NATIONAL STUDENT RESEARCH FORUM

52nd ANNUAL MEETING
April 21 – April 22, 2011

Sponsored by:
The University of Texas Medical Branch
Galveston, Texas
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Special Thank You to the
2011 National Student Research Forum Supporters

The awards presented at the 2011 National Student Research Forum are generously funded by many organizations, individuals and UTMB Department Chairs. We appreciate your continued support!
The primary source of support for the Forum is the:

THE UNIVERSITY OF TEXAS MEDICAL BRANCH AT GALVESTON
UTMB encourages progress and excellence in medical education and research!

Department of Biochemistry and Molecular Biology
Department of Dermatology
Department of Neuroscience and Cell Biology
Department of Internal Medicine, Division of Cardiology
UTMB Global Health Education Program
Department of Pediatrics
Department of Pharmacology and Toxicology
Department of Preventive Medicine and Community Health
Department of Orthopaedic Surgery and Rehabilitation
Department of Radiology
Department of Surgery
Department of Otolaryngology
UTMB Center to Eliminate Health Disparities
The Oliver Center for Patient Safety and Quality Healthcare
Department of Microbiology and Immunology
Department of Obstetrics and Gynecology
Department of Internal Medicine Division of Hematology and Oncology
School of Medicine, Office of Student Affairs and Admissions
School of Medicine, Office of the Provost
Dear Forum Participants:

Welcome to the 52nd Annual National Student Research Forum at the University of Texas Medical Branch. We are excited to have each of you in Galveston to continue the great tradition of bringing together young medical and graduate students, interns, and residents in the biomedical sciences from around the world to present research and receive critical feedback and recognition of their efforts from peers and established scientists. It is the mission of UTMB to improve health for the people of Texas and around the world, so it is an honor to host so many up-and-coming scientists who also are committed to advancing health and health care.

This year’s keynote address will feature Clyde F. Barker, M.D., on Thursday, April 21 at 4 p.m. in the William C. Levin Hall main auditorium. Among Dr. Barker’s numerous recognitions are the 2009 Lifetime Achievement Award of the Society of University Surgeons and the Thomas E. Starzl Prize in Surgery and Immunology of the Starzl Institute at the University of Pittsburgh. In 2010 he received the Medawar Prize, the highest award of the International Transplant Society. Dr. Barker also will be part of the noon Bench to Bedside luncheon panel, joined by Drs. Kristene Gugliuzza, Richard Dixon and Geoffrey Land, and Ms. Tamra Lewis.

Every year, we look forward with great anticipation to the National Student Research Forum and we encourage you to take full advantage of the 2011 event. We hope you will return to your home schools having gained both valuable presentation experience and a renewed sense of camaraderie with your fellow scientists. Welcome to Galveston and to UTMB!

Sincerely,

David L. Callender, MD, MBA, FACS
President
INTRODUCTION AND HISTORY

BACKGROUND
The National Student Research Forum is organized and run by students for the discussion of student research papers in a scientific atmosphere. Originating in 1960 at the University of Texas Medical Branch in Galveston, the first Forum had participants from Texas, Louisiana, Arkansas, and Tennessee. Last year approximately 140 students from 50 medical schools and hospitals throughout the United States and Canada presented papers. The National Student Research Forum now affords young scientific investigators one of their major opportunities to participate in a scientific meeting and the 2011 Forum is expected to be represented in several major fields of medical research.

During the 1959-60 academic year, a small group of medical students involved in research approached Dr. James V. Warren, then-Chairman of the Department of Internal Medicine, for his help in setting up a forum for the presentation of their work. Supported by the Executive Committee of the Faculty of Medicine, Dr. Warren recruited both the James W. McLaughlin Committee, which supports research in infection and immunity, and the Galveston Chapter of Sigma Xi, which is dedicated to the encouragement of research, to help finance and organize the first Forum. That meeting was open to medical students in the southwestern United States and was held at the Hotel Galvez in March 1960. The success of the first effort led to yearly Forums organized, directed, and presented by students.

In 1963, Dr. Benedict E. Abreu, then Chairman of the Department of Pharmacology, became faculty advisor to the Research Forum. Dr. Abreu's goal was to have the Forum become national in scope, which would provide a much-needed opportunity for the presentation of research by students. By 1963, the Forum had already grown into a project too large for its two original supporters. Dr. Abreu persuaded Mead Johnson Laboratories to become a major supporter of the Forum, and by 1964, twenty-two drug companies were contributing, thanks to Dr. Abreu's active solicitation.

When Dr. Abreu died in January of 1965, the Forum sought administrative support from UTMB. Planning and management remained the responsibility of the students and, in 1968, representatives from the National Office of the Student American Medical Association agreed to officially designate the program the SAMA-UTMB National Student Research Forum. Sixty nine medical schools were represented in 1968, and the Forum continued to grow in size and diversity. In 1978, a truly national Forum was realized, with 135 papers presented in 17 sessions. Today, more than 151 abstracts and papers will be presented in 10 group sessions.

PURPOSE AND OBJECTIVES
The primary purpose of the National Student Research Forum, now in its fifty-second year, is to provide a national scientific assembly, planned and managed by students for presentation of research by medical students, interns and residents, and graduate students in the health sciences. The Forum recognizes excellence in research by means of awards, based upon the judgement of a panel of medical scientists selected from the UTMB faculty. The Forum provides an opportunity for young health scientists to receive meaningful and pertinent discussion of their research efforts by their peers and by established scientists in an atmosphere encouraging the highest scientific standards. The leadership of the National Student Research Forum has encouraged and will continue to encourage the establishment of local and regional student research forums. The prize-winning papers from the regional Forums are automatically accepted for presentation at the National Student Research Forum.
David Clifton grew up in Fort Worth, Texas where he attended TCU and graduated with a Bachelor of Science in Neuroscience with departmental Honors in research. After college, he worked as a physician scribe consultant for one year prior to entering medical school at the University of Texas Medical Branch. He is currently a third year medical student with aspirations of a career in Interventional Radiology. His current research interests include a project investigating circadian rhythms and the stress response funded by the AMA Foundation as well as a project compiling radiologic and anatomic correlates. This year, David Clifton has served as the Senior Co-Director of the 52nd Annual National Student Research Forum and has enjoyed organizing such a worthwhile event.

Kelli Sleeth is a third year student in the School of Medicine at the University of Texas Medical Branch in Galveston. Kelli originally grew up in Dallas and completed her undergraduate education at Austin College in Sherman, Texas where she majored in Psychology. She graduated magna cum laude in 2007 and was inducted into the Psi Chi Honor Society. Kelli currently serves as the community outreach officer in UTMB’s Student Psychiatry Organization and plans to pursue a career in Psychiatry. Kelli is also involved in the Pediatric Student Association and was recently chosen to be a member of the Gold Humanism Honor Society for excellence in clinical care, leadership, compassion and dedication to service. Kelli has enjoyed her role as a Co-Director for this year’s National Student Research Forum and is excited to welcome all participants, judges, and speakers to the UTMB campus!
Kristopher McCall grew up in the small city of Lufkin, Texas, where his parents were born and raised. He spent the majority of his time playing baseball and doing activities outdoors like lifeguarding, hunting, and hiking with the local Boy Scouts troupe. He knew early on that he wanted to become a physician through close interactions with a family doctor because of inner ear infections. After graduating from high school, he began his path toward medicine at Texas A&M University where he graduated magna cum laude with a degree in Biomedical Science. He is currently a third year medical student at the University of Texas Medical Branch and plans to enter a residency in Orthopedic Surgery. Kristopher completed research during college on mantle cell lymphoma and is currently working a case report in Orthopedics. He enjoys most anything outdoors including fishing, hunting, swimming, scuba diving, and hiking. He also enjoys reading, traveling and spending time with his family.

