-coracoid CT axial images as well as axillary X-rays. A Pearson correlation coefficient, unpaired two-sample t-test, and repeated-measures ANOVA were used to determine correlation, significance, and effect size between measurement techniques, respectively. Results: The average difference in measured glenoid component retroversion between the gold-standard post-operative CT and our radiograph-based novel projection method was 1.56 degrees (0.01-4.85 deg) with very strong correlation (r=0.958,
There was significant improvement in the accuracy of our novel method over traditional CT measurements, including 3D-corrected, mid-glenoid, and inferior-to-coracoid, as well as over axillary XR measurements. These differed significantly from the gold-standard post-operative CT by 3.26 degrees (p=0.023), 4.36 degrees (p<0.01), 11.04 degrees (p<0.01) and 7.73 degrees (p<0.01), respectively. A post-hoc power analysis found that the study had a 95% power to detect a 4.0 degree difference in version, which represents an effect size of 0.43. **Conclusions:** Our novel projection method utilizes routine TSA post-operative clinical imaging to provide an accurate glenoid component retroversion measurement to within 1.56 degrees of the gold-standard post-operative CT measurement. It is also significantly more accurate than traditional post-operative CT measurement techniques. With the validation of our novel method, post-operative glenoid version may be used to study and inform TSA patient outcomes and implant longevity without the additional patient radiation and cost of post-operative CTs.

**COLLAPSING-TYPE FSGS AND THE QUESTIONABLE APPEARANCE OF SYPHILIS: A CASE REPORT**

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**Introduction:** Collapsing-Type Focal Segmental Glomerulosclerosis (FSGS) is a rare subtype of FSGS, a type of Nephrotic Syndrome, and is characterized by sclerosis of some glomeruli. Secondary causes of this disease may include HIV, Diabetes Mellitus, and IV drug abuse. Patients diagnosed with Collapsing-type FSGS are more likely to progress to end-stage renal disease compared to other types of Nephrotic Syndrome. An important association with this disease is the genetic Apol1 risk variants, especially in individuals of African descent. **Methods:** A 43-year-old African woman presented with a blood pressure of 170/90 stating that she was concerned about her kidney function after consuming an herbal fertility tonic in western Africa in October of 2016. Upon hospitalization at that time due to bilateral pitting edema in her legs and face, her Creatinine was measured at 3.4mg/dL. Additionally, she had been treated for Malaria and received IV treatment. Urinalysis and blood work indicated Nephrotic Syndrome prompting an HIV test. Clinical suspicion prompted a Hepatitis profile and RPR test. A biopsy was done to confirm disease process.

**Results:** HIV test was negative and patient denied IV drug abuse. GFR was measured at 22 mL/min/1.73 m², thereby establishing a diagnosis of Chronic Kidney Disease, Stage 4. Kidney biopsy was notable for tubular atrophy and degeneration, interstitial fibrosis, and burgeoning podocytes, thus confirming a diagnosis of the collapsing variant of FSGS. Negative Hepatitis profile and Positive RPR warranted Syphilis treatment with IM Benzathine Penicillin G. She was also started on Prednisone 120 mg every other day and Cyclosporine 50 mg twice daily to prevent rejection of kidneys. In theory, treatment to eradicate Syphilis in this patient should improve the disease process as we see this as a symptom of the infection rather than a separate disease altogether. Although uncommon, secondary Syphilis may also cause similar, but distinct types of Nephrotic Syndrome such as Membranous Glomerulonephropathy and Minimal Change Disease. **Conclusion:** Syphilis is not commonly associated with the collapsing variant of this disease. This case exemplifies the multi-faceted approach necessary to diagnosing pathologies of the kidney and the importance of complete histories. This patient presented without symptoms of Syphilis and provided no history to indicate such an infection had occurred. Thoroughness may prevent or slow the progression of very devastating and debilitating diseases such as this.
MEDIASTINITIS IN POST-OPERATIVE PEDIATRIC CARDIOTHORACIC PATIENTS: A CASE SERIES

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Introduction/Aim: Infection of the mediastinum is a rare but highly morbid and lethal complication that may result from life-saving cardiothoracic (CT) surgery. There is sparse research regarding mediastinitis in pediatric patients who have undergone cardiothoracic surgery. The objective for this study is to identify commonalities between patients in this population who developed mediastinitis. By teasing out characteristics shared amongst patients who developed the infection, we hope to reveal potential modifiable risk factors amongst the cohort. This information can help lay the groundwork for future placebo-controlled prospective trials, with the goal of reducing incidence of mediastinitis by modifying pre-, intra-, and post-operative risk factors. Methods: The study group includes individuals up to 26 years of age who developed mediastinitis following cardiothoracic surgery at Holtz Children’s Hospital between January 1st, 2000 and August 31st, 2015. We reviewed electronic medical records and paper charts and logged relevant pre-, intra-, and postoperative variables. We excluded patients who were more than 26 years of age and those who underwent non-cardiovascular procedures. Results: From our search, we found 13 pediatric cardiothoracic surgery patients who developed postoperative mediastinitis. Of the 13 total, five (38.5%) were male and eight (61.5%) were female. The median age at surgery was 160 days with a range of 0-26 years. Nine (69.2%) patients had cyanosis prior to surgery. Four patients (30.8%) underwent closed-heart surgery compared with 9 (69.2%) who underwent open-heart surgery. Four patients (30.8%) underwent an additional emergency operation prior to diagnosis of mediastinitis. Three patients (23.1%) had more than one CT procedure concurrently. All cases (100%) involved implantation of a foreign body within the mediastinum. Wound culture was positive in 10 patients (76.9%). Blood culture was positive in 4 (30.8%) patients. Wound VAC was utilized in 11 cases (84.6%). The cohort had undergone a median of 1 prior CT surgery before the operation which resulted in mediastinitis. The average length of hospital stay for these patients was 44.1 days. The average length of antibiotic therapy following infection was 35.0 days. There were two cases (15.4%) that died prior to discharge. Conclusion: A diagnosis of mediastinitis resulted in extended hospital stays and lengthy duration of antibiotic therapy in pediatric cardiothoracic surgery patients. To reduce morbidity and mortality, further research into identification and prevention of factors leading to mediastinitis is warranted.

OSTEOPONTIN DEFICIENCY AMELIORATES DIASTOLIC DYSFUNCTION, PLAQUE BURDEN, AND HEARING DEFICIT IN A GENDER-BASED MANNER IN OLD AThEROGEnIC ApoE<sup>−/−</sup> MICE

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Introduction/Aim: Osteopontin (OPN) is a bone protein that is shown to increase in the atherosclerotic lesions and plays a pathological role in the progression of atherosclerosis. In the current study, using the aged Apolipoprotein-E deficient (ApoE<sup>−/-</sup>) mouse model of atherosclerosis we investigated the effects of OPN deficiency on plaque formation, cardiac function, and hearing ability. Methods: Male and female ApoE<sup>−/−</sup> mice at 12-14 months of age were used on normal chow, with or without homozygous deletion of OPN. Plaque burden was quantified using en face Oil Red O staining in isolated intact aortas and carotids. Echocardiography, Pulse-Wave Doppler and strain analysis were utilized to study cardiac function. Hearing function was assessed using auditory-evoked brainstem response (ABR) and distortion product otoacoustic emission (DPOAE) tests. Results: Consistent with the published literature, we show OPN protein overexpression in human atherosclerotic arteries and confirm that OPN deficiency ameliorates aortic plaque burden only in female ApoE<sup>−/−</sup> mice. We found that similar to aortic plaque burden, carotid plaque burden is only prevented in the female ApoE<sup>−/−</sup> OPN<sup>−/−</sup> mice. Moreover, we show that aortic root lesion area and acellular necrotic zones were significantly decreased in female ApoE<sup>−/−</sup> OPN<sup>−/−</sup> mice without affecting plaque stability. In the aortic root lesions, we observed no difference in total collagen content or fibrous cap thickness between ApoE<sup>−/−</sup> versus ApoE<sup>−/−</sup> OPN<sup>−/−</sup> mice. While cardiac function remained normal in male ApoE<sup>−/−</sup> mice, female mice developed diastolic dysfunction as shown by prolonged isovolumetric relaxation time (IVRT; 28.22±0.62ms in female ApoE<sup>−/−</sup> vs 13.66±1.23ms in female wild type group, p<0.0001), and increased ratio of early transmitral flow to early diastolic annular velocity (E/A', 53.37±3.37 in female ApoE<sup>−/−</sup> vs 25.62±0.97 in female wild type group, p<0.01) – all reflecting elevated LV filling pressures. Female ApoE<sup>−/−</sup> mice also demonstrated myocardial deformation as shown by impaired global circumferential strain (GCS), and myocardial asynchronicity as shown by a sharp increase in maximal opposing wall delay. However, all these cardiac measures were normalized to control levels in female OPN deficient ApoE<sup>−/−</sup> mice.
mice. Moreover, our data show that male but not female ApoE-/- mice develop high frequency sensorineural hearing deficit as an increased hearing threshold at 32kHz (p<0.0645). However, this pathology is also reversed by OPN deficiency in male ApoE-/- mice (p<0.05). DPOAE recordings did not reveal any differences in the genotypes nor genders. Conclusions: Collectively, our findings reveal, for the first time, the beneficial role of OPN deficiency in the carotid plaque burden, cardiac pathology and hearing loss in ApoE-/- mice, implicating OPN as a major causative player in the pathophysiology of atherosclerosis and its comorbidities. Further studies are required to scrutinize the mechanisms underlying protective effects conferred by the lack of OPN.

ACUTE HIV INFECTION DETECTED BY SCREENING IN THE EMERGENCY DEPARTMENT IN MIAMI

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Introduction/Aim: One in seven Human Immunodeficiency Virus (HIV) positive individuals do not know that they are HIV positive, and these unknown positives account for as many as 2 out of 3 of new infections. Acute HIV infection is the early phase of infection characterized by high viral loads and absence of antibody to HIV. Acutely infected individuals are more likely to transmit HIV due to their high viral loads, but less likely to be detected because many HIV tests detect circulating antibodies rather than the virus directly. Miami-Dade County has the highest rate of new HIV infections in the country, which makes the identification of newly infected individuals of paramount importance. Additionally, it is hypothesized that Miami-Dade County has a higher acute HIV prevalence rate than the overall United States. Methods: In a newly implemented opt-out screening protocol in the Jackson Memorial Hospital Emergency Department (ED), all patients who had blood drawn and did not refuse testing were screened for HIV. This protocol uses an opt-out model and integrates routine HIV screening into the existing ED workflow to identify HIV positive patients and attempt to link or re-link them to care. Results: From its inception in June through the month of September, 32,415 unique patients visited the ED. Of these, 8197 were tested, for a screening rate of approximately 25%. 195 HIV positive individuals were identified (2% of those screened). 7% of positive patients did not know their HIV status prior to testing. To date, 37 (19%) have been successfully linked to care. 3 cases of acute HIV were identified, for an acute HIV prevalence of 0.04%. Only one of the three presented to the ED with symptoms that suggested acute HIV infection. Conclusions/Discussion: High clinical suspicion and appropriate screening tests are critical in the identification of HIV infections, particularly acute cases. Early detection of HIV infection allows patients to receive risk-reduction counseling and treatment during the period when he/she is most contagious, which may decrease viral loads and reduce transmission. The cases demonstrate that patients with acute HIV may present with nonspecific symptoms that are hard to diagnose as acute HIV, and that clinicians must remain vigilant regarding diagnosis of acute HIV. The high rate of acute HIV infections (0.04%, compared to 0.02% in the United States overall) highlights the need for comprehensive screening protocols in high-prevalence areas throughout the United States to slow the spread of HIV infection.