Patricia Stone grew up in The Woodlands, TX. She graduated from the Academy of Science and Technology at Oak Ridge High school in 2004. She attended Austin College in Sherman, TX where she played NCAA varsity soccer and club lacrosse. She received a BA in Biology in 2008. Patricia is currently a third year medical student at UTMB. She is a 2nd Lieutenant in the US Army and will enter an Army residency upon graduation from medical school. She plans to pursue a career in Otolaryngology.
Michael Kueht
Co-Director

Michael Kueht graduated from the University of Houston in 2006 with a Bachelor of Science in Exercise Science where he studied effects of obesity and exercise on the immune system in the Laboratory of Integrative Physiology. After graduation, he worked at the Children’s Nutrition Research Center in the Texas Medical Center utilizing high-throughput genotyping technology to study polymorphisms in various populations. He is currently a third-year medical student at UTMB and looks forward to applying his background in Genetics and Immunology as a transplant surgeon. This is his first year serving as a Co-Director for the National Student Research Forum.

Janese Laster
Co-Director

Janese Laster is a third year medical student at the University of Texas Medical Branch. She is originally from Birmingham, Alabama and graduated from Spelman College in Atlanta, Georgia with a degree in Psychology Pre-Medicine. Before matriculation into medical school, she worked as a Clinical Research Coordinator with various trials in pain management and orthopedics. She has been the Class of 2012 Student Curriculum Representative for the past three years; was accepted as a John P. McGovern Osler Student Scholar in 2009; inducted into the Gold Humanism Honor Society in 2011; and is a 52nd Annual National Student Research Forum Co-Director. Some volunteer activities include: Director of annual Miles for Melanoma charity and walk; personal mentor for first year medical students; and student ambassdor. She has an interest in preventative medicine and indigent care. She hopes to apply for residency in the specialty of Internal Medicine and to continue to embody compassion and humanistic values that have been fostered while at UTMB.
Cynthia Miranda
Co-Director

Cynthia Miranda attended the University of Texas – Pan American where she majored in Biology and Chemistry. Following graduation in 2009, she entered the UTMB School of Medicine and is now a second year medical student. Cynthia plans to go on to residency in Pediatrics. This is Cynthia’s first year serving as a Co-director for the National Student Research Forum.
2011 Faculty Advisors

Cheryl J. Ellis Vaiani, Ph.D.

Dr. Vaiani is currently an assistant professor in the Institute for Medical Humanities and clinical ethicist in the Institutional Ethics Service at the University of Texas Medical Branch in Galveston where she is involved in clinical consultation, teaching, and serves as co-chair of the Institutional Ethics Committee. Dr. Vaiani is Co-director of the Practice of Medicine 2 course in the School of Medicine. She received her doctorate in medical humanities at UTMB in Galveston in 1998 and was recognized with the Dean's Award for Academic Excellence. Her research concerned anencephalic infants and use of their organs for transplantation. She then completed a postdoctoral fellowship in clinical ethics at UTMB. Dr. Vaiani is active in the Galveston community serving as president of the Galveston Historical Foundation, a member of the Galveston County Historical Commission, and as chair of the City of Galveston Ethics Commission.

Ahmed El-Sayed Ahmed, Ph.D.

Dr. Ahmed El-Sayed Ahmed graduated from Cairo University in Cairo, Egypt with a Bachelor of Science in Pharmacology in 1966 and received his Ph.D. in Medicinal Chemistry from the University of Minnesota in 1975. He finished his post-doctoral fellowship at the University of Minnesota in 1975 and a summer fellowship at MIT in Boston, Massachusetts in 1978. From 1982 – 1983 he was a Swedish Medical Research Council Fellow at the University of Uppsala in Uppsala, Sweden. He has published over 100 articles and has particularly focused on the impact of chemicals in the environment and human health. Dr. Ahmed is currently a professor at UTMB in the Departments of Pathology, Pharmacology and Toxicology, and Preventive and Community Health.
2011 Senior Faculty Advisor

Jeffrey P. Rabek, Ph.D.

Dr. Rabek received a B.A. in Zoology from Drew University in Madison, New Jersey in 1971 and a Ph.D. in Biochemistry from Princeton University in 1976. He did postdoctoral work at Oak Ridge National Laboratory, Oak Ridge, Tennessee. Dr. Rabek is the Assistant Dean for Student Affairs and Admissions in the School of Medicine, an assistant professor in the Departments of Biochemistry and Molecular Biology and Family Medicine, and a Fellow in the Sealy Center for Aging at UTMB. Dr. Rabek’s major research interests lie in the control of the temporal and tissue-specific expression of specific genes during development and aging, and in response to stress. Control mechanisms acting at the level of the induction and regulation of gene transcription and messenger RNA translation are of particular interest. Dr. Rabek’s research interests also include a longitudinal study looking at protein markers and protein damage in tissue from muscles paralyzed after stroke, through functional recovery. Dr. Rabek has been particularly active in the educational mission of UTMB in both the Graduate School of Biomedical Sciences and the School of Medicine. He lectures in numerous graduate school courses and serves as a course director. In the medical school, he has served as co-director of the Molecules Cells and Tissues module, is a member of the Family Medicine Clerkship Committee, and has served as Co-Chairman of the Course Directors Committee and as a member of the Curriculum Committee. He also serves on the Advisory Committee for the UTMB and UTMB-UT Austin MD/PhD Combined Degree Programs. Dr. Rabek’s has ongoing educational research interests in the analysis of factors that affect the admission of underrepresented minority and economically disadvantaged applicants into medical school and the factors that affect the performance of academically at-risk students in the medical school curriculum. At the state level, Dr. Rabek serves on the Advisory Council for the Joint Admissions Medical Program (JAMP) and the Advisory Board for the Texas Medical and Dental School Admissions Service (TMDSAS).
2011 52nd National Student Research Forum
Schedule of Events

WEDNESDAY, April 20, 2011

6:00 pm – 8:00 pm  Kick-off Party with Refreshments and Appetizers  
                    Poolside – Hilton Galveston Island Resort

8:00 pm – 10:00 pm  Hospitality Suite Open  
                    Hilton Galveston Island Resort

THURSDAY, April 21, 2011

7:30 am – 4:00 pm  Registration Table Open  
                    Foyer – Levin Hall

7:30 am – 8:30 am  Continental Breakfast  
                    Foyer – Levin Hall

8:30 am – 9:00 am  Welcome Address:  
                    Courtney M. Townsend, Jr., M.D.  
                    Professor, Department of Surgery  
                    John Woods Harris Distinguished Chairman  
                    Distinguished Chair in General Surgery  
                    Levin Hall Main Auditorium

9:30 am – 11:30 am Oral Session A:  
                    Cell Biology  
                    Levin Hall:  3.320

Oral Session B:  
Radiology  
Levin Hall:  3.324

Oral Session C:  
Surgery and Hematology and Oncology  
Levin Hall:  Main Auditorium

12:00 pm – 2:00 pm  Bench 2 Bedside  
                    Levin Hall Dining Room

2:00 pm – 4:00 pm  Poster Session 1  
                    Levin Hall Foyer

4:00 pm – 5:00 pm  Abreu Keynote Memorial Lecture:  
                    Clyde Barker, M.D.  
                    Is the Physician Scientist Dead?  
                    Lessons from Pancreatic Islet Transplantation.  
                    Levin Hall Main Auditorium
7:00 pm – 10:00 pm  Hospitality Suite Open –
Hilton Galveston Island Resort

FRIDAY, April 22, 2011

8:00 am – 12:00 pm  Registration
Foyer – Levin Hall

7:30 am – 8:30 am  Continental Breakfast
Foyer – Levin Hall

8:30 am – 10:30 am  Poster Session 2
Foyer - Levin Hall

11:00 am – 12:00 pm  Lunch
Levin Hall Dining Room

12:00 pm – 1:00 pm  Oral Session D:
Neuroscience
Levin Hall:  3.320

Oral Session E:
Immunology
Levin Hall:  North Auditorium

Oral Session F:
Orthopedics
Levin Hall:  South Auditorium

1:00 pm – 3:30 pm  Breakout Sessions:
Levin Hall:  South Auditorium

6:00 pm - 8:00 pm  Awards Banquet
Closing Remarks:
Garland D. Anderson, M.D.
Executive Vice President and Provost
Dean School of Medicine
Thomas N. & Gleaves T. James Distinguished Chair
Hilton Galveston Island Resort
Hilton Grand Ballroom

8:00 pm – 10:00 pm  After Party
Poolside
Hilton Galveston Island Resort

SATURDAY, April 23, 2011

8:00 am – 10:00 am  Breakfast
Hilton Galveston Island Resort
IN APPRECIATION

The 2011 National Student Research Forum Committee wishes to thank the following individuals and organizations for helping to make this year’s forum a success:

• University of Texas Medical Branch administration for their never-ending help in all aspects of making the NSRF great.

• Faculty at the University of Texas Medical Branch and various off-campus institutions for their enthusiastic efforts in evaluating manuscripts, poster and oral presentations.

• Medical students at the University of Texas Medical Branch who served in many essential capacities.

• Dr. David L. Callender, President of the University of Texas Medical Branch, for his enthusiastic support and help with the NSRF.

• Dr. Garland Anderson, Provost and Dean of Medicine at the University of Texas Medical Branch, for his advocacy and support of the NSRF.

• Dr. Cary Cooper, Dean of the Graduate School of Biomedical Sciences at the University of Texas Medical Branch, for his continued advocacy and support of the NSRF.

• Dr. Lauree Thomas, Associate Dean for Student Affairs and Admissions, School of Medicine at the University of Texas Medical Branch, for her enthusiastic encouragement.

• Dr. Jeffrey Rabek, Assistant Dean for Admissions, School of Medicine at the University of Texas Medical Branch, for his years of dedication and support of the NSRF.

• Dr. Courtney Townsend, John Woods Harris Distinguished Chairman of Surgery at the University of Texas Medical Branch, for his advocacy and support of the NSRF.

• Drs. Ahmed E. Ahmed and Cheryl E. Vaiani, the 2011 National Student Research Forum Faculty Advisors, for their commitment, guidance, and dedication to the Forum.

• Dr. Clyde Barker, the 2011 National Student Research Forum Keynote Speaker.

• Drs. Clyde Barker, Kristene Gugliuzza, Richard Dixon, Geoffrey Land, and Ms. Tamra Lewis for their participation in the Bench to Bedside panel discussion.

• Drs. Horacio E. Adrogué, Ioannis Pavlidis, Harold Fields, Jason Glenn, and Ms. Tamra Lewis for their time and efforts in speaking at the Forum.

• The Moody Medical Library staff, especially Sarita Oertling, for providing tours of the Blocker History of Medicine Collection.

• Christen Miller, MPAff of the Global Health Education Program and the UTMB Center to Eliminate Health Disparities.

• Meridith Masel, Ph.D., MSW, and the Oliver Center for Patient Safety and Quality Health Care.

• The staff of the Office of Student Affairs and Admissions at the University of Texas Medical Branch for their assistance and dedication to the Forum.

• Elisabeth Sanders for her dedication to making this year’s NSRF a success. Without her many hours of dedicated work, there would be no Forum.
The NSRF Co-Directors would like to thank the physicians and scientists who agreed to take time out of their busy schedules to review manuscripts and judge presentations. Their dedication to the future physicians and scientists is greatly appreciated.

*NOTE: Some NSRF judging assignments had not been completed at the time of printing.*

### Oral and Poster Judges
- Xioyong Bao, PhD
- Malavosklish Bikram, PhD
- Darren Boehning, PhD
- Miriam Falzon, PhD
- Nisha Garg, PhD
- Zbigniew Gugala, MD/Ph.D.
- Winifred Hamilton, PhD, SM
- Hal Hawkins, MD
- Raleigh Johnson, PhD
- Brent Kelly, MD
- Joseph Knezetic, PhD
- Brian Knoll, PhD
- Charles Kuszynski, PhD
- John Ladbury, PhD
- Scott LeMaire, MD
- Eastwood Leung
- Jere McBride, PhD
- Bradley McConnell, PhD
- Tatiana Nanovskaya, PhD/DDS
- Vinod Panchbhavi, MD
- Richard Puzdrowski, PhD
- Jeffrey Rabek, PhD
- Sharon Raimer, MD
- Koto Ramana, PhD
- Bill Rampy, DO, PhD
- Adrian Recinos, PhD
- Roy Riascos, MD
- Judith Rowen, MD
- Laura Rudkin, PhD
- Catherine Schein, PhD
- Edward Sherwood, MD/PhD
- Kizhake Soman, PhD
- Misha Syed, MD
- Giulio Tagliatela, PhD
- MariVi Tejada-Simon
- Cheryl Vaiani, PhD
- Gustavo Valbuena, MD/PhD
- Richard Wagner, MD

### Manuscript Reviewers
- Ahmed Ahmed, MD
- Lance Barton, PhD
- Wei Cao, PhD
- Susan Carlton, PhD
- Diane Chico, PhD
- Patricia Dahia, MD/PhD
- Zbigniew Gugala, MD/PhD
- Hal Hawkins, MD
- Fred Huang, MD
- Kristina Hulten, PhD
- Sunil Jain, MD
- Raleigh Johnson, PhD
- Thomas Jones, MD
- Lois Killewich, MD
- Charles Kuszynski, PhD
- Philip Lee, MD
- James Lee, PhD
- Simon Lewis, PhD
- Chin-Yo Lin, PhD
- Michael Malloy, MD
- Brian McFarlin, PhD
- Daniel O'Connor, PhD
- Thomas Presseley, PhD
- Richard Puzdrowski, PhD
- Jeffrey Rabek, PhD
- Krishna Rajarathnam, PhD
- Peggy Redshaw, PhD
- Jose Rojas, PhD, RRT
- Lory Santiago-Vazquez, PhD
- Gary Shaw, DrPH
- Phillip Thomas, MD
- Yi Wang, PhD
The Oslerian Award for Translational Research

William Osler Scholar, John P. McGovern Academy of Oslerian Medicine

“The…greatest glory is that the leaves of the tree of science have availed for the healing of the nations. Measure as we may the progress of the world – intellectually in the growth and spread of education, materially in the application to life of all mechanical appliances, and morally in a higher standard of ethics between nation and nation, and between individuals, there is no one measure which can compare with the decrease of disease and suffering in man, woman and child.”

-Sir William Osler

Man’s Redemption of Man: A Lay Sermon, 1910

The John P. McGovern Academy of Oslerian Medicine was created in 2001 as a result of the combined visions of Dr. John McGovern and Dr. John Stobo. The Academy was founded to foster the ideals for which Sir William Osler is most revered: scientifically based medical practice, personalized care of patients with emphasis on the doctor-patient relationship, and a commitment to professionalism. As part of its mission, the Academy supports faculty and student Osler scholars. Dr. Aronson, a pathologist, was elected to the Academy in 2004. She sponsors the Oslerian Award for Translational Research to recognize those NSRF participants who best articulate the relevance of their research to Oslerian principles of science, compassion, and humanism.