AN EXPLORATORY STUDY ON THE PREVALENCE OF OPIATE USE, ABUSE AND TREATMENT IN TUHC

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Introduction/Aim: Opioid use disorder has become a healthcare problem over the last two decades. Albania’s lack of access to prescription opioid as a treatment modality, associated with high costs of opioid treatment has contributed to heroin use. Despite opioid abuse, there is only one specialized public drug treatment facility in Albania. Our aim is to describe the prevalence of opioid use/abuse across different groups through analysis of the TUHC patient population as well as describe treatment and follow-up care. Methods: Demographics, substance use, days of treatment, and improvement status data was extracted from 521 patients admitted to TUHC from January 2012-December 2016. Inclusion criteria included patients admitted for opioid or multi-substance abuse. Patient charts were analyzed to look at treatment protocols, outcome, and follow up plan. Percentages were used for descriptive statistics and Pearson Chi-square was used to test for associations between variable such as age groups, sex of patient, diagnosis, primary drug of use, days in treatment, and improvement status post treatment. Results: Preliminary results show the majority of patients are urban dwelling (85.4%) unemployed (77%), uninsured (83.2%), males (94.4%), 21-30 years of age.
(56.6%) suffering from withdrawal (74.1%), mainly heroin (64.3%), receiving an average 6-10 days of treatment (46.8%). A significant difference exists between gender and diagnosis with most males’ experiencing withdrawal (75.6%) while females experience withdrawal (48.3%) and overdose (44.8%) equally ($X^2 (4)=69.27, p<.001$). Sex was also related with days of treatment received as 48% of males received 6-10 days while 58.6% of females only 1-5 days ($X^2 (3)=16.83, p<.005$). While most patients (50.5%) with withdrawal stay for 6-10 days, the majority (71.1%) of those with overdose stay only 1-5days ($X^2 (12)=68.27, p<.001$). The majority of patients were treated using buprenorphine (69.5%) vs methadone (16.9%) with follow up care to occur within 7-14 days.

**Conclusion:** These data suggest the majority of opioid users are unemployed, uninsured, males centered in urban environments. The differences between male and female patients and days of treatment suggest a possible disparity that should be addressed. These data could further be used to advocate for substance use services currently lacking as well as be insightful to countries working on future policies addressing similar concerns.

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**BARRIERS TO HEPATITIS C SCREENING: A COMPARISON OF HEPATITIS C AND HUMAN IMMUNODEFICIENCY VIRUS SCREENING RATES AT A COMMUNITY STD CLINIC IN MIAMI, FL**

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**Introduction/Aim:** Hepatitis C virus (HCV) is the most prevalent chronic blood borne infection in the United States. There are approximately 4 million individuals infected in the U.S. and 170 million infected globally. In comparison, there are approximately 1.2 million and 36.9 million people infected with HIV in the U.S. and worldwide, respectively. Despite a higher prevalence of HCV as compared to HIV, most HCV infections are undiagnosed. Mortality from HIV has been declining in the U.S. while mortality from HCV is increasing. **Methods:** From June 2014 to February 2015, 357 community residents in Miami, FL were screened for HCV using the OraQuick HCV rapid point of care antibody test. Participants were asked to report if they had previously been screened for HCV and HIV. **Results:** Of the 357 participants, 21 (5.88%) were found to have HCV (confirmed by RNA analysis), a number slightly higher than the estimated national prevalence. Only 15.1% (n = 54) had been screened for HCV before whereas 83.8% (n = 299) had been screened for HIV. Of the patients who had previously been screened for HCV (n = 54), 98.2% of these patients had previously been screened for HIV as well. Of the patients who had never received a previous HIV test (n = 45), only 1 participant (2.2%) had previously been tested for HCV. Among people who knew their prior testing history, the observed 17% increase in the HCV screening rate, in those who were previously tested for HIV (19%) relative to those without prior testing (2%), is statistically significant (OR: 10.6, 95% CL: 1.4–79, p < 0.004) **Conclusion:** This data demonstrates that there may be a low prevalence of HCV screening in high-risk populations in Miami, FL. HCV screening rates appear to be lower than that for HIV. This suggests that pertinent CDC guidelines to screen all high-risk adults for HCV are not being implemented. The data also suggests that participants who had previously received an HIV screening test were more likely to report receiving a prior HCV screening. When individuals are unaware of their infection, they are more like to transmit their infection, less likely to benefit from early treatment and thus prone to increased morbidity and mortality of the disease. Recent treatment advances have made HCV a curable disease. In order to decrease HCV related mortality, we propose offering HCV testing in conjunction with HIV testing to facilitate screening in high-risk populations that are already linked to care.

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**THE DEVELOPMENT AND IMPLEMENTATION OF A NATIONAL PHYSICAL ACTIVITY INTERVENTION IN COLOMBIA**

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**Introduction:** Physical inactivity is a major risk factor for many non-communicable diseases, causing at least 3 million preventable deaths per year worldwide. In 2011, the Colombian government started a nationwide program, Hábitos y Estilos de Vida Saludable program (HEVS; Healthy Life Habits), to provide free physical activity classes for over 60,000 individuals across Colombia. This study describes the HEVS program, participant baseline characteristics, and changes in their anthropomorphic and health measures following participation in the program. **Methods:** Data on program participants was collected from HEVS programs across all states of Colombia during 2016. Individuals
completed surveys before and after participating in the HEVS program that included questions on their demographic information, current health status, lifestyle habits, and anthropomorphic measures. Data for individuals 18 years and older were aggregated and analyzed using R software. Anthropomorphic and health measurements before and after HEVS program participation were compared using a paired t-test and McNemar’s Test, respectively. **Results:** A total of 56,472 participants enrolled in the HEVS program (females: 86.5%, males: 13.5%). The greatest proportion of male and female participants were between the ages of 18-34 (35.5%), with a decreasing number of participants in each successive age group. Prior to participating in HEVS, the mean BMI was 26.3 kg/m² and the mean waist circumference was 85.7 cm. Post-program data was collected on 17,145 individuals. HEVS participation resulted in statistically significant decreases in BMI (26.3 to 25.9 kg/m², \(p<0.001\)), waist circumference (85.7 to 83.7 cm, \(p<0.001\)), and the proportion of patients with self-reported hypertension (16.8 to 13.4%, \(p<0.001\)) and diabetes (6.7 to 6.0%, \(p<0.001\)). **Discussion:** The HEVS program successfully engaged a large number of Colombians and resulted in significant improvements in their health status and anthropomorphic measures. These results indicate the national reach and effectiveness of a government-supported program engagement in community-based physical activity programs. These findings could be strengthened further by improved participant follow-up. Lessons learned from the HEVS program can serve as a valuable guide for the development of similar large scale, community-based physical activity programs in other international settings.

**IMPROVING HOSPITAL FLOW BY IDENTIFYING AND REDUCING DISCHARGE DELAYS AND ROOM TURNOVER TIME: A QUALITY IMPROVEMENT PROJECT**

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**Introduction/Aim:** Delays in hospital discharge and room turnover have been shown to cause prolonged emergency room times, which are associated with increased patient mortality, morbidity, and length of stay (LOS). Further, LOS is associated with reduced hospital reimbursement. It is estimated that the University of Colorado Health (UCH) spends $2721 for every inpatient day. To reduce LOS, this study aims to identify and reduce inefficiencies in the patient discharge and room turnover processes through quality improvement approaches utilizing PDSA (Plan-Do-Study-Act) cycles on the Medical Health Services Unit, a new inpatient unit at UCH. **Methods:** To identify areas for improvement we interviewed staff (n=10) and patients (n=13) and mapped the discharge and room turnover processes (n=10). We found that: 1) providers are 44% accurate at predicting next-day discharges, 2) 60% of identified patients do not know they are being discharged the next day, and 3) it can take up to 68 minutes before the hospital is informed that the discharged patient left the unit. The following quality improvement approaches were implemented: 1) a discharge delay tracker was developed, 2) a patient-centered discharge checklist was given to patients identified for discharge, and 3) a sign was given to discharging patients to leave at the front desk communicating that they had left the unit. Discharge delays were tracked (n=15) and events in the room turnover process were timed before (n=9) and after intervention (n=10). **Results:** We found that: 1) most discharge delays (27%) are due to changes in patient’s medical status, 2) utilizing a patient-centered discharge checklist reduced delayed discharges by 24%, and 3) eliminating communication requirements among unit staff reduced the average room turnover time by 16%. **Conclusion:** This study identified and reduced discharge delays on the medicine unit at UCH by utilizing our discharge delay tracker and patient-centered discharge checklist. Additionally, this research demonstrated that room turnover time can be reduced by eliminating staff communication requirements. We recognize that a small sample size and confounding variables, such as staff awareness of the project, are limitations of this study. However, this study identified patient discharge and room turnover delays, evaluated quality improvements using PDSA cycles, and demonstrating enhancements in these processes. We suggest that future work utilize and improve upon these interventions with larger sample sizes to improve hospital flow, reduce LOS, and improve patient mortality and morbidity.

**EVALUATION OF THE IMPACT OF A SAFE SPACE LESBIAN, GAY, BISEXUAL, TRANSGENDER AND QUEER (LGBTQ) SENSITIVITY TRAINING PROGRAM**

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**Introduction/Aim:** Recent examination of lesbian, gay, bisexual, transgender, and queer (LGBTQ) health has
enhanced awareness of LGBTQ discrimination in educational and professional settings. An important area of investigation is medical education and clinical practice, which are not exempt from LGBTQ bias and discrimination. In fact, homophobic and transphobic climates perpetuate the exclusion of sexuality and gender issues from medical curriculum and contribute to unique challenges faced by LGBTQ medical students. The Association of American Medical Colleges and individual researchers have published proposed interventions focused on the inclusion of LGBTQ health content in medical curricula, exposure to LGBTQ patients, and LGBTQ-specific support services. Of particular interest are educational interventions developed to foster LGBTQ inclusive learning environments as well as to train medical professionals, both in practice and in training, about the issues pertinent to the LGBTQ community and healthcare. These trainings are designed to enhance sensitivity and inclusivity of the LGBTQ community by educating participants on components of sexual orientation and gender identity, skills to support LGBTQ students, and knowledge of resources available to LGBTQ individuals. Our study aims to evaluate the impact of a Safe Space educational training program on the attitudes and knowledge of LGBTQ issues amongst our institution’s faculty, staff, and administration. Methods: From 2015 to 2016, the Safe Space Training program was available to university faculty and staff. Participants completed pre- and post-evaluations that asked about their perception of LGBTQ discrimination on campus and their understanding of gender, gender identity, sexual orientation, and comfort handling situations in which these topics are discussed. The pre- and post-evaluations were composed of a 7-item questionnaire including quantitative questions measured by a Likert scale and 2 questions requiring qualitative responses. Results: Of the 215 participants, 93.4% rated training session as either informative or very informative, and 80.6% believed they would change their language or behavior following the program. When comparing participant responses prior to and after the training, four of the five areas of evaluation demonstrated notable changes. Following the training, participants felt more knowledgeable of the challenges and discrimination faced by LGBTQ individuals and more comfortable dealing with issues related to sexual orientation or gender identity. Additionally, more participants felt knowledgeable of the resources available to LGBTQ individuals at UMMSM after the training. Conclusion: The Safe Space Training program increased the awareness of participants to LGBTQ experiences and challenges, as well as knowledge of gender, gender identity, sexual orientation, and institutional resources for LGBTQ individuals.
ASSESSING SUICIDE AND HOMICIDE RATES BY FIREARM AFTER “STAND YOUR GROUND” LAW IMPLEMENTATION

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Introduction/Aim: In the wake of the Pulse Nightclub mass shooting in Orlando in 2016, the American Medical Association declared gun violence to be a “public health crisis” in the United States, adding to a growing call for additional gun violence research and more restrictive gun control. However, progressive policies adapting gun control have been thwarted, as gun use has long been protected by the United States government. In fact, states have expanded self-defense laws since 2006 to allow people to use lethal force in situations in which they feel threatened both inside and outside of the home. These laws, dubbed “stand your ground” laws, were initially written to decrease the number of home invasions and homicides. But in practice, these laws have the potential to contribute to the gun violence crisis. This study aims to explore the correlation between these state-level “stand your ground” firearm policies and the proportional mortality from firearms to understand if and how “stand your ground” self-defense laws affect rates of homicide by firearm.

Methods: CDC-derived data was modeled using an interrupted time series design, exploring the monthly rates of suicide and homicide by firearm in Alabama, Arizona, Georgia, Louisiana, and Michigan from January 1999 to December 2015. A two-pronged approach was then used to evaluate the outcomes: 1) Comparison of homicide rates by firearm in states with “stand your ground” laws before and after 2006 and 2) comparison of suicide rates by firearm in states with “stand your ground” laws before and after 2006. Results: The 2006 implementation of “stand your ground” laws in Alabama, Arizona, Georgia, Louisiana, and Michigan did not significantly increase the rate of homicide by firearm. However, the rate of suicide by firearm did increase in states with “stand your ground” laws following the implementation. Conclusion: The original rationale for the implementation of the “stand your ground” laws throughout many states was to decrease the overall homicide rate. However, more than a decade after passing the laws, we are observing an increase in suicide rates by firearm in states with these laws. In practice, “stand your ground” laws may have unintentional consequences involving gun culture that further contribute to the epidemic gun violence that pervades the United States.