To compete for this award, the applicant will write an original 1000-word essay describing the implications and potential importance of his/her research avenue or discovery for the betterment of human health. The successful essay should explicitly link results of the applicant’s scientific inquiry with humanistic ideals espoused by Osler and emulated to this day. Judging will be based both on the applicant’s essay and submitted abstract. Up to five winners will receive this award.
DETERMINATION OF AWARDS

The National Student Research Forum offers several categorical and overall awards. Each poster presentation is evaluated by the average score from three different on-site judges. Each oral presentation is evaluated by a combined score from three on-site judges and three off-site manuscript judges. The manuscript average score accounts for 60% of the overall score, with the average of the presentation scores making up the remaining 40%. Presenters are then ranked based on their scores and the top ones are qualified for awards in their field of competition. All comments of evaluators are taken into consideration when determining ties among presenters.

Participants are eligible to compete for only one Categorical Award in their respective field of research and for only one or Overall Award.

Any faculty member participating in the National Student Research Forum as an oral/poster presentation judge cannot be listed as an author on any paper competing for an award in the session for which they are a judge.

Best Oral/Poster Awards

These awards are given to three oral and three poster presenters who exhibit the highest scores in their respective presentation.

Categorical Awards

These awards are given to presenters who exhibit the highest scores within their respective categories of research.
Medical Humanities and Health Disparities Awards

Global Health
This division highlights original research on topics related to global health, including health-related issues affecting low-income and middle-income countries as well as the impact of globalization processes on health in all countries. Research can be of any type, including basic science, clinical, public health, social science, humanities, etc. Awards will be based on the number and quality of entries.

Global Health Research Award First Place
Global Health Research Award Second Place

Health Disparities
Original research on topics related to health disparities (not only racial/ethnic but also other disparities) or social determinants of health, either in the U.S. or in other countries. Research can be of any type, including clinical, public health, social science, humanities, etc. Topics might include issues related to health care services, health impact assessment, implementation research, measurement and monitoring issues, links to human rights, advancing health in all policies, or other issues.

Health Equity Research Award First Place
Health Equity Research Award Second Place
National Student Research Forum Awards

The purpose of the awards program is to encourage and recognize outstanding research in basic and clinical sciences. Availability of an award does not necessarily guarantee its presentation. Research presentations must be judged to be of sufficient quality to merit receipt of an award.

Awards for Best Oral Presentations

UTMB School of Medicine, Office of Student Affairs Outstanding Oral Presentation First Place
NSRF Outstanding Oral Presentation Second Place
NSRF Outstanding Oral Presentation Third Place

Awards for Best Poster Presentations

UTMB School of Medicine, Office of Student Affairs Outstanding Poster Presentation First Place
NSRF Outstanding Poster Presentation Second Place
NSRF Outstanding Poster Presentation Third Place

Categorical Awards

UTMB Cancer Center Award in Oncologic Research
Biochemistry and Molecular Biology Award for Research Excellence
  Best Poster Presentation in Oncology
  Best Oral Presentation in Neuroscience and Cell Biology
  Excellence in Radiology Research Oral Presentation
  Best Oral Presentation in Microbiology and Immunology
  Best Oral Presentation in Surgery
  Best Poster Presentation in Neuroscience and Cell Biology
  Excellence in Radiology Research Poster Presentation
  Best Poster Presentation in Public Health
  Best Poster Presentation in Dermatology
  Best Poster Presentation in Surgery
  Best Poster Presentation in Pharmacology and Toxicology
  Best Poster Presentation in Cardiology Award
  Best Oral Presentation in Orthopaedic Surgery
  Best Poster Presentation in Orthopaedic Surgery
  Best Poster Presentation in Genetics
Dr. Barker's numerous recognitions include the presidency and the medallion for scientific achievement of the American Surgical Association, the presidency and the Pioneer Award of the American Society of Transplant Surgeons, and the Sheen Award of the American College of Surgeons. He has been elected to memberships in the Institute of Medicine of the National Academy of Sciences, the American Philosophical Society (Vice President, 2005-2011) and the American Academy of Arts and Sciences. His clinical interests are focused in transplantation and vascular surgery. His research interests are transplantation biology and diabetes. His research has been funded through NIH grants since 1974, including a MERIT grant from 1987 to 1995. He has been and continues to be a mentor and role model for a generation of surgeons.

Dr. Barker's memberships in scientific societies include the American Surgical Association (President, 1996-97); Society of University Surgeons, The Society of Clinical Surgery, Halsted Society (President, 1986-87); the Society for Vascular Surgery, the American Society of Transplant Surgeons (President, 1992); the International Surgical Group (President, 1994-94). He is also a member of the Institute of Medicine of the National Academy of Sciences, the Association of American Physicians, the American Academy of Arts and Sciences, the American Philosophical Society, and the International Transplantation Society. He has authored more than 400 scientific papers. He is recognized as one of the leading investigators in the transplant field in the United States. He initiated HUP's transplant program in 1966 and is credited with building it into the largest and most successful program in the area. In 2009 Dr. Barker received the Lifetime Achievement Award of the Society of University Surgeons and the Thomas E. Starzl Prize in Surgery and Immunology of the Starzl Institute at the University of Pittsburgh. In 2010 he received the Medawar Prize, the highest award of the International Transplant Society.
Oral Presentations

All participants in the oral presentation category that submitted a manuscript for review will be considered for Overall Awards and Oral Categorical Awards. Information regarding how the awards are selected can be found on page 20 of this program.
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<th>Session</th>
<th>Speaker</th>
<th>Institution</th>
<th>Title</th>
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<td>A - 7</td>
<td>Chin, Jocelyn</td>
<td>Stanford University School of Medicine</td>
<td>METFORMIN ACTIVATION OF AMPK PROTECTS AGAINST ACUTE CARDIAC REJECTION THROUGH INHIBITION OF INTRINSIC APOPTOSIS</td>
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<tr>
<td>9:45</td>
<td>Baumann, Brian</td>
<td>University of Pennsylvania School of Medicine</td>
<td>&quot;BUSTING THE BLOOD BRAIN BARRIER OF BRAIN TUMORS&quot;: A NEW MOUSE MODEL SYSTEM TO TEST RADIATION-AUGMENTED TREATMENT STRATEGIES USING A NOVEL NANOPOLYMER</td>
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<tr>
<td>10:00</td>
<td>Beauregard, Mariejka</td>
<td>Laval University</td>
<td>IDENTIFICATION OF RARE GENETIC VARIANTS OF THE DICKKOPF 1 GENE IN PAGET’S DISEASE OF BONE</td>
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<td>10:15</td>
<td>Al-Lahham, Rabab</td>
<td>University of Texas Medical Branch</td>
<td>MITOCHONDRIAL-GENERATED ROS, THROUGH ACTIVATION OF THE P38 STRESS-RESPONSE PATHWAY, DOWNREGULATES THE INSULIN SIGNALING PATHWAY</td>
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<td>10:30</td>
<td>Wiraszka, Tomasz</td>
<td>University of Texas Medical Branch</td>
<td>STREPTOZOTOCIN TOXICITY TO RETINA IN AN ANIMAL MODEL OF TYPE I DIABETES.</td>
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<td>11:00</td>
<td>Barash, Alexander</td>
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9:30 *Baylor College of Medicine*  
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*Department of Radiology, UTMB*  
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University of Alabama at Birmingham
9:30  MYRISTOYLATED ALANINE RICH C-KINASE SUBSTRATE (MARCKS) IS A CRITICAL REGULATOR OF GLIOBLASTOMA GROWTH AND RADIATION SENSITIVITY THAT PREDICTS FOR PATIENT SURVIVAL

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9:45  COMPLICATIONS AND RISK FACTOR ANALYSIS OF OMMAYA RESERVOIR PLACEMENT – A TERTIARY CARE CANCER HOSPITAL EXPERIENCE IN 837 PATIENTS

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10:30  THE EFFECT OF TAMOXIFEN AND RALOXIFENE ON ESTROGEN METABOLISM AND ENDOMETRIAL CANCER RISK

C - 133  Trust, Marc D.
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12:00  University of Cincinnati
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"BUSTING THE BLOOD BRAIN BARRIER OF BRAIN TUMORS": A NEW MOUSE MODEL SYSTEM TO TEST RADIATION-AUGMENTED TREATMENT STRATEGIES USING A NOVEL NANOPOLYMER
Brian Baumann, Dr. Jay Dorsey, Dr. Gary Kao
University of Pennsylvania School of Medicine, University of Pennsylvania, Radiation Oncology, University of Pennsylvania, Radiation Oncology

Background: The prognosis of glioblastoma (GBM) remains poor despite the addition of chemotherapy. The relative ineffectiveness of chemotherapy has been partly attributed to the inability to achieve therapeutic intra-tumoral drug concentrations due to the tumor blood-brain barrier (T-BBB). Novel drug delivery systems using nanocarrier polymers loaded with chemotherapy may increase serum half-life but are still limited by the T-BBB. Based on preliminary evidence that radiation therapy (RT) increases the permeability of the T-BBB, we tested the efficacy of combined RT & nanopolymerized paclitaxel (NP) for treating GBM via a novel bioluminescent orthotopic mouse model.

Objective: 1) To develop an orthotopic animal model with human GBM cells to facilitate investigations of strategies for modulating the T-BBB. 2) To investigate the efficacy of NP to treat orthotopic GBM xenografts +/- RT-induced T-BBB disruption.

Methods: U251 GBM cells were established to express green fluorescent protein (GFP, to be distinguishable from normal tissue) & luciferase (to enable optical imaging of tumor). These cells were stereotaxically injected into nude mice brains. Successful tumor implantation was confirmed by luciferin-induced luminescence on bioluminescent imaging (BLI). Serial BLI measured tumor growth & response to treatment. Mice were evenly distributed based on tumor BLI signal to 1 of 4 treatments: IV NP, whole brain RT (WBRT) to 16 Gy in 4 fractions, concurrent WBRT + NP, or controls. BBB integrity was assessed via the extravasation of IV Evans Blue (EB) dye which fluoresces, allowing co-imaging with GFP-expressing tumor. Dynamic contrast-enhanced MRI of tumors is ongoing. Results: EB integrity was assessed via the extravasation of IV Evans Blue (EB) dye which fluoresces, allowing co-imaging with GFP-expressing tumor. Dynamic contrast-enhanced MRI of tumors is ongoing.

Conclusions: This novel orthotopic GBM model should facilitate studies of new therapeutic strategies targeting GBM. Preliminary results suggest that RT usefully disrupts the T-BBB & together with NP results in the greatest tumor response.

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IDENTIFICATION OF RARE GENETIC VARIANTS OF THE DICKKOPF 1 GENE IN PAGET'S DISEASE OF BONE
Mariejka Beauregard, Mrs. Edith R Gagnon, Mr. Jean Morissette, Mr. Jacques P Brown, Mrs. Laetitia Michou
Laval University, CHUQ Research Centre (CHUL), Laval University, CHUQ Research Centre (CHUL), Laval University, Department of medicine, Laval University, CHUQ Res, Department of medicine, Laval University, CHUQ Res

Introduction: Paget's disease of bone (PDB) has an autosomal-dominant mode of inheritance with incomplete penetrance in a third of cases. Several mutations of the Sequestosome-1 gene have been identified, but only account for 37% of familial and 10% of sporadic forms of PDB, suggesting other gene involvement. The Dickkopf 1 gene (Dkk1, locus 10q11.2), expressed by osteoblasts and osteocytes, encodes a secreted protein that inhibits Wnt signaling, which helps regulate bone remodelling. An increased expression of DKK1 is found in pagetic osteoblasts and stromal cells and increase serum levels of DKK1 protein in pagetic patients. The objective of this study was to identify rare genetic variants of DKK1 and to test for genetic association of this candidate gene with PDB in a French-Canadian population.

Materials and methods: The four exons of DKK1, the promoter and the exon-intron junctions from 30 French-Canadian patients suffering from familial PDB and four healthy individuals were amplified and sequenced. All variants identified in at least one individual and absent from NCBI's SNP database were considered potential rare variants. In addition, an association study was conducted by genotyping three common variants (tag SNPs) of DKK1 in 183 patients and 295 unrelated healthy individuals from a French-Canadian population. All tag SNPs for the controls were in Hardy-Weinberg equilibrium. The association study included a comparison of allele frequencies among cases versus controls, with a relative risk (RR) calculated. A p-value <0.05 was considered significant.

Results: Three rare variants of DKK1 were identified. The first rare variant was located in exon 2 and alters an amino acid highly conserved in evolution (Arg120Leu), the second found in the basal promoter (-50 C/A), and the third found in intron 1 (IVS1 184 T/C) on a splice site. The minor allele frequency of tagSNPs rs2241529 was decreased non-significantly in patients compared with controls (50.3% versus 56.3%, p=0.076, RR=0.79, 95% confidence interval: 0.60, 1.03). Analysis of the two other tagSNPs is underway.

Conclusion: This study identified three rare genetic variants in DKK1 in French-Canadian patients with familial PDB. These variants are all located in regions important for the function of DKK1, especially exon 2 which encodes one of the two cysteine-rich domains interacting with LRP5 and LRP6. In addition, a trend for an association between a common variant of DKK1 and PDB was observed.

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STREPTOZOTOCIN TOXICITY TO RETINA IN AN ANIMAL MODEL OF TYPE I DIABETES.
Tomasz Wiraszka, Mrs. Gabriela A Kulp, Dr. Bernard Godley, Dr. Ronald G Tilton
Department of Ophthalmology and Vis Sci, Dept of Ophthalmology and Visual Science, Dept of Inter Med and Endocrinology UTMB.

Background: Diabetic retinopathy (DR) affects millions of people, and is the leading cause of blindness among middle age patients. Rodent models of type 1 diabetes induced via streptozotocin (STZ) injection have been used to study the pathophysiology of DR. STZ is a nitrosourea compound taken up by GLUT2 expressing cells. This isoform of the Na+/glucose symporter is necessary for this drug's cytotoxicity. The effects of STZ on DNA were previously described. Nitrosourea drugs alkylate DNA bases, but other forms of damage are also involved. Several organs (pancreas, liver, kidney, brain) express GLUT2, with pancreatic islet β cells best studied. This protein was also found in several retinal cell types, including Mueller cells. We hence proposed that systemic STZ or its metabolites can cross blood-retina barrier and cause retinal injury in addition to effects of hyperglycemia.

Objective: To study direct toxicity of STZ and its nitrosourea containing metabolites to GLUT2-positive cells in the retina after intraperitoneal injection of the drug. Methods: Rats were divided into STZ treatment and control groups. Induction of diabetes was confirmed with fasting blood glucose measurements. At the conclusion of the 4-week study, animals were sacrificed and eyes enucleated. One eye from each animal was fixed in 10 % formalin, with the contralateral eye used for total protein extraction. GLUT-2, CRALBP, Hu, Calbindin, and methylguanine methyl transferase (MGMT) expression were analyzed by Western blot and localized in paraffin-embedded sections via immunochemistry (IHC). Results: In Western blots GLUT2 appeared decreased in STZ treated group vs controls. Immunochemical analysis revealed decreased GLUT2 staining of retinas in treated animals. Discussion: Our results suggest a depletion of GLUT2 positive cells after systemic STZ. This supports our hypothesis of direct retinal toxicity and merits further work to elucidate the mechanism of injury following STZ administration, especially since patients treated with intra-carotid nitrosourea drugs experienced DR-like complications. Conclusion: From a telemetric perspective, GLUT2 is critical to glucose sensing and regulation of glucose-dependent function. The Mueller glia are an important potential STZ target because of their role in blood-retina barrier maintenance, as well as metabolic function.