FACTORS AFFECTING ADHERENCE TO TREATMENT AND HCC SCREENING AMONG HEPATITIS B PATIENTS IN WUHAN, CHINA: A QUALITATIVE STUDY

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Introduction/Aim: For chronic Hepatitis B patients, regular screening is essential for early detection of hepatocellular carcinoma (HCC), particularly in patients with advanced fibrosis or cirrhosis. However, screening adherence is globally low. The reasons for the low adherence rates have not been clearly elicited. We used qualitative methods to identify factors affecting screening adherence among Hepatitis B patients at Wuhan Union Hospital, a major academic medical centre in central China. Methods: We conducted semi-structured interviews with 16 chronic Hepatitis B patients recruited from an outpatient clinic in Wuhan Union Hospital. Results: Participants identified several barriers to screening, including financial and logistical barriers, lack of trust in doctors and Western medicine, social stigma associated with having Hepatitis B, and lack of knowledge. Notably, almost all participants (15/16) used Baidu, a Chinese search engine that shows websites approved by government censors, as their primary source of knowledge. Family was a variable factor: some participants’ families did not support their attempts to adhere to treatment, while other participants’ family members encouraged them to adhere to medications and screenings. For female participants in particular, the prospect of pregnancy was a strong motivating factor for compliance with all aspects of Hepatitis B treatment, including routine screening. Conclusions: Measures to improve screening adherence must address financial and logistical barriers, as well as stigma associated with having Hepatitis B, patients’ lack of trust in doctors, and lack of knowledge. Motivating factors may also be harnessed to improve adherence.
SOCIAL DETERMINANTS AND BARRIERS TO OPTIMAL HEALTH OUTCOMES AND COMPLIANCE IN A MEDICALLY UNDERSERVED POPULATION IN CHENNAI, INDIA

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Introduction/Aim: The health of individuals within a population is dependent on their own biological variations, choices, and behaviors—inequities—as well as external factors beyond their control—inequities. Prior studies have identified correlations between social determinants of health and prevalence, awareness, and control of various illnesses. However, there is limited research on this relationship regarding hypertension and diabetes, two of the most prevalent chronic conditions in India, in the context of Indian society. The aim of this study was to identify social determinants that may contribute to suboptimal health outcomes among lower income hypertensive and diabetic patients at the Free Medical Clinic in Manapakkam, Chennai, India.

Methods: This study utilized a survey containing sociodemographic and 5-point Likert scale questions to assess some of these social determinants of health in hypertensive and/or diabetic adult patients at the Free Medical Centre in Manapakkam, Chennai, India. Volunteers were used to accommodate varying literacy levels and languages spoken. Data was analyzed using SPSS and Excel.

Results: 351 voluntary responses were collected from 396 eligible patients. 67.3% reported an education level of middle school or below. 62.1% were worried about their health, 53.5% admitted to knowingly making decisions injurious to their health, and 57.3% admitted that they forget to take their medications. Over 80% reported that they did not understand their diagnoses or the role of their medications. Stress was a common theme. 26.7% reported violence at home.

Conclusion: This survey sheds light on social barriers to compliance and management of health among low- and middle-income patients diagnosed with chronic conditions. Even within this smaller, voluntary sample there appears to be a large need for counseling and education to improve patient health literacy as well as the management of stress and safety. Future studies may focus on the efficacy of such interventions.

NARCOTICS ARRESTS IN MIAMI-DADE COUNTY DEVIATE FROM COUNTY AND NATIONAL TRENDS OF OPIOID DRUG USE

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Importance: Over the past decade, the United States has witnessed a rise in the number of individuals addicted to opioids. In 2016, two million Americans were addicted to prescription pain relievers, and 591,000 had a substance use disorder involving heroin. The majority of those addicted are young/middle-aged (25-52 years), non-Hispanic white males. Opioid use in Miami-Dade County (MDC) reflects the trends seen on a national level. Objective: We hypothesized that trends in narcotics arrests in MDC would mirror the trends of opioid use in this region. Methods: Public data accessed through the Miami-Dade County Police Department was analyzed. This data included information on all arrests made between 2005-2016 due to narcotics. Data included date of arrest, sex and race of perpetrator, and the location of the arrest. Statistical analysis on this data will include linear regression on narcotics arrests from 2005-2016 and Fisher’s Exact Test to determine statistical significance of narcotics arrests based on sex and race. Results: From 2005-2016, 50,491 narcotics arrests occurred in MDC. Of these, 49% of arrests involved black males and 35% involved white males. Narcotics arrests increased from 2,014 arrests in 2005 to 6,067 arrests in 2008. After 2008, there was a steep decline in narcotics arrests to 3,193 in 2011. Since 2011, arrests have been increasing once again and reached 4,144 in 2016. Though arrests have occurred in all regions of MDC, the majority have occurred in Overtown (33%), Little Havana (11%), Little Haiti (11%), and Model City (10%). Discussion: Narcotics arrests in MDC do not reflect county and national opioid abuse trends. The decrease in number of arrests from 2008-2011 does not reflect the county and national rise of individuals addicted to opioids during this same time period. This discrepancy may be the result of a decrease of funding to the MDC Police Department, however, further investigation will need to be pursued. Additionally, nearly half of all narcotics arrests in MDC involved black men, which is disproportionate to the racial demographics of users. Nationally, African Americans represent only 12.5% of illicit drug users, but make up 29% of drug offenses, and 33% of state facility incarcerations for drug offenses. These discrepancies may be due to the demographics of narcotic suppliers, racial profiling among police officers, distribution of police assignments in various neighborhoods, or the increased visibility of homeless addicts in lower income areas. The ultimate objective of this study is to better understand the nature of narcotics arrests and to create a targeted approach to address opioid substance abuse in MDC.
Conclusion: to 84.8%.

Cardiac death. Among those suffering from cardiac arrest, the proportion of sudden cardiac death ranges from 39.5%.

2 were found to suffer from sudden cardiac death. In infants with Wolf-Parkinson-White, 0.8% died from sudden cardiac death. The proportion of infant mortality due to sudden cardiac causes in those with underlying cardiac disease included in our review. We found that the proportion of infant mortality attributing to sudden cardiac causes ranges from 0.4% to 11%. The proportion of infant mortality due to sudden cardiac death in the general US population attributing to sudden cardiac causes by searching PubMed.

Making it challenging to determine the true magnitude of this problem. Thus, we reviewed the proportion of infant deaths attributing to sudden cardiac causes in the United States. Studies that do not have a clear definition of sudden cardiac death or clear distinctions between sudden cardiac death and sudden infant death syndrome were excluded. The reviewers then extracted data from included studies using a piloted data extraction form. Due to the heterogeneity of the included studies, we did not perform a meta-analysis.

Out of 7,730 studies retrieved, 14 studies involving 949,706 US infants were screened and appraised by at least two reviewers according to the protocol that was published a priori. Briefly, all retrieved studies were screened and appraised by the reviewers against the inclusion and exclusion criteria. To meet our inclusion criteria, all longitudinal or cross-sectional studies must contain peer-reviewed primary data related to the proportion of infant deaths attributing to sudden cardiac causes in the United States. Studies that do not have a clear definition of sudden cardiac death or clear distinctions between sudden cardiac death and sudden infant death syndrome were excluded. The reviewers then extracted data from included studies using a piloted data extraction form. Due to the heterogeneity of the included studies, we did not perform a meta-analysis.

Results: Out of 7,730 studies retrieved, 14 studies involving 949,706 US infants were included in our review. We found that the proportion of infant mortality attributing to sudden cardiac causes ranges from 0.4% to 11%. The proportion of infant mortality due to sudden cardiac death in those with underlying cardiac conditions ranges from 85% to 100%. None of the infants with restrictive cardiomyopathy or long QT syndrome type 3 were found to suffer from sudden cardiac death. In infants with Wolf-Parkinson-White, 0.8% died from sudden cardiac death. Among those suffering from cardiac arrest, the proportion of sudden cardiac death ranges from 39.5% to 84.8%.

Conclusion: Overall, our review observed a scarcity and variability in studies examining infant mortality.
attributing to SCD in the US. These findings suggest a need for more studies and consistent reporting of SCD in infants in order to provide accurate and current data for better awareness and prevention of SCD in our youngest patient population.

A META-ANALYSIS OF PATIENT REPORTED OUTCOMES OF FAT GRAFTING TO THE BREAST: DO OUR MEANS JUSTIFY THEIR ENDS?

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Introduction: Since its introduction, autologous fat grafting has become increasingly popular in the field of reconstructive surgery for its utility as an “ideal filler.” Despite the inconsistencies of graft take, fat grafting has developed into an indispensable tool that has a role in most modern operating rooms. Unfortunately, the process of lipoaugmentation often requires several iterations before a satisfactory result is achieved. Thus, it is important to recognize the patient perspective in this process to further justify the utility of this procedure. Many studies have used validated questionnaires to evaluate patient satisfaction, but this has revealed variable results. The purpose of our study is to conduct a meta-analysis of the published data to better understand patient satisfaction following autologous fat grafting. Methods: Meta-Analysis was conducted according to PRISMA guidelines. A PubMed/MEDLINE, Web of Science, and Embase search was conducted for all publications from January 1st, 2000 to October 1st, 2017 containing the phrase “autologous fat grafting” and related terms. Initial search yielded 2255 results and review of this literature revealed significant heterogeneity of results reported so the BREAST-Q, a validated patient-reported outcome measure, was selected for analysis. A total of 16 publications utilized this metric, and of these 7 were included based on availability of raw data. Pooled data were analyzed to compare satisfaction to those who did not undergo fat grafting. Results: The total number of patients included in the meta-analysis is 2,243, of those 310 received fat grafting and 1,933 did not. The mean age of patients included is 48.8. The questionnaire was filled out anywhere from 3 to 30 months post-operatively. When compared to patients who did not undergo fat grafting, on a scale from 1 to 100, results demonstrated lower satisfaction with breast (63.2 vs. 66.1), lower psychosocial well-being (69.9 vs. 75.2), and lower physical well-being (74.3 vs. 76.8) in patients who received fat grafting. The only domain in which fat-grafting scored higher was sexual well-being (57.9 vs. 55.7). Conclusions: This meta-analysis demonstrates that, according to the available studies with quantifiable data, fat grafting to the breast does not necessarily improve patient satisfaction. Although surprising and counter intuitive, this may be explained by the selection bias inherent in these studies. Further, the data are severely limited by the lack of consistent baseline scoring to evaluate improvement over time. Further level I studies evaluating patient satisfaction after fat grafting in the setting of breast reconstruction are required.

A SINGLE INSTITUTION STUDY: ARE REPEAT CT SCANS NECESSARY FOR EVALUATING SMALL BOWEL OBSTRUCTION?

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Introduction: Patients admitted for small bowel obstruction (SBO) will typically receive a non-contrast CT in the ER when first admitted. However, CT with contrast – the gold standard – can provide data that is crucial for determining the management of patients with SBO – surgical vs. medical. The first purpose of this study is to retrospectively compare outcomes of patients that had non contrast CT followed by CT with contrast and determine if the second CT changed the management. The second purpose was to prospectively patients admitted to the surgery service with SBO and had received either CT with contrast, CT without contrast, or both, and were followed to determine if CT with or without contrast made a difference in their management or length of stay in the hospital. Methodology/Results: At our institution, we retrospectively queried the medical record data base from January 1, 2015 to January 1, 2017 for patients admitted for small bowel obstruction and received 2 or more CT scans. From there, patients that received non-contrast CT followed by CT with contrast were included in the study. Patients who received only one kind of CT or CT with contrast followed by CT without contrast were excluded. Additionally, from October 1, 2017 to January 1, 2018 we prospectively followed patients admitted to the surgery service who were admitted for SBO. We then followed these patients to identify what type of scans they received during their admission, and determined how their management or length of stay was changed. Results: There were 536 patients who had CT scans performed for SBO. 110 patients (20.5%) were scanned 2 or more times, and 70 of those patients (63.6%, overall 13.1%) had CT without contrast followed by CT with contrast. Of the 70 patients that met criteria for having both types of scans in the correct order, X patients were managed on the surgical team (as opposed to GI or other medical teams). We found that X
(data pending) percent of patients had their management changed (non surgery to surgery) by the additional CT scan with contrast. In the prospective part of the study, we found patients X patients had received CT without contrast, Y patients had received CT with contrast, and Z patients had received both. Length of stay was X, Y, Z, for each group, respectively. X patients from group X, Y patients from group Y, and Z patients from group underwent surgery. **Discussion:** From this study, it appears that most patients who underwent both CT scans did not have their management changed by the additional CT scan (proposed). Additionally, there was no change in management or statistical difference in LOS of patients who received CT with or without contrast in the prospective group (Proposed). **Conclusion:** While CT scans with contrast are the gold standard, they do not play a significant role in treating SBO. The cheaper, quicker option of CT scan without contrast may suffice in the management of patient with SBO.

### CAN PREOPERATIVE FSH PREDICT UPGRADE SEMEN PARAMETERS IN MEN WITH SEVERE OLIGOSPERMIA WHO UNDERGO VARICOCELE REPAIR?

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**Introduction:** Follicle-stimulating hormone (FSH) can be used to predict improvement in semen parameters following varicocele repair. Couples with Total motile sperm counts (TMSC) less than 5 million are destined for invasive assisted reproductive techniques. Varicoceleectomy can potentially upgrade semen quality making patients eligible for less invasive therapies. Few studies have evaluated predictors of upgrading semen in men with TMSC <5 million after varicocele repair. We hypothesized that men with TMSC <5 million and normal FSH will have a greater chance of upgrading semen quality. **Methods:** We identified men with TMSC <5 million (at least on 2 semen analyses) who underwent microscopic subinguinal varicocelectomy between May 2015 to April 2017. We evaluated age, FSH (normal 2-8 ng/dL), testis size, grade of varicocele, preoperative and post-operative semen parameters (3-6 months after surgery). Significant improvement was defined as upgrading of semen quality based post-operative total motile sperm count: IVF (<5million), IUI (5-9million) and natural pregnancy (greater than 9million). Data were analyzed using Microsoft excel, p<0.05 was considered statistically significant. **Results:** A total of 22 men with severe oligospermia and TMSC <5million underwent varicocele repair. Among the 22 men, 10 had preoperative FSH < 8ng/dL and 12 had >8ng/dL. TMSC in men with FSH <8 ng/dl improved significantly post operatively (1.46 to 9.437million p< 0.05). In addition, men with FSH >8 also improved significantly post operatively (0.56 to 6.67million, p<0.05). Interestingly 50.0% of men with TMSC<5 million and FSH<8 upgraded semen quality to natural pregnancy range, whereas only 33.3% of men with TMSC < 5million and FSH>8 upgraded semen quality (Table). Age, testis size and grade of varicocele did not appear to be associated with upgrading semen quality. **Conclusions:** Up to 40.9% of men with TMSC <5 million upgraded into the natural pregnancy range (TMSC > 9million) after varicocelectomy. Men with normal FSH and TMSC <5 million appear to have a greater chance of upgrading semen quality following varicocele repair. Preoperative FSH can be used to counsel couples who are planning to undergo varicocele repair +/- assisted reproduction.

### PIPELINE EMBOLIZATION DEVICE FOR TREATMENT OF INTRACRANIAL PSEUODOANEURYSMS

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**Introduction:** Intracranial pseudoaneurysms are rare, accounting for 1% of intracranial aneurysms. However, they are associated with high rupture rates of up to 60% prior to definitive treatment, which can result in a significant mortality rate ranging from 31% to 54%. These aneurysms are often due to blunt, penetrating, infectious, or iatrogenic injury. Traditionally, treatment consists of sacrifice of the parent vessel either by endovascular methods including coil occlusion or polymer or glue embolization, or open vessel deconstruction with or without intracranial bypass. While, there have been a few case reports of the successful use of flow diverting stents for treatment of iatrogenic intracranial vascular injuries, the role of the Pipeline embolization device (PED) remains unclear. In the largest case series to date, we present our multi-institutional experience with endoluminal reconstruction of intracranial pseudoaneurysms using the PED. **Methods:** The authors reviewed a retrospective cohort of intracranial pseudoaneurysms that were treated with PED between 2014 and 2017 at 7 institutions. Data collection included demographic data, indications for treatment, number and size of flow diverting stent used, pre-operative and post-operative angiographic and clinical outcomes. Simple statistical analysis was carried out using SAS. **Results:**
11 patients with a mean age of 56.8 years old (range 16-75) underwent PED placement for intracranial pseudoaneurysms. 5 patients suffered iatrogenic intracranial vascular injuries from transsphenoidal surgery, 3 patients had injuries associated with surgical intervention for invasive sinus infections involving mucormycosis, aspergillosis, and histoplasmosis and 3 patients presented with traumatic pseudoaneurysms. Of these 11 patients, 8 demonstrated diminished pseudoaneurysm filling or resolution on follow-up imaging. 1 patient was noted to have an intraluminal thrombus and underwent ICA sacrifice. 2 patients were found to have pseudoaneurysm progression and also underwent subsequent ICA sacrifice. No patients developed any further neurologic deficits or complications after PED placement. Conclusions: Parent vessel sacrifice remains the preferred treatment for intracranial pseudoaneurysms. However, in patients who cannot tolerate parent vessel sacrifice or open surgical bypass, PED may be a feasible alternative and possible future treatment replacement. Nevertheless, given the high morbidity and mortality associated with pseudoaneurysms, we recommend short-term follow up within 1 week with repeat angiography for evaluation of pseudoaneurysm progression.

IGF-1 TREATMENT TO ENHANCE NERVE REGENERATION AND MINIMIZE MUSCLE ATROPHY IN LIMB TRANSPLANTATION

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Introduction/Aim: Following limb transplantation, functional recovery is dependent on nerve regeneration. The extent and speed in which the recipient’s axons regenerate into the transplanted limb and re-innervate muscle and skin determines the degree of motor and sensory function gained. Treatments to enhance nerve regeneration and functional recovery are lacking. IGF-1 is a naturally occurring peptide hormone that stimulates cellular growth and prevents apoptosis in almost all body tissues, including nerve, muscle and blood vessels. We hypothesize that IGF-1 treatment will enhance functional recovery following limb transplantation through enhanced nerve regeneration and decreased muscle atrophy. Methods: All animals received orthotopic allogeneic hind limb transplants from Brown Norway (BN) to Lewis (LEW) rats and received FK506 for graft maintenance. There were two groups (n=5 per group), one receiving daily subcutaneous IGF-1 (1 mg/kg/day) and one control group. Animals were sacrificed at 21 days for quantitative nerve and muscle histomorphometry. Results: Nerve histomorphometry demonstrated significantly greater total fiber number (p=0.004) and fiber density (p=0.023) in the IGF-1 treated animals as compared to controls. Histomorphometric analysis of myofiber cross-sectional area as a measure of muscle atrophy is pending. Conclusions: IGF-1 treatment significantly enhanced nerve regeneration as measured by quantitative nerve histomorphometry. Muscle histomorphometry may also demonstrate diminished muscle atrophy and increased vascularity in treated animals (data pending). This study highlights the promise of IGF-1 as a function-enhancing therapy in limb transplantation. Future studies at later time points with direct functional assessments are needed.
Department of Public Health Sciences Showcase

POSTER SESSION
FEBRUARY 23, 2018
9:00 AM – NOON
ANALYSIS OF A FREE ORAL AND HEAD AND NECK CANCER SCREENING: CHARACTERISTICS OF PATIENTS AND FINDINGS

Misha Armstrong, Prashant Angara, Brandon Burroway, Brianna Cohen, Adam Kravietz, Simon Menaker, Kush Panara, Zoukaa Sargi MD MPH. University of Miami Miller School of Medicine, Miami, FL 33136, Department of Otolaryngology, University of Miami Miller School of Medicine, Miami, FL 33136.

Introduction/Aim: Over 60,000 Americans are diagnosed with head and neck cancer (HNC) every year. An estimated 75% of HNCs are associated with tobacco and alcohol use. However, public awareness regarding risk factors associated with these cancers is poor. Community-based screenings are an effective intervention for delivering services to underserved populations. Studies have shown that community-based screenings attract significantly more patients with HNC risk factors than hospital-based screenings. Screenings in the community allow for education, increased awareness of symptoms, early detection, and provision of ENT services that otherwise would not be available. Methods: Four screening fairs over a one-week period took place in the local South Florida community and at local hospital sites (n=240). Participants completed 35 survey questions regarding demographics, knowledge of HNC, risk factors, and symptoms prior to screening. All participants were eligible to complete the survey. Summary statistics were performed using SPSS. Results: In total, 240 individuals were screened with 164 participating in the survey (response rate 68%). Only thirty percent of participants had at least a college diploma, 42% reported making less than $10,000/year, and 35% reported having no health insurance. About a third of participants (28%) had a history of smoking, 33% used alcohol, and 18% reported having at least three symptoms associated with HNC. Referrals were given for further head and neck evaluation or general ENT follow up (33%), with 17% of referrals for other specialty care. The majority of the ENT follow up recommendations were for benign conditions. However, 17% of the ENT referrals were for conditions requiring immediate consultation. Conclusion: Free HNC screenings provide specialty services to underserved communities and an opportunity to increase awareness regarding risk factors. Although the majority of participants do not have the typical risk factors for HNC, there is still an increased risk due to low SES, lack of insurance, and reporting of symptoms. In concordance with existing literature, most patients have benign or non-emergent ENT findings. However, in our sample 17% of referrals were for immediate intervention due to suspicion of malignancy or disease with risk of complications. Further evaluation is necessary to determine the number of participants receiving follow up care and barriers to follow up care.

PLANNING FOR OUTCOME AND IMPACT LEVEL RESULTS IN THE SALUD MESOAMERICA INITIATIVE

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Introduction/Aim: Women and children of the poorest quintile of Central America carry a disproportionate burden across various health outcomes. Despite improvements in maternal and neonatal health in the last decade, maternal and child mortality rates remain among the highest in the hemisphere. Global maternal and child health initiatives often claim to follow results-based planning; however, the results sought by most programs typically do not exceed products, activities or outputs. Deliverables such as equipment purchased, training sessions provided, or hospital units furnished can be monitored using standard project management tools, and do not necessarily translate into desirable outcome- and impact-level results. Salud Mesoamerica Initiative (SMI), a health financing initiative administered by the Inter-American Development Bank (IDB), guides and implements policies and interventions that promote maternal, antenatal, neonatal and child health care, as well as structural reform and policy dialogue for sustained long-term success and health impact in Central America. The aim of this project was to delineate and describe SMI’s planning for results methodology. Methods: The study was undertaken through extensive staff interviews and comprehensive reviews of in-house documents, such as memos, notes, manuals, and guidelines. This was supplemented by country missions and meetings with Ministry of Health officials, highlighting the extent to which
planning for results has impacted SMI’s progress since its activation. Derived methods and descriptions of SMI’s planning framework were continually contrasted with common approaches to project planning and management, highlighting strengths and adaptations of SMI’s rigorous evidence-based methodology. **Results:** Planning per SMI encompasses a delicate balance between choosing inputs, accelerating processes, prioritizing activities, and adapting efficiently while maintaining focus on greater targets. SMI countries are required to achieve results at these levels within very short time-frames. With typical project management tools, countries would likely not meet health indicators to ensure returns on their investments. **Conclusion:** The planning framework will serve a primary purpose in loan decisions by IDB health specialists. Secondarily, it will serve as a planning model for ministries of health and international development organizations. Thirdly, methods may be complemented by in-depth analyses of specific SMI interventions. Although operationalized in the context of financial incentives for health, SMI’s planning principles, tools and methodologies will aid decision makers in any results-based project, both in and outside of health. They are intended for anyone who has to identify and operationalize rational solutions to complex and dynamic problems, particularly under resource constraints.

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3 A SURVEY OF HEALTHCARE WORKERS ATTITUDES AND RECOMMENDATION PRACTICES TOWARD MOSQUITO-REPELLENT IN SOUTH FLORIDA AMID THE ZIKA VIRUS OUTBREAK

**Natalie A. Cain**, Paola Lichtenberger MD, Naresh Kumar PhD, University of Miami Miller School of Medicine Department of Public Health Sciences.