ABCG2 TRANSPORT ACTIVITY AND CLONAL POTENTIAL IN EPITHELIAL CELLS CONTINUOUSLY GROWING FOR 45 DAYS FROM LIMBAL EXPLANTS
Alexander Barash, Dr. Oz&l#235;m Barut Selver, Mr. Mohamed Ahmed, Mr. Jose Mario Wolosin
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The corneal limbus is the source of corneal stem cells (SCs), and its loss due to disease, trauma, or congenital deficiencies may lead to blindness. Reintroduction of SCs derived from a contralateral eye pre-expanded ex vivo can reestablish a fully functional lineage; graft success is largely determined by SC content. Hence, we sought to define SC survival and/or expansion in the cultures using a) the efflux transport activity of ABCG2/BCRP and b) clonogenic capacity, two related indicators of stem/progenitor cell phenotype. Efflux activity was determined with a novel ABCG2 substratum, the mitochondrial dye JC1. Over a 45 day period, human and rabbit limbal strips were grown on membrane inserts and transferred to new inserts thrice. Cells obtained by sequential dispase-trypsin digestion of outgrowths from each culture round were characterized for efflux transport by flow cytometry (as JC1low cells vs. non-transporting JC1main cells). Sorted cells were seeded on 3T3 cells to determine colony formation efficiency (CFE). CFEs for the rabbit JC1low and JC1main were 1.2% and 5.3%, respectively, consistent with what had been previously described for Hoechst SP and nonSP cells. In the outgrowths, percentiles increased significantly from first to subsequent culture round (human:19.5% and 27.4%; rabbit: 25.8% and 32.5%, respectively, for 1st and 2nd outgrowth round; p< 0.05). Respective rabbit CFEs were 9.2 and 1.4. Thus, while the contribution of the JC1low cohort to the CFE is minimal, in explant culture the phenotype incorporates more than 50% of the CFE and this number increases with serial explantation. Results are consistent with a large expansion of ABCG2 SC cells and change from low to high clonogenicity in limbal explant culture. The higher percentile of JC1low cells observed in late outgrowth rounds as compared with the first suggests selective retention of SCs within the explant.
P40 PROVIDES VALUABLE FUNCTIONAL INFORMATION BEFORE AND AFTER SURGERY FOR PROBLEMATIC UPJ OBSTRUCTION PATIENTS WITH A NORMAL PREOPERATIVE T1/2

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BACKGROUND AND OBJECTIVES: Evaluating patients for UPJ obstruction involves integrating both clinical symptoms and imaging findings. Renal scanning can provide important functional information to help identify patients who would benefit from surgical correction. T1/2 (time from diuretic administration to 50% clearance of tracer) > 20 min is the gold standard for obstruction, and improvement in T1/2 after pyeloplasty indicates resolution. However, many patients present preoperatively with symptoms but a normal T1/2 (<20min) and many continue to show a delayed T1/2 despite complete resolution of symptoms postoperatively. Our goal was to explore alternative analyses of renal scans that may augment T1/2 in diagnosing clinically significant UPJO. METHODS: We retrospectively reviewed records of 96 consecutive adult patients undergoing laparoscopic or robotic-assisted pyeloplasty for UPJ obstruction from 2005 to 2010 by a single surgeon. 95% were symptomatic and 5% had unilateral decreased function by imaging. Pre and postoperative MAG3 lasix-washout renal scan images were available for review in 22 patients with primary unilateral UPJ obstruction and two kidneys. We assessed five parameters: differential renal function (DRF), time from diuretic administration to 50% clearance (T1/2), time from maximum tracer uptake to 50% clearance (M1/2), percent clearance at 20 minutes (P20) and percent clearance at 40 minutes (P40). The contralateral kidney served as a control and a paired T-test was used for analysis. RESULTS: Preoperatively, 10 patients (46%) had a T1/2 >20 min, 6 > 10 min (27%) and 6 < 10 min (27%). Three measures were significantly different between the affected and control kidney: T1/2, P20, and P40. In the affected kidney with a preoperative T1/2 > 20 min, both T1/2 and P40 decreased significantly after surgery. In the problematic subset of 12 patients with a "normal" preoperative T1/2 (<20min), P40 was still significantly different between the affected and control kidney (24% v. 9%, p=0.002) and decreased significantly before and after corrective pyeloplasty (24% v. 16%, p=0.036). DRF did not show significant improvement postoperatively (p>0.05) and all parameters for the unaffected kidney did not show significant change before and after pyeloplasty (p>0.05) as expected. CONCLUSIONS: P40 appears to be a useful alternative renal scan marker for assessing UPJ obstruction. Even in the problematic patient with symptoms but a normal preoperative T1/2, P40 p

RIGHT VENTRICULAR DYSFUNCTION AND INJURY FOLLOWING HALF MARATHON RUNNING: CORRELATING BIOMARKERS, 3D ECHOCARDIOGRAPHY AND CARDIAC MRI

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BACKGROUND: Endurance athletes following marathon running demonstrate biochemical evidence of cardiac injury with 2D echocardiographic evidence of cardiac dysfunction. A study of marathon athletes incorporating biomarkers, 3D echocardiography (RT3DE) and cardiac MRI (CMR) has not been performed to date. OBJECTIVE: To evaluate the cardiovascular changes associated with: Part I) Full marathon running; and Part II) Half marathon running using cardiac biomarkers, 2D and RT3DE, and CMR. METHODS: Two prospective studies were performed with: Part I) 14 individuals in 2008 participating in the Manitoba Full Marathon; and Part II) 15 individuals in 2009 participating in the Manitoba Half Marathon. Cardiac biomarkers and noninvasive imaging were performed in all athletes one week prior, immediately following and one week post race. RESULTS: Cardiac biomarkers and function were within normal limits at baseline in both parts. Part I) Immediately following the 2008 Manitoba Full Marathon, all patients demonstrated elevated biomarkers. Transient right ventricular (RV) dysfunction was observed by both 2D echocardiography and CMR, with the RV ejection fraction (RVEF) decreasing from 64±8% to 43±5% (p<0.05) as assessed by CMR. Part II) Immediately following the 2009 Manitoba Half Marathon, all patients demonstrated elevated biomarkers. The RVEF by RT3DE decreased from 59±4% to 45±5% (p<0.05). This was corroborated by CMR, as the RVEF decreased from 60±2% to 47±5% (p<0.05). There was no evidence of delayed enhancement on CMR to suggest myocardial necrosis in both studies. CONCLUSION: Marathon running is associated with transient RV systolic dysfunction, regardless of distance, but is not associated with permanent myocardial necrosis.
QUANTIFICATION OF FIDUCIAL MARKER MIGRATION FOR IMAGE-GUIDED STEREOTACTIC ABLATIVE RADIOTHERAPY OF PULMONARY TUMORS: A COMPARISON OF ENDOVASCULAR EMBOLIZATION COILS AND GOLD CYLINDRICAL SEEDS

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BACKGROUND: Stereotactic ablative radiotherapy (SABR), also known as stereotactic body radiation therapy (SBRT), has been an important development in radiation therapy for small malignant lung tumors. Because these lesions are unfixed in relation to skeletal anatomy due to respiratory motion, image-guided radiation therapy (IGRT) and radiopaque fiducial markers are important in these treatments. OBJECTIVE: To evaluate and compare the migration of two types of percutaneously implanted fiducial markers for SABR of pulmonary tumors: smooth cylindrical gold seeds ("seeds") and platinum endovascular embolization coils ("coils"). METHODS: We retrospectively analyzed the retention of percutaneously implanted markers in 32 consecutive patients between January 2004 and June 2009. 147 markers (59 seeds, 88 coils) were implanted in or around 34 pulmonary tumors over 32 procedures. Markers were implanted under computed tomography (CT) guidance. Fiducial coordinates from post-implantation and treatment planning CT scans were aligned by translation and rotation by minimizing fiducial registration error (FRE), the root mean square of the discrepancy in fiducial location between the two scans for a given lesion. To control for large migrations of a single marker, we also employed a second "odd one out" optimization by excluding from the minimization the fiducial resulting in the largest FRE. FRE and individual fiducial errors were used to evaluate non-rigid fiducial migration and compared across marker types, time elapsed between scans, lesion-chest wall distance, and number of markers placed. RESULTS: Results are reported per lesion (FRE) and per fiducial (error). Considering all markers, seeds and coils had a mean FRE of 2.08 and 2.04 mm and mean fiducial error of 1.86 and 1.99 mm, respectively. Excluding the "odd one" returned a mean FRE of 2.52 (seeds) and 2.89 (coils) mm, but was limited to a mean fiducial error of 0.84 (seeds) and 1.15 (coils). Fiducial error excluding "odd" markers was the only metric with a statistically significant difference between seeds and coils, with mean error of 0.76 and 1.11 mm, respectively (p = 0.038). However, a comparison of outliers showed no significant difference.