**Introduction/Aim:** Zika virus (ZV) is a vector-borne flavivirus transmitted by the *Aedes* species mosquito, which are aggressive urban, daytime biters that also thrive at night. Use of insect repellent is strongly recommended by the CDC and EPA to prevent ZV infection. Healthcare workers (HCW) are a unique group of individuals with the responsibility of providing pertinent information to patients seeking health-related advice. This study describes the knowledge and attitudes of HCW in South Florida on insect repellent usage and recommendation as a protective measure against ZV for their patients. **Methods:** An evidence-based survey tool was created based on a PubMed literature review encompassing previously validated survey questions on insect repellent usage and ZV transmission. The survey tool was distributed via an online email platform and printed copies to HCW in teaching hospitals in South Florida. Participants received a monetary incentive for their participation. Survey results were stored in a password-protected database and analyzed through Pearson’s Chi Squared test and ANOVA on SPSS Statistical Software. **Results:** A total of 144 HCW participated in the research study. The demographics were 57.6% medical students, 31.9% resident physicians, 9% attending physicians and 1.5% other (medical assistant and registered nurses). 56.9% of participants have recommended insect repellent to their patients and 13.2% responded “I don’t know enough about repellent to recommend it” (mean 1.868, p=.0884, CI 1.075-1.425). Overall, participants answered 41.8% of the fund of knowledge questions correctly (p=.0672, CI .985-1.251). Participants reported an average confidence level of 2.632 on a five-point scale in prescribing and giving detailed instructions on insect repellent appropriately (p=.0944, CI 2.445-2.819). 77.8% of participants felt they should have more information about the use and safety of repellent to recommend it more comfortably to their patients (mean .236, p<.0493, CI .139-.333). **Conclusion:** This study demonstrates a significant knowledge gap in insect repellent concepts and recommendations for ZV prevention among the HCW population. Participants also show a lack of confidence in their ability to recognize ZV and recommend repellent appropriately. The study shows HCW desire more accessible information about repellent for their patients’ needs. Limitations to this study include a small sample size. Based on these results, intervention among this population is warranted to inform HCW of insect repellent information, appropriate recommendation approaches and availability of resources for ZV prevention.
UTILIZATION OF PSYCHOSOCIAL SCREENING TOOL FOR MENTAL HEALTH REFERRAL IN AN UNINSURED, MINORITY POPULATION FROM THE UNIVERSITY OF MIAMI'S PEDIATRIC MOBILE CLINIC: A FACTOR ANALYSIS APPROACH.

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Introduction/Aim: In the US, mental disorders have become common among children. Florida Health surveys indicate the gravity of mental health issues among children parallels national trends. To mitigate such trends, some clinics utilize tools like the Pediatric Symptom Checklist (PSC) which asks questions regarding the behavior of the child. Amongst children suffering from mental health issues, reports indicate that unmet needs are emphasized in minority and uninsured populations. With additional funding received by the Pediatric Mobile Clinic (PMC), the capacity of PMC mental health services has increased along with the growing population need. This study aims to inform the PMC on its psychological patient profile, assess construct validity of the PSC, and compare results to studies found in literature. Methods: Children between 4-12 years whose parents/guardians completed a PSC during a routine visit to PMC (August-2015--December-2016) were included in this retrospective cohort study. The patients’ electronic medical charts including sociodemographic characteristics were linked with PSC questionnaire data and US Census neighborhood poverty data based on patients’ residency at the time of PMC visit which were utilized in grouping participant’s residency by zip code according to the federal poverty thresholds. Exploratory data analysis and exploratory factor analysis were conducted using the 17-item-PSC extracted from the 35-item-PSC. The PSC questionnaire were entered into REDCap database, linked with sociodemographic and US census data to analyze with SASv9.4. Results: A total of 562 children satisfied eligibility criteria. A majority of the patients were Caucasian (68.57%) and self-identified as Hispanic (92.88%). Agreement between the PSC-17 and PSC-35 was moderately high (Kappa statistics=67.3%, 95% CI: 55.6%, 79.1%). Extraction of PSC-17 from PSC-35 revealed that 20 patients who did not meet cut-off score for referral in the PSC-35 did qualify with the PSC-17. Of the subscales found in PSC-17, attention issues were most prevalent. In the exploratory factor analysis, three items did not load on subscales found in comparison studies. Conclusion: Our analysis showed the screeners were not always completed, which could improve from the medical provider and parent standpoints. We can conclude that using the PSC-17 in the clinic will be sufficient in comparison to the PSC-35. Although the significant loadings that we did find were mostly distributed on the same factors, the loadings were not as strong as those found in a comparison study. This may mean that the questions are not conducive to the constructs in the 17-item PSC as well as they have been found to be in other populations.

ASSESSING RISK FACTORS FOR DEMENTIA AMONG OLDER ADULTS: THE AGING, DEMOGRAPHICS, AND MEMORY STUDY (ADAMS)

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Introduction: The prevalence of dementia is expected to double in the United States (US) by 2050. There is no curative treatment and all approved medications focus on reducing problematic symptoms. However, research has identified many risk factors that are associated with dementia. This study assesses non-modifiable and modifiable risk factors for dementia. It also identifies which modifiable risk factors should be reduced in order to significantly decrease the probability of dementia in older adults within the US. Methods: The Aging, Demographics, and Memory Study (ADAMS) consists of a nation-wide, population-based sample of older adults (>70 years) from 2001-2008 (n=856). Participants were interviewed and in-home assessments were conducted. A multivariable logistic regression model was used to identify risk factors for dementia by including apolipoprotein ε4 genotype (APOE e4), along with other non-modifiable (gender, age, ethnicity) and modifiable (BMI, education, history of alcohol and smoking, traumatic brain injury (TBI), hypertension, depression, hypercholesterolemia, diabetes). Adjusted odds ratios (aOR) and corresponding 95% confidence intervals (95%CI) were calculated. Data management and statistical analysis were
performed by SAS version 9.4. **Results:** Out of 856 participants, 648 were included in our study. The majority were female (57.56%), non-Hispanic white (73.60%), and aged 80-89 years (43.21%). Diagnostic evaluations resulted in nearly 30% demented, 30% with cognitive impairment not dementia (CIND), and 40% normal cognitive function. Multiple risk factors significantly predicted dementia in older adults: presence of APOE e4 (aOR=2.81, 95%CI: 1.62-4.87), less than high school degree (1.83, 1.06-3.15), history of TBI (3.56,1.61-7.88), history of depression (4.16, 2.39-7.24), and no history of hypercholesterolemia (2.15, 1.24-3.71). In comparison to 70–79 year olds, those who were 80–89 years were more likely (5.82, 3.37-10.04), and those aged older than 90 years (37.59, 14.35-98.45) were significantly more likely to have dementia. Likewise, in comparison to those with underweight/normal BMI, overweight (0.37, 0.21-0.65) and obese (0.22, 0.11-0.46) participants were significantly less likely to have dementia. **Conclusion:** This assessment revealed significant modifiable and non-modifiable risk factors to predict dementia in older adults. Further research should be conducted to determine the impact of reducing these identified risk factors on risk of dementia.

6 CENTERING PREGNANCY FOR HEALTH LITERACY

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**Introduction:** Centering Pregnancy is an evidence-based model for group prenatal care designed to provide health education reduce maternal and infant morbidity in disadvantaged populations throughout the US. Since 2014 the Centering Pregnancy site in Lantana FL has administered tests in to patients prior to and after completing the curriculum, but until now the data from these pre- and post-tests has not been analyzed. The purpose of this project was to evaluate pre- and post-tests given by the Lantana site for Centering Pregnancy between 2014 and 2016 to assess changes in knowledge regarding maternal health promotion and disease prevention, as well as fetal and infant health promotion and disease prevention following completion of the curriculum. **Methods:** 196 Cumulative pre- and post-test pairs, and 227 Family Planning pre- and post-test pairs administered between 2014 and July 2016 were evaluated. The change in average total score and average number of questions left unanswered were calculated and assessed using the T-test. This analysis was repeated to evaluate the change responses between pre- and post- Family Planning tests. The change in average accuracy of responses for individual questions between pre- and post-tests was then analyzed and evaluated using the McNemar’s test. **Results:** The average total score for the cumulative exam increased from 12.6 on the pre-test to 17.9 on the post-test of a possible 20 points, while the average number of questions unanswered decreased from 5.2 to 1.2 (P<.01). Similarly, the average score for the family planning exam increased from 4.5 to 6.0 out of a possible 7 points, and the average number of questions unanswered decreased from 1.7 to 0.24 (P<0.01). The greatest increases were seen in questions regarding maternal health promotion, with an increase from 51% of respondents answer questions correctly on the pre-test to 80.9% correct responses on the post-test (p=.01). This indicates a consistent and significant improvement in health knowledge among the women served by Centering Pregnancy. **Conclusion:** Our findings suggest that the Centering Pregnancy model of prenatal care combined with group education and social support can be an effective method for improving health knowledge in underserved populations. It may be worthwhile to similarly evaluate other Centering sites to assess the generalizability of these results.
EVALUATION AND MONITORING OF THE PATIENT NAVIGATION INITIATIVE FOR IMPROVING CARE CONTINUITY AFTER SCREENING AT A STUDENT-RUN HEALTH FAIR

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Introduction: The Department of Community Service (DOCS) at the University of Miami is a student-run organization with the goals of improving the health of underserved populations and of training medical students. While over 2500 patients are screened each year at DOCS’ health fairs, few high-risk patients receive follow up care. The Patient Navigation Initiative (PNI) was developed with the goal of improving continuity of care for high risk patients. Community based participatory research was used in developing the initiative. A competency based patient navigation education program was developed to provide training to students to be patient navigators.

Aim: To evaluate the impact of patient navigators on connecting high and average risk patients to follow up health care appointments after screening at the DOCS Liberty City Health Fair. Methods: A randomized controlled trial was conducted. A “high risk” patient (HR) had systolic blood pressure >160 mmHg, fasting glucose >200 mg/dL, or abnormal findings from any other station. An “average-risk” (AR) patient was any patient who attended the health fair who did not meet these criteria. All 29 HR patients were given patient navigators. The first 41 AR patients were enrolled in the study and randomized, using permuted random block design, to receive patient navigation (n=20 treatment) or to not receive navigation (n=21 control). Patient navigators called their patients approximately every week for three months to help address barriers to obtaining and attending a follow up health care appointment. Data were recorded on original REDCap forms that were adapted from The George Washington Cancer Center’s Patient Navigation Barriers and Outcomes Tool (PN-BOT) to fit our program. Outcome measures of patient navigation were the ability to make contact, counseling the patient on phone, healthcare appointment made, and healthcare appointment attended. Results: Complete data was collected on 23 HR patients, 11 AR patients with navigation, and 17 AR patients with no navigation. When comparing all patients receiving navigation (high risk plus treatment group) and the control group, navigation improved both contact (88.2% navigated vs 47.1% control, p<0.05) and counseling (73.5% navigated vs 47.1% control, p<0.05). There was a suggestion of improvement in appointments made (47.6% navigated vs 41.2% control, p=0.22) and attended (29.4% navigated vs 11.8% control, p=0.11), that did not reach statistical significance. In contrast, there was not a significant difference in any outcome between HR and AR treatment groups, who both received navigation (87% HR vs 90.9% AR contacted, p=0.42; 73.9% HR vs 72.7% AR counseled, p= 0.32; 47.8% HR vs 45.5% AR appointment made, p=0.90; and 30.4% HR vs 27.3% AR attended appointment, p=0.31). Conclusion: Patient navigators have the potential to increase attendance at follow up health care appointments for high and average risk patients.

DIFFERENCES IN CHARACTERISTICS AND RISK BEHAVIORS AMONG PEOPLE WHO INJECT DRUGS PARTICIPATING IN FIXED-SITE SYRINGE EXCHANGE VERSUS MOBILE SYRINGE EXCHANGE IN MIAMI, FLORIDA

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Introduction: In March 2016, Florida passed the Infection Disease Elimination Act (IDEA), legalizing the formation of the first syringe exchange program in Florida, which opened in December 2016 at a fixed site in Overtown, Miami. Since that time, the exchange expanded in April 2017 to include a mobile van unit that provides the same services at different locations throughout Miami-Dade County. The aim of this study was to present differences in key variables among people who inject drugs (PWID) surveyed at the fixed site versus those surveyed at the mobile unit. Methods: Trained interviewers obtained informed consent and conducted face-to face interviews from all first-time participants at the IDEA Syringe Exchange, both at the fixed site and the mobile unit. The interviews took approximately 20 minutes and consisted of questions to identify participants’ demographic characteristics, drug injection and sexual behaviors, and HIV/Hepatitis C (HCV) status. Descriptive statistics were generated using Stata® software. Results:
Compared to participants at the fixed site, a greater percent of participants at the mobile site were African-American (24.5% vs 4.1%, p < .001), homeless (71.9% vs 40.9%, p < .001), and uninsured (62.3% vs 55.9%, p = .006). Participants at the fixed site were more likely to report injecting heroin (47.2% vs 34.6%, p = .001) and using prescription painkillers before ever initiating injection drug use (65.9% vs 48.3%, p = .01). Mobile exchange participants were more likely to report injecting in public areas (69.6% vs 48.5%, p = .02), sharing needles when injecting (72.4% vs 39.3%, p = .04), and unprotected sex (80.0% vs 67.3%, p = .01). They were also more likely to have a prior diagnosis of HIV-positive (15.91% vs 9.33%, p = .03) or HCV-positive (57.78% vs 43.3%, p = .02).

**Conclusion:** Participants at the fixed site and mobile site report differences in socioeconomic status, drug injection and sexual behaviors, and HIC/HCV status. Taken together, these results suggest that the mobile unit is capturing a subset of PWID in Miami that the fixed site is not, and vice-versa. As the opioid crisis extends into all demographics, such multimodal efforts to target PWID should be kept in mind, especially when unveiling future syringe exchanges in Florida.

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9 **RIVERSIDE PARK – A BETTER PARK LEADING TO A BETTER COMMUNITY**

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**Introduction:** Violence and crime have a large public health impact, affecting multiple health outcomes such as mortality, injury, mental health and physical activity. Miami’s Little Havana neighborhood is a community where violence and crime are seen daily. The Riverside Park Workgroup, made up of various organizations and community residents, is working to reduce crime and violence around Riverside Park. This public park has the potential to be a place where people can engage in behaviors that promote health and well-being. The purpose of this capstone project was to inform park improvement work by analyzing existing crime data and community members’ self-reports regarding the park. **Methods:** Secondary data analyses and a literature search were conducted. The secondary analyses were conducted with existing crime data from two time periods: 1) December 2015-June 2016, the time period before the Workgroup began its interventions, and 2) December 2016-June 2017, the time period following the start of the interventions. Analyses were also conducted on 313 self-report surveys by community residents near the park regarding perceptions of the park, and barriers to park use. A literature search was conducted to identify which evidence-based interventions could be used in a community such as Little Havana. **Results:** Perceptions of the park prior to the interventions were negative with 76% of respondents stating the park was unsafe. Barriers to park use were: limited safety, lack of lights, closed restrooms, and limited activities. Before the Workgroup interventions began, there were 187 crimes in the quarter-mile radius around the park, and afterwards there were 131 crimes, indicating a 30% decrease following park improvement interventions. In the latter time period, crimes were also not as highly clustered around the park, and there were much fewer crimes on the perimeter of the park. Evidence-based crime prevention interventions and tools from the literature were summarized so they could be used by the Workgroup in Little Havana. **Discussion:** The crime data suggests that crime has decreases in the areas surrounding the park following the Workgroup’s interventions. While this cannot be attributed solely to the Workgroup’s interventions, it does suggest that the area is now a safer place. Moreover, many of the barriers to park use mentioned by the community members have been addressed. These findings should be reported to residents who live in this community, as it may help encourage park utilization and health. Continued community involvement in keeping the park safe is needed.
MIAMI IDEA EXCHANGE PILOT PROGRAM: A ONE YEAR EVALUATION OF SHORT-TERM GOALS

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Introduction: Miami has one of the highest heroin usage rates and HIV incidence of any city in the United States. In December 2016, the Miami IDEA Exchange was opened with the goal of providing clean drug injection equipment, as well as clean needles in exchange for dirty ones. Furthermore, the Exchange performs HIV and HCV testing, linkage to treatment and drug use treatment centers, and harm reduction education. Methods: Participants were assessed for demographic characteristics and baseline sexual and drug use behaviors with an initial enrollment behavioral survey. Behaviors were reassessed at three month intervals with a quarterly assessment. Daily transactions were also recorded. Participants could either exchange needles at a fixed site, located in Overtown, Miami, or at the mobile unit, a van that parks in remote and underserved neighborhoods in Miami. Results: 506 participants visited either the fixed site or the mobile unit. There were 3,162 participant visits, exchanging 71,170 needles. 73.72% of participants were male, 73.66% were Caucasian, 63.81% were currently unemployed and 40.93% were homeless. 45.67% of participants used heroin as their drug of choice and 63.03% report having been addicted to painkillers prior to injecting drugs. 55.72% of participants reported reusing their syringes or needles every time they inject, while 60.00% report never sharing needles or syringes with other injection drug users. 100% (162/162) of participants whose last HIV test was negative, and 100% (4/4) who did not know their prior test results, tested negative. 22/83 participants who had a prior negative HCV test, tested positive at enrollment. Overall, 85.07% of participants felt that the Exchange has enabled them to take greater responsibility for their health, and 95.06% were very satisfied with the Exchange. Conclusions: In the year since the Exchange opened, the program has been successful in providing clean needles and drug injection equipment, harm reduction services, and linkage to care. Though most participants do not share needles with each other, most reuse their own needles, a risk factor for soft tissue infections. Though no newly positive HIV participants have been diagnosed, there were 22 participants with a new diagnosis of Hepatitis C.

EFFECTIVE CONTRACEPTION EDUCATION FOR WOMEN EXPERIENCING HOMELESSNESS

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Introduction: Women experiencing homelessness are a particularly vulnerable group when it comes to unintended pregnancy. Our data shows that of women aged 18-44 who have been pregnant at Lotus House Women’s Shelter, 82% has experienced an unintended pregnancy. The reason for this statistic is multifactorial, but includes limited education on methods of contraception, barriers to accessing their desired forms of contraception, and low health literacy affecting their attitudes about and knowledge of different forms of contraception. Methods: In order to create an effective contraception education intervention at Lotus House Women’s Shelter in Miami, a qualitative literature review was done to identify key components proven successful in other contraception education interventions previously. A total of 22 pieces of literature met criteria and were analyzed for an outcome of increased education on contraception, increased use, or a change in the attitudes or beliefs about contraception. These findings were then compared to surveys and focus groups done at Lotus House to assess the beliefs, attitudes, and knowledge about contraception in order to create a tailored intervention to the needs of the women at Lotus. Results: The 5 main outcomes for successful contraception interventions obtained from the literature review were 1) physician education, training, and communication 2) using a systems based approach 3) utilization of multidisciplinary teams 4) culturally competent materials and 5) multifactorial approach to education. The surveys and focus groups done at Lotus House showed themes of the main concerns which should be addressed in the intervention, which include 1) sexually transmitted infections 2) side effects of each method 3) cost 4) ease of access and 5) ease of use. Conclusion: In order to create an effective contraception education intervention for the women of Lotus, the findings from the comprehensive literature review of past interventions will be integrated with the data about concerns and beliefs about
contraception gathered by the surveys and focus groups. This will allow us to create a tailored, effective, sustainable contraception education intervention for the women of Lotus House.

12 SUBSTANCE ABUSE DISORDERS AMONG PATIENTS WITH DIABETES RECEIVING CARE AT THE UNIVERSITY OF MIAMI HEALTH SYSTEM

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Introduction: Effective diabetes management often presents enormous challenges. Furthermore, managing multiple conditions could also lead to worse diabetes care by distracting from diabetes care goals. Substance abuse disorders (SUDs) could affect diabetes care by compromising patient’s adherence to treatment, exacerbating other medical conditions, and increasing diabetes-related hospitalizations. The purpose of this study is to determine the prevalence of substance use disorders in patients with diabetes receiving care at the University of Miami Health (UHealth) System. Methods: We conducted a cross-sectional analysis of 5 years of electronic health record data of the UHealth system (January 1, 2012 to December 31, 2016) which included all patients with diagnosis of diabetes. The diagnostic variables were based on ICD-9 codes. First, we determined the means and the frequencies for demographics variables by SUDs status. Then, χ² tests (categorical variables) or independent t tests (continuous variables) were used to examine the differences between patients with and without SUDs with regards to demographic characteristics. Statistical significance for all tests were defined at p<0.05. Results: Overall, 10.5% of patients with diabetes (n = 9748) had a SUD. The prevalence of SUDs was higher in the group of patients between 45 and 64 years (12.9%), and among men (13.4% vs 7.6% in women). Compared with their non-SUDs counterparts, more patients with diabetes and comorbid SUDs were younger (62.4 years (SD=15.0) vs. 63.9 years (SD=12.8)), male (64.1% vs 49.6%), Hispanic (43.2% vs 41.3%) or Black (31.1% vs 26.5%), had a public health plan coverage (57.6% vs 51.9%) or were uninsured (2.7% vs 0.9%), and were HIV-positive (5.1% vs 1.7%) (All p<0.001). Conclusions: The prevalence of SUDs in this study is consistent with US estimate. However, ethnic minorities and publicly insured and uninsured patients were disproportionately affected in this large diverse sample. In order to identify the full impact that SUDs have on diabetes care, we will analyze a set of well-accepted diabetes quality indicators (HEDIS® measures) in a subsequent study. Our findings also highlight the need for healthcare systems to develop strategies to address this problem.

UNDERSTANDING BARRIERS TO HUMAN IMMUNODEFICIENCY VIRUS (HIV) TESTING/SCREENING AMONG PARENTS IN A MOBILE CLINIC SETTING

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Introduction: Among all the sexually transmitted diseases (STDs) in the United States (USA), HIV infection/acquired immunodeficiency syndrome (AIDS) is one of the most common and prevalent public health issues among adults in the USA as well as in Miami-Dade County. The rate of HIV infection in adults is amongst the highest for any age group, which is why this group should have ample opportunities to get tested. Sexual networks is a major determining factor for HIV risk in the USA, because with the population at a high risk to HIV tending to have sexual relations with people in their communities. Some other social determinants of health like lack of access to care, low health literacy, discrimination, homophobia, stigma, and poverty. Therefore, parents of youth visiting the Pediatric Mobile Clinic (PMC) are also at risk of HIV because of the social determinants of health. Evidence suggests that some of the interventions to prevent HIV among parents are to understand barriers to HIV testing and counseling. Understanding these barriers is essential to ensure that interventions are well targeted and maximally effective. The purpose of this study was to know some barriers to HIV testing and gain a better understanding whether the parents want to take/accept the HIV and other STI testing services if offered at PMC. Methods: To further understand factors that act as barriers to HIV testing and counseling among parents, In-Depth/Individual Interviews and rapid assessment qualitative
analysis (Matrix template) was conducted to characterize parents who do not accept the HIV and other STI testing and to better understand the barriers. **Results:** Most of the Creole-speaking parents mentioned barriers such as fear, embarrassment, privacy, stigma, and stress. On the other hand, Spanish-speaking parents concern was transportation, fees, shame, accessibility to testing sites, rejection of not accepting the positive test results, fear of positive test result, insecurities, a sick feeling of having AIDS and if insurance covers the test. This data reveals a deeper insight into the insecurities and fear of parents regarding HIV. **Conclusion:** The results show the importance of HIV pre, and posttest counseling, as most of the parents/guardians, was not aware of prevention, and treatment options as well as linkage to care for HIV positive individuals. HIV pre-test counseling would motivate parents to get tested for HIV by boosting their confidence and helping them to overcome their fear. Further, post-test counseling would help parents to deal with the positive test results by giving them the moral and medical support to increase their understanding of the resources available as well as the prognosis once they are linked to care. Improving knowledge of the disease and preserving privacy was essential concerns of parents that should be acknowledged. In my opinion, arranging small in-person informative sessions at PMC can guide the parents about HIV, privacy issues and how to get tested for it. Hence, by better understanding these barriers, the team can further help to make recommendations regarding expanding the current PMC HIV and STD testing in securing funding through grant development to develop the HIV testing program and offer HIV testing and counseling to parents as well.