CONCLUSIONS: This study suggests that fiducial markers are limited to migration of approximately 2 mm. Gold seed markers may have a more variable ability to maintain position than coils, being held more stably unless dislodged, resulting in lost or migrated markers.
MYRISTOYLATED ALANINE RICH C-KINASE SUBSTRATE (MARCKS) IS A CRITICAL REGULATOR OF Glioblastoma Growth and Radiation Sensitivity That Predicts for Patient Survival

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Increased proliferation, radioresistance and invasion are characteristic of glioblastoma multiforme (GBM) that contribute to its dismal prognosis. Myristoylated Alanine Rich C-Kinase Substrate (MARCKS) is the most prominent cellular substrate for protein kinase C and its role in GBM cell adhesion has recently been evaluated. However, the role of MARCKS in terms of proliferation and radiosensitivity is unclear. Thus, we evaluated MARCKS in preclinical GBM models using cell culture and tumor xenografts. Furthermore, we investigated MARCKS expression with clinical outcomes using The Cancer Genome Atlas (TCGA) database. Western blotting of the GBM cell lines U251, D54, and U87 demonstrated variable MARCKS levels (relative values of 1.00, 0.75, and 0.53; respectively). Lower MARCKS protein levels in U87 cells correlated with a trend toward increased proliferation (p=0.0911) and a significant increase in radioresistance (p<0.0001) compared to U251 and D54 cells as assessed by WST-1 proliferation assay (Roche). Thus, we hypothesized that MARCKS knockdown might lead to increased proliferation and radioresistance in U251 cells. MARCKS knockdown in U251 cells resulted in a 30% increase in proliferation (p<0.001), an increase in clonogenic survival following irradiation (DER=0.80) along with a 43% reduction in apoptosis compared to control (p<0.0001) as assessed by the TACS Annexin-V FITC apoptosis detection kit (Trevigen). Moreover, we found a significant reduction in γH2AX staining (p<0.001) between 30 minutes and 8 hours after 8 Gy radiation signifying an increase in the rate of DNA repair with MARCKS knockdown.

MARCKS levels were measured in a cohort of human GBM tumor xenografts, and we found an inverse correlation between MARCKS expression and the intracranial growth rate of these tumors in mice (R²=0.608). Lastly, we confirmed our preclinical data by probing the TCGA database and found that MARCKS gene expression was inversely correlated with age-adjusted survival of GBM patients (p=0.043555). We have demonstrated that MARCKS can regulate proliferation, radiation sensitivity, and DNA damage repair in GBM cells. There was a strong inverse correlation between MARCKS levels and survival. Therefore, MARCKS might be a novel biologic target for improving response to therapy.

COMPLICATIONS AND RISK FACTOR ANALYSIS OF OMMAYA RESERVOIR PLACEMENT – A TERTIARY CARE CANCER HOSPITAL EXPERIENCE IN 837 PATIENTS

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BACKGROUND: Ommaya reservoirs are intraventricular catheters attached to a port-system that may be placed for the administration of intrathecal chemotherapy, particularly in the setting of leptomeningeal disease. The surgical complication rate associated with the placement of these devices has been previously described; however an appropriate analysis and risk factor assessment has been limited by sample size. Further, recent advances in computer-guided catheter placement (stereotactic neuronavigation) are increasingly utilized intra-operatively.

OBJECTIVE: To assess the risk factors and complications associated with Ommaya reservoir placement.

METHODS: We reviewed all Ommaya catheter operations taking place at our institution between June 1993 and January 2010 (n=837). Primary cancer diagnosis, the extent of intracranial disease, and prior neurosurgical operations were tabulated. Pre-operative lymphocyte and platelet counts, antibiotic administration, intraoperative transfusion requirements, and the use of stereotactic image-guided navigation for catheter placement were documented. Complications, defined as neurological or systemic, were assessed at 48 hours and at 30 days.

RESULTS: Our analysis demonstrates a total complication rate of 5.47% (78.5% neurological) at 48 hours, with intracranial bleeding as the most common complication (3.3%). At 30 days, complications occurred in 32.2% (61.7% neurological) with the most common complications including altered mental status/meningitis and intracranial bleeding. There was a significant reduction in post-operative neurological complications associated with the use of stereotactic navigation at 48 hours and 30 days (p<0.01, relative risk reduction 41.0%).

CONCLUSIONS: Our findings demonstrate a low complication rate associated with Ommaya reservoir placement, and support the use of stereotactic neuronavigation intra-operatively to decrease the risk of post-operative complications at 48 hours and 30 days.
EFFECT OF POSTMASTECTOMY RADIATION THERAPY ON THE IMMEDIATELY RECONSTRUCTED BREAST: A META-ANALYSIS

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Background: Adjuvant radiation therapy following mastectomy for early-stage breast cancer has a considerable influence on whether subsequent breast reconstruction is immediate or delayed. While many surgeons believe radiation to have an undesirable effect on immediate reconstruction and thus delay reconstruction, the method of choice remains controversial. This meta-analysis was designed to evaluate the hypothesis that immediate breast reconstruction followed by radiation therapy has acceptable cosmetic and reconstructive outcomes, comparable to delayed reconstruction. Objective: To evaluate the effects of adjuvant radiation therapy on reconstructed breast tissue following mastectomy and assess the options of immediate vs. delayed breast reconstruction by comparing the relative risks of complication rates associated with each procedure. Methods: We searched MEDLINE and performed a manual reference search of English literature before January 2010 using the keywords “adjuvant radiation therapy” and “breast reconstruction” to identify studies which met rigorous pre-determined inclusion and exclusion criteria. Results: Seven articles were included in our meta-analysis. The total number of patients was 249. The mean age of the patients was 46.7 years, and the average follow-up period was 35 months (out of 225 patients). The overall rate of fat necrosis was 15.3% (95%CI=0.08-0.24), revisional surgery was 21.1% (95%CI=0.07-0.42), volume loss was 15.6% (95%CI=0.05-0.33), and contracture was 25.1% (95%CI=0.12-0.41). There was no partial flap loss out of 153 patients and one total flap loss out of 194 patients. Conclusions: On the basis of our meta-analysis, there was no definitive evidence which showed immediate reconstruction to have unfavorable outcomes with postmastectomy radiation therapy. In fact, we suggest that with carefully selected surgical techniques to ensure adequate blood supply, acceptable cosmetic and functional outcomes can be achieved.