**HOW DO PUBLIC SCHOOLS IDENTIFY AND MANAGE STUDENT ALCOHOL USE?**

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**Introduction:** Underage alcohol use amongst adolescents is associated with a wide range of negative developmental outcomes and transcends limits of gender, race, ethnicity, socioeconomic status, parental education, and geographic region. The purpose of this qualitative study was to examine the role of public schools in identifying and managing underage alcohol use through interviews with assistant principals, guidance counselors, social workers, and school-associated health care professionals. This study also assessed the feasibility of school-wide alcohol screening using a brief alcohol screening tool. **Methods:** Participants were recruited from schools across Miami-Dade County. Staff responsible for responding to student alcohol use events were approached in person among 15 schools in distinct neighborhoods of Miami-Dade County. Of those approached, 15 participants were recruited from four senior high and four middle schools. One-on-one, open-ended interviews investigated both the current school response to student alcohol use and the potential for future school-wide alcohol screening. **Results:** Between senior high and middle schools, it was generally true that student alcohol use was more common amongst senior high students, with rare events occurring amongst middle school students. A model emerged from these interviews for how both senior high and middle schools typically handle alcohol related incidents, with more than ten separate interventions and respective barriers identified. An important distinction was found between students presenting to campus in possession of alcohol and students revealed to consume alcohol off-campus. Specifically, in acute events of alcohol possession decisions were made in light of danger and liability whereas in cases of chronic alcohol consumption effort was made to contact parents and intervene. With respect to the potential for universal alcohol screening, common concerns emerged including the validity of students’ self-reports of alcohol use, schools’ legal responsibilities for reporting alcohol use, maintaining students’ confidentiality and the potential for a Hawthorne effect. School-wide screening was viewed as potentially serving an important need, more so at the senior high level. **Conclusion:** Through these interviews, it was found that public schools appear to play an important role in identifying and managing adolescent alcohol use. Both senior high and middle schools were already found to employ a variety of similar interventions for students using alcohol. Individual school-policy and discretion of the administrator, and not uniform policy across Miami-Dade County Public Schools, more often determine the management of student alcohol use. Alcohol screening at the senior high level will be difficult. Future school-based interventions should take heed of the complexity of the relationship between schools and student alcohol use.
SUCCESSES AND CHALLENGES OF THE ACTION, CARE, TRANSPORT (ACT) FOR CHILD HEALTH STORYTELLING PROJECT IN RURAL UGANDA

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Introduction: The prevention of child and maternal mortality are significant medical and public health challenges with increasing disparities between developed and developing countries. Specifically, in Uganda the maternal mortality ratio was 274 deaths per 100,000 live births while the neonatal death rate was 27 per 1000 live births in 2011. Intervention development, planning, and implementation efforts to decrease maternal and child mortality are often constructed around the Three Delay’s Model. The Three Delay’s model is constructed as follows: the decision to seek care (Phase 1); the infrastructure involved in reaching a medical facility (Phase 2); and finally, the receipt of appropriate and adequate treatment (Phase 3). Delays result from actual barriers at the care facility, such as lack of skilled birth attendants, technological equipment and medical supplies. This project aims to collect and analyze qualitative (1) narrative interviews and (2) direct participant observation data from residents of rural Uganda. Findings will inform the development of delivery methods for storytelling in communities affected by maternal and child mortality. Methods: A narrative analysis approach will be used to examine stories and recurring meanings within the data collected. Drawing on Polkinghorne’s two forms of narrative analysis, paradigmatic analysis of narratives and narrative analysis, this project will emphasize the utility of using narratives as a means of uncovering the lived experiences of women, men and other community members. Rather than discovering and creating themes from within the text, the project recognizes that the stories in which the community members tell are to convey a meaning intended for impact and change. Results: Interviews revealed four major themes prompting increase in seeking medical guidance and care from certified health centers after ACT: (1) increased knowledge in labor and delivery, (2) increased attendance in antenatal care and immunization sessions, (3) utilization of midwives during labor in place of traditional birthing attendants, and (4) utilization of community support groups during pregnancy. Conclusion: Continuation of the project is possible as it provides the support for intervention recommendations, particularly the solution to increase awareness of successful interventions and to improve on the challenges still being faced. The dissemination of information to target populations and communities will foster improved communication, and a more in depth understanding of the impact maternal and child mortality has on the health of the individual, significant partner and community. Finally, findings will aid in the understanding of the successes and challenges of maternal and child intervention programs in rural Uganda.

SYSTEMATIC LITERATURE REVIEW OF THE RELATIONSHIP BETWEEN POLYCHLORINATED BIPHENYLS (PCBs) AND COGNITIVE DEVELOPMENT IN CHILDREN

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Introduction: Prenatal exposure to environmental toxicants has been linked to cognitive deficits in children, with evidence particularly strong that mercury and other heavy metals are associated with reduced cognitive functions. However, less is known about the impacts of prenatal exposure to polychlorinated biphenyls (PCBs) on children’s cognitive development. It has been suggested that PCB concentrations in the order of 1000 ug/kg of lipids in maternal plasma, may increase the risk of mental or motor deficits in children. Prior research has identified inconsistent patterns of result but has not specifically broken down the result by cognitive domain or cognitive test, which may account for these inconsistencies in the literature. The purpose of this study is therefore to conduct a systematic literature review on the relationship of prenatal PCB exposure to children’s cognitive functioning, and whether this relationship varies within and across cognitive domains. Methods: A systematic literature review was conducted in the fall of 2017 using PubMed/Medline and Web of Science, on whether prenatal exposure to PCBs was linked to cognitive functioning in children. The focus of the review is on child cohort studies in peer-reviewed journal articles, in English, published from 1990 to November 2017. Standardized methods are employed for converting volume-weighted PCB
concentrations into plasma lipid-adjusted concentrations, as described previously in the literature. Studies were retained that measured any of the following 5 cognitive domains: attention, memory, IQ, language, and executive function. The pattern of results across studies is described for each cognitive domain. In addition, further follow-up analyses examine the pattern of results by cognitive sub-domain and cognitive test administered. The results of each article will be grouped by cognitive domain, and by cognitive test, to evaluate the statistical significance between and within groups. These results will be shown in tabular and graphical form for each domain. **Results:** An initial search found 193 articles, of which, 30 articles were identified that fit the inclusion criteria. Analyses comparing the association of converted PCB concentrations in maternal plasma to cognitive functions, subdivided by cognitive domain and test, are currently underway, with results expected by early February 2018. **Conclusion:** Based on previous research, the evidence is currently unclear regarding the strength and/or consistency of the associations between PCB concentrations in maternal plasma and subsequent child cognitive outcomes. The current systematic literature review is an attempt to bridge this gap in the literature, by breaking down these relationships within a specific cognitive domain or for a specific cognitive test. A further explication of the results will therefore be provided in terms of the specific associations of prenatal PCB exposure for each cognitive domain and test, as well as discussing implications of these findings for future research in this area.

THE PREVALENCE OF MENTAL HEALTH DIAGNOSIS AND REFERRALS IN THE CHILD AND ADOLESCENT HISPANIC POPULATION USING PEDIATRIC MOBILE CLINIC SERVICES

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**Introduction:** The Pediatric Mobile Clinic (PMC) works to reduce disparities in the availability and accessibility of mental health services in underserved communities of Miami Dade County. One out of 5 children and adolescents living in the United States are affected by mental, emotional, and behavioral (MEB) disorders. Twenty-two percent of Latino youth report depressive symptoms, a rate higher than any minority group. Only 8% of Hispanic parents report that their children have ever used mental health care services. The mental health team at the PMC is responsible for achieving three main goals: screening children as a first assessment for brief intervention, linking to community providers who can provide ongoing mental health counseling; and psychoeducation and advocacy on US cultural value and school system. These aims are accomplished utilizing two validated screening tools, the Pediatric Symptom Checklist (PSC) and the Guidelines for Adolescent Prevention Survey (GAPS). The PSC’s primary purpose is to alert pediatricians regarding further assessments a child needs based on parent’s responses to the screening items. The GAPS Survey questionnaire assists healthcare providers in identifying behavioral health and lifestyle concerns regarding adolescents. **Methods:** Scores on the PSC, GAPS survey, and coding referrals for the PMC were analyzed. The data was collected via their initial visitation to the PMC. There were no duplicated patients in the data. All demographic information was collected by the medical assistant and nurse practitioner. The GAPS survey was completed by the adolescent and the PSC was completed by the parent for children upon arrival. The diagnosis referral codes for social work or psychological services were entered by treating physician. **Results:** The PMC served a total number of 2210 unique Hispanic patients seen from January 2016 to June 2017. Of those patients seen, 222 were referred to services. A regression analysis was conducted to identify contributions of referral codes and mental health needs in the Hispanic community to prevalent diagnoses in this population. Results indicated a strong prevalence of behavioral diagnoses also known as disruptive behavioral disorder. Anxiety-related disorders were the second most common diagnosis amongst those referred. The most common secondary diagnoses were adjustment disorders and attention deficit disorder. **Conclusion:** In comparison to the total population seen in the PMC, Hispanics had a higher rate of referrals and MEB diagnoses. MEB disorders have been associated with negative outcomes which compromise the mental, physical, and social welfare of individuals.
TOXICITY OF FINE AND ULTRAFINE PARTICULATE MATTER EXPOSURE: A MURINE MODEL PILOT STUDY

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Introduction: There has been an unprecedented increase in airborne particulate matters ≤ 2.5 µm in aerodynamic diameter (PM2.5) from anthropogenic sources, including automobile combustion and trash burning, in the urban areas of developing countries. Using PM2.5 collected onto the filters from Delhi (India) this study uses a murine model to explore PM2.5 toxicity. Methods: Sprague-Dawley male rats (N=31) were exposed to PM2.5 intravenous injections every 7 days +/-3 days. Rats were housed in control (N=7) condition (i.e. phosphate buffer saline [PBS] injection) and treatment (N=24) condition (metal or non- metal dominant PM2.5) condition. The treatment was subdivided into sedentary (N=12) and exercise rich environment (ERE) (N=12) conditions. At 12 weeks, biological manifestations, namely peripheral cell and lipid analyses, of the effects of PM2.5 exposure were examined using descriptive and regression analyses. Results: Excluding two (potentially) infected rats, the results of this study suggests that exposed rats in sedentary condition (SC) observed elevated white blood cell (WBC) count (12.2 x 10^3/µl ± 3.13 x 10^3/µl at 95% confidence interval [CI]), red blood cell (RBC) count (8.7 x 10^6/µl ± 3.7 x 10^6/µl at 95 CI), segmented neutrophils (20.9% of WBC ± 1.8%) and cholesterol (70.5 mg/dl ± 9.0 mg/dl) levels as compared to controls (8.64 x 10^3/µl ± 3.13 x 10^3/µl), (8.0 x 10^6/µl ± 2 x 10^6/µl), (14.8% ± 1.8%) and (67.6 mg/dl ± 22.5 mg/dl), respectively. Within the exposed group, increasing exposure from 50 µl (with 0.006µg of PM2.5 dose)/week to 600µ (with 0.06µg of PM2.5)/week dose WBC, RBC, segmented neutrophils and cholesterol increased significantly. In comparison to rats in SC, exposed rats in ERE showed reduced effects of exposure on WBC, RBC, segmented neutrophils and cholesterol. The peripheral cells and lipid profile of exposed rats in ERE were identical to the rats in the sedentary control condition. ERE showed a significant (p<0.01) inverse association with WBC, RBC, segmented neutrophils and cholesterol levels. Conclusion: This study investigated the toxicity of airborne particles (PM2.5) that people routinely inhale in Delhi, India which has witnessed unprecedented increase in air pollution in recent years. While elevated levels of RBC and WBC indicate reduced oxygen level and oxidative stress, elevated levels of segmented neutrophils indicate towards acute phase of inflammatory responses due to PM2.5 exposure. Among observed rats, exercise reduces oxidative stress and inflammatory responses, and improved lipid profile. Further research is needed to assess whether exercise interventions in areas with high concentrations of PM2.5 counteract adverse health effects of PM2.5 exposure.

FOCUS GROUPS IN RETIRED FIREFIGHTERS: UNDERSTANDING PERCEPTIONS OF HEALTH AND WELLNESS

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Introduction: In 2016, the Firefighter Cancer Support Network released data showing that 371 out of 756 (49%) South Florida retired firefighters were diagnosed with cancer in 2011 alone. Furthermore, a 2006 retrospective cohort study conducted by Dr. David Lee indicated that female firefighters had increased rates of overall cancer and cervical cancer. These data seem to suggest that the firefighter occupation may increase the risk of cancer and that these effects may become most apparent after retirement. Therefore, it is imperative that data be gathered about the experiences of retired firefighters in regards to their health and risk for cancer. The present study aim to collect qualitative information of risk perceptions of retired firefighters related to safety and health hazards through the use of focus groups. Methods: Participants were recruited through email with the use of a study flyer. Eligible participants needed to be retired firefighters that had worked in Palm Beach County and be fluent in English. Focus groups consisted of 6-10 firefighters and a semi-structured script was utilized to guide the discussion. Focus group questions encompassed topics such as firefighting experience, perceived work hazards, healthcare access, and perceived cancer risk from job
exposures. Firefighters also completed a short demographic questionnaire prior to the focus group. All participants were compensated with a $25 gift certificate after completion of the focus group. Results: To date, three focus groups have been conducted consisting of a total of 20 retired firefighters. All participants thus far have been male, with the average age of 61 years old (SD = 5.85). On average, participants had worked as firefighters for 31.25 years (SD = 3.10) and had been retired for 5.6 years. Common themes that emerged included lack of personal protective equipment, lack of awareness of health hazards early in their careers, sleep disturbances during retirement as a result of the firefighting occupation, increased utilization of health resources after retirement, and increased knowledge about cancer risk and prevention following retirement. Many participants expressed concern that they had been exposed to blood-borne pathogens and inhaled pollutants due to lack of knowledge or access to personal protective equipment, such as oxygen masks or gloves. Conclusion: Retired firefighters can provide valuable insight into the exposures and health practices that experienced firefighters may have encountered. Themes that emerge from the focus group discussions can be utilized to develop interventions targeting the retired firefighter populations, such as increased screening for cancers for which inhaled smoke or exposure to blood-borne pathogens are risk factors. Additional interventions, such as education about sleep disturbances or counseling on traumatic events experienced during a career, may help to improve the transition to retirement.

SURVEYING ALIMENTARY BEHAVIORS AND OCCUPATION-SPECIFIC RISK (S.A.B.O.R) IN CONSTRUCTION WORKERS


Introduction: Construction jobsites operate under tight time constraints with the greatest pressure and stress often felt by the worker. A way in which construction workers compensate for delays and time-loss at the worksite is by either eliminating or reducing the number of breaks (i.e., breakfast and lunch) taken throughout their workday. This worksite climate potentially affects dietary behaviors by increasing consumption of unhealthy meals from fast-food restaurants and lunch trucks at the jobsite. Evidence has shown that although construction workers perform physically-demanding tasks, the type of activity includes very limited cardiovascular exercise oftentimes lending to construction workers being overweight or obese. This pilot project aims to identify factors that contribute to their food choices, dietary habits, and risk for obesity, with the goal of informing the design of targeted programs and interventions that promote healthy foods in this occupational setting. Methods: An anonymous paper-based questionnaire was administered to a non-probabilistic sample of 101 construction workers at two South Florida construction jobsites. The survey instrument included sociodemographic measures, as well as validated measures on nutritional intake, dietary choices, and food-seeking behaviors (i.e., the Latino Dietary Behavior Questionnaire, the Brief Dietary Assessment Tool for Hispanics, and the Assessment of Perceived Food Availability). Objectively measured height, weight, and waist circumference were also collected using the NHANES Anthropometry Procedures Manual. Study participants were given a $10 incentive after both the survey and anthropometric measurements had been collected. Survey responses were entered in a relational database and analyzed using IBM SPSS Statistical Software. Results: Study participants were mostly male (96.0%), white (45.5%), and Hispanic (82.7%) with a mean age of 37.0 years (standard deviation=11.5 years). When categorized by Body Mass Index (BMI), 13.3% of the sample was normal weight, 49.0% were overweight, and 37.8% were obese. Of those who purchase food at work at least some days, 13.9% were normal weight, 50.6% were overweight, and 35.4% were obese. The number of workers with normal body weight that reported fair to poor fat intake (61.5%) was significantly greater than the number of workers workers categorized as overweight/obese (23.5%, p=0.005). A significantly greater proportion of workers that only brought food from home were married (80.1%) when compared to non-married workers (20.0%, p-value=0.04). Conclusion: Although BMI as a classification tool has many limitations, findings from this preliminary study suggest that although construction workers have high physical activity levels, they are exposed to high fat foods at their worksite and face increased disease risk due to weight status. We found fat intake was surprisingly higher in normal weight workers relative to their overweight/obese counterparts. Further research is necessary to characterize diet and its relationship to body habitus in construction workers.
IMPLEMENTATION OF THE URBAN INNOVATION PROGRAM IN AN UNDERSERVED COMMUNITY IN MIAMI-DADE COUNTY, FLORIDA: DETERMINING ACCEPTABILITY, BARRIERS AND FACILITATORS OF COMMUNITY ENGAGEMENT

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Introduction: It is estimated that more than 190 million individuals, nearly 59% of the US population, suffers from one or more chronic diseases and are at increased risk of developing others. These are often preventable health problems whose risk is increased by physical inactivity and poor nutrition, among other behaviors. Although chronic diseases are found in individuals of all races and income levels, individuals living in low income communities represent a disproportionate number of those with chronic diseases. UI Zones is a program designed to empower community members to transform their neighborhood streets into safe play areas that serve as drivers of health, social connection, and well-being for their children and families. A UI Zone entails temporarily closing a low-traffic street and turning it into a gathering space and play area where children and families can safely engage in physical activity. This program was implemented in an underserved and predominantly Hispanic/Latino community in Miami-Dade County: Little Havana. The purpose of this research was to assess community residents’ thoughts about the Urban Innovation (UI) Zones program and how to tailor it to their community’s needs. Methods: Three focus groups (n=16 residents) with accompanying individual surveys were conducted before the UI Zone program to assess the acceptability of the program, as well as barriers and facilitators to community engagement, park use, and physical activity. One focus group (n=8) was conducted after the first program to evaluate it and identify areas for improvement. Qualitative analyses using a general inductive approach were used to analyze the data and derive themes. Results: Approximately 69% of participants reported having a park less than one mile from their home and attending once or twice per month, 56% reported no recent physical activity. Qualitative analyses revealed that perceived benefits from UI Zones were increasing opportunities for children to play outside and reduce computer and video games use. Perceived barriers that prevented individuals in the community from engaging in physical activity were lack of safety and time. Barriers that prevented community engagement in the program included language barriers, skepticism, and fear. Additionally, participants indicated that group programs motivate participation. Conclusion: Findings show there was a need for the UI Zones program, as evidenced by limited physical activity and several perceived benefits of the program. The successful engagement of community members and implementation of the program shows that it is feasible in this community. The UI Zones program has promising potential to help create healthier communities by removing barriers to physical activity and creating sustainable environments that promote active and healthy living.

A QUALATATIVE STUDY: ACCEPTANCE OF PATIENT NAVIGATORS AT DOCS HEALTH FAIR COMMUNITIES

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Introduction: Socioeconomic status (SES) greatly affects health outcomes. Patients who are uninsured and underinsured have greater health disparities (Freeman, 2011). In South Florida, the Department of Community Services (DOCS) at the University of Miami has been eliminating the barriers that low SES patients face through free health fairs and clinics. While these health fairs have been a great success towards improving community health, few high risk patients receive follow up care. Barriers such as, knowledge, distrust and understanding the flow of the health care system may still be a factor that feeds into low follow up rates. Lack of follow up care highlights the need for interventions that can improve health disparities. Purpose: The purpose of this descriptive qualitative study was to assess the acceptance of introducing patient navigators in four of the eight DOCS Health fairs. Acceptance is defined as patient willingness to have a patient navigator assigned to them after attending the health fair. This study provides the information that substantiates the need for follow-up care in the form of patient navigations after community health fair. Methods: Focus groups were held in three South Florida communities. Participants were members of the communities (n=13) who were 18 and over. Sessions were audio recorded, transcribed and coded by 4 team members.
General inductive approach was used for analysis. This approach was used to condense the extensive and varied raw text data into a brief summary format and to establish clear links between the research objectives and summary findings (Thomas, 2006). **Results:** Theme 1: Challenges of navigation of the Health Care System. Participants highlighted lack of health insurance as a barrier to good health (1.1). Additionally, other participants identified that not speaking the same language as their health care provider, is also a barrier for a better health (1.2). Theme 2: How Patients Access Health Care. When participants were asked if they have ever used services offered in the community, most of the participants stated that they resort to their primary doctor or hospital, when a health problem presents (2.1). Few, participants mentioned that they have used the services offered on free clinics (2.2). When asked about how they learned about the services offered in the community, participants mentioned that it was through referrals from their family members or friends (2.3). Theme 3: Desire for Resourceful and Accessible Patient Navigator. Participants felt that this program, will fill that need of having someone that would assist them with follow-up medical appointments (3.1).

A SUSTAINABLE MODEL FOR HEALTH-CENTERED EDUCATION IN DOMESTIC VIOLENCE SURVIVORS

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**Introduction:** One in three women and one in four men in the United States have experienced domestic abuse. Survivors of domestic violence suffer from a myriad of mental and physical health issues as a result of the abuse; domestic victimization is correlated with a higher rate of depression and suicide and is a risk factor for HIV infection and other STI’s. Currently, there are few trauma-informed resources that provide support or education for survivors once they leave a domestic violence shelter. Aid to Victims of Domestic Abuse (AVDA) is an organization in Palm Beach County that aims to identify and help individuals who have been in abusive situations. They offer services such as a 24 hour crisis hotline; emergency and transitional housing; advocacy; and counseling and support. **Objectives:** 1. Assess the health-focused educational needs of the domestic violence survivor population at AVDA. 2. Review pertinent literature and existing materials for survivors. 3. Create a manual for instructional workshops that educate survivors about a healthy life after domestic violence. 4. Create or identify accompanying documents to guide participants in connecting with local resources. 5. Evaluate appropriateness and flow of workshops with test-runs with shelter residents and AVDA employees. **Methods:** A focus group was conducted at AVDA, after which eight health-related topics were selected. After a literature review, eight multimedia workshops were written utilizing a variety of validated resources such as Planned Parenthood, CDC, and the American Academy of Pediatrics. Background for each workshop was provided for the instructor, and a workshop was composed to elicit participation from attendants. The workshops varied in form from discussion-based to interactive worksheet to PowerPoint presentations. Each workshop was reviewed by an expert in the field, as well as by faculty mentor Dr. Julia Belkowitz and AVDA management, for accuracy and sensitivity. Before finalization, each workshop was test-run with residents and AVDA employees. **Conclusion:** A completed manual with eight workshops and accompanying materials was created for use by AVDA. Expectations moving forward include the continued utilization and assessment of the eight workshops and possible expansion of the manual to other domestic violence shelters. No objective assessment of the effectiveness of these workshops has been done as yet, but should be completed upon implementation of these workshops.
Development of a Patient Navigation Training Program for the Patient Navigation Initiative of the Department of Community Service at the University of Miami

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Introduction: The University of Miami Department of Community Service (DOCS) Health Fairs and Clinics reach over 2500 patients annually, providing screening services for patients traditionally disconnected from the health system. Despite the large reach of the DOCS program, many patients never attain follow up after positive health screenings. As many DOCS patients are uninsured or live near the poverty line, they often do not seek care due to the various barriers facing patients with lower socioeconomic status. The Patient Navigation Initiative (PNI) was created in response to this low attainment of follow up after health fairs. The PNI seeks to train and employ student volunteers as patient navigators for elevated risk patients. Methods: To meet the training goals of the PNI, a multimodal approach to training is being developed and tested with prospective patient navigators. Training competencies were adapted from existing patient navigation training programs, with a focus on choosing competencies essential to the theory of patient navigation as well as competencies specifically needed for our prospective patient navigator base. Results: A 3-module, 8-hour training class was developed from the aggregated competencies. Module 1 focuses on the knowledge and resources needed to be a patient navigator. Module 2 focuses on patient navigation specific skills. Module 3 focuses on data and personal management skills. Each lesson was developed using 3 different types of media (PowerPoint, written training manual, and video) to ensure uniform training of patient navigators. Roughly 55% of the live training involves Problem Based Learning, student run activities, or group discussions, with the remaining 45% being a lecture. Supplemental materials were included for each lesson to allow for learners from different levels of prior training to explore materials. Conclusion: While the PNI training program is still early in its development, over 50 patient navigators will have been trained by some version of the program by the end of its second year. The accessibility of the modules allows for easy access by prospective patient navigators from various skill levels, ensuring a low barrier to entry for prospective navigators. The flexibility of the program allows for rapid alteration of materials to meet the changing goals of DOCS, as well as respond to patient navigator feedback. As the PNI training program continues to develop, more study into the efficacy of the various training methodologies will be completed.
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### Department of Public Health Sciences Showcase

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