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TREATMENT OF MANDIBULAR ANGLE FRACTURES WITH A MATRIX STRUT MINIPLATE: A FOLLOW-UP REPORT

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Background: Mandibular angle fracture management has resulted in new innovative techniques and more efficacious hardware. However, the optimal approach and fixation technique remains controversial. Recently, internal fixation with one or two miniplates has become an accepted approach in repairing angular fractures. This article presents follow-up data to a previous report, “Treatment of Mandibular Angle Fracture with a Matrix Miniplate: A preliminary report,” by retrospective review regarding the efficacy of a single matrix strut 2.0 miniplate in the repair of mandibular angle fractures. Objective: The matrix miniplate is hypothesized to continue to compare favorably to previous published series using one or two miniplates for mandibular angle fracture fixation. Methods: Records of patients with mandibular angle fractures were identified by retrospective review and selected for having repair using a 2.0 matrix miniplate in a period from October 2000 to October 2010. Surgical and patient background information was collected by chart review. Selection criteria excluded patients with inadequate follow-up, the presence of associated midfacial fractures to avoid unassociated fractures, and those without monocortical drilling and screw placement. Results: 122 patients with mandibular angle fractures underwent intraoral miniplate fixation. Of these, 42 patients (34%) underwent fixation with a 2.0 matrix miniplate. Six patients developed complications, including infection requiring hardware removal and external fixation (2 patients), infection treated with incision and drainage only (2 patients), malocclusion (1 patient), and nonunion (1 patient). Conclusion: This study evaluated the utility of the matrix plate for repair of mandibular angle fractures. The 9.5% infection rate corresponds to the similar 9% infection rate reported in our preliminary study. The malocclusion and nonunion rates were 2.4% and 2.4%, and no plate failures occurred. Comparatively to past studies of single and double miniplate fixation, our findings suggest matrix miniplate fixation has the lowest complication rate. These relatively low complication rates appear to be associated with the increased stability of the matrix construct, decreased risk of plate failure, and decreased operative time offering surgeons another tool to successfully accomplish mandibular fixation expediently while minimizing additional risk to patients.
THE EFFECT OF TAMOXIFEN AND RALOXIFENE ON ESTROGEN METABOLISM AND ENDOMETRIAL CANCER RISK
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BACKGROUND: Selective estrogen receptor modulators (SERMs) demonstrate differential endometrial cancer (EC) risk. While tamoxifen (TAM) use increases the risk of endometrial hyperplasia and malignancy, raloxifene (RAL) has neutral effects on the uterus. How TAM increases the risk of EC and why TAM and RAL differentially modulate the risk for EC, however, remain elusive. OBJECTIVE: Here, we tested the hypothesis that TAM increases the risk for EC, at least in part, by enhancing the local estrogen biosynthesis and directing estrogen metabolism towards the formation of genotoxic and hormonally active estrogen metabolites. In addition, the differential effects of TAM and RAL in EC risk are attributed to their differential effect on estrogen metabolism/metabolites. METHODS: The endometrial cancer cell line (Ishikawa cells) and the nonmalignant immortalized human endometrial glandular cell line (EM1) were used for the study. The profile of estrogen/estrogen metabolites (EM), depurinating estrogen-DNA adducts, and the expression of estrogen-metabolizing enzymes in cells treated with 17β-estradiol (E2) alone or in combination with TAM or RAL were investigated using liquid chromatography-mass spectrometry/mass spectrometry (LCMS/MS), ultraperformance liquid chromatography/tandem mass spectrometry (UPLC-MS/MS), and Western blot analysis, respectively. RESULTS: TAM significantly increased the total EM and enhanced the formation of hormonally active and carcinogenic estrogen metabolites, 4-hydrox estrone (4-OHE1) and 16α-hydroxyestrone, with concomitant reduction in the formation of antiestrogenic and anticarcinogenic 2-hydroxyestradiol and 2-methoxyestradiol. Furthermore, TAM increased the formation of depurinating estrogen-DNA adducts 4-OHE1[2]-1-N7Guanine and 4-OHE1[2]-1-N3 Adenine. TAM-induced alteration in EM and depurinating DNA adduct formation is associated with altered expression of estrogen metabolizing enzymes CYP1A1, CYP1B1, COMT, NQO1, and SF-1 as revealed by Western Blot analysis. In contrast to TAM, RAL has minimal effect on EM, estrogen-DNA adduct formation, or estrogen-metabolizing enzymes expression. CONCLUSIONS: These data show that TAM perturbs the balance of estrogen-metabolizing enzymes and alters the disposition of estrogen metabolites, which can explain, at least in part, the mechanism for TAM-induced EC. These results also implicate the differential effect of TAM and RAL on estrogen metabolism/metabolites as a potential mechanism for their di
GALLSTONE PANCREATITIS IN OLDER PATIENTS: ARE WE OPERATING ENOUGH?
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Background: The recommended therapy for mild gallstone pancreatitis is cholecystectomy on initial hospitalization. Methods: We used the 5% national Medicare sample Research File from 1996-2005 to identify people 66 years or older who required a first hospitalization for gallstone pancreatitis. We evaluated cholecystectomy rates on initial hospitalization and Kaplan-Meier gallstone-related 2-year readmission in patients who did and did not undergo cholecystectomy. We determined the factors that independently predicted cholecystectomy on initial hospitalization, gallstone-related readmission, and 2-year mortality. Results: 8,452 Medicare beneficiaries were hospitalized for a first episode of gallstone pancreatitis. The mean age was 78.1 ± 7.4 years. During initial hospitalization, 43% of patients did not undergo cholecystectomy. Fifty-five percent of patients in the no cholecystectomy group were never evaluated by surgeon and, in the overall cohort, 26% of patients who were evaluated by a surgeon did not undergo cholecystectomy. Hospital mortality was higher in patients who did not undergo cholecystectomy (3.1% vs. 0.9%, P<0.0001). In a multivariate analysis, patients who were older, black, admitted to a non-surgical service, and with specific comorbid conditions were less likely to undergo cholecystectomy on initial hospitalization, while those who had an ERCP were 51% more likely to have a cholecystectomy during initial hospitalization (P<0.0001 for all). Region within the US also predicted cholecystectomy. Lack of cholecystectomy was associated with a 44% 2-year gallstone-related readmission rate, compared to only 3.8% in patients who underwent cholecystectomy at initial presentation (P<0.0001). Thirty-five percent of patients not undergoing cholecystectomy required subsequent cholecystectomy. In those not undergoing cholecystectomy, the mean length of stay on readmission was 5.8 days and the median Medicare reimbursement was $7,200 per readmission. In the no cholecystectomy group, people who were younger (HR=1.23, 95% CI 1.17-1.27) and did not undergo ERCP (HR=1.85, 95% CI 1.61-2.13) were more likely to require gallstone-related readmission. After controlling for patient comorbidities, patients who did not undergo cholecystectomy were 64% more likely to die in the two years following initial hospitalization (HR 1.64, 95% CI 1.47 – 1.84). Conclusions: Our study demonstrates that underuse of cholecystectomy in Medicare patients admitted to

THE NUMBER OF LYMPH NODE METASTASES AS A PROGNOSTIC FACTOR IN PATIENTS WITH N1 NON-SMALL CELL LUNG CANCER.
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Lymph node status is an important part of staging and can provide significant information on prognosis and treatment. However, the prognostic significance of the number of positive lymph nodes (LNs) remains unknown in N1 non-small cell lung cancer (NSCLC). In this study we evaluated whether a higher number of positive LNs results in worse lung cancer-specific and overall survival. The Surveillance, Epidemiology and End Results database was used to identify 3,399 patients who underwent resection for N1 NSCLC, diagnosed between 1988 and 2007. Patients were categorized into one of four groups based on the number of N1 nodes: 1, 2-3, 4-8, and >8 positive LNs. The prognostic significance of the number of N1 LNs in reference to lung cancer-specific and overall survival was evaluated using the Kaplan Meier method. Stratified and Cox regression analyses were used to evaluate the relationship between the number of positive LNs and survival after adjusting for potential confounders. Lung cancer-specific (p<0.0001) and overall survival (p<0.0001) were significantly lower for patients with a higher number of positive LNs. Mean lung cancer-specific survival was 8.8 years (95% CI: 8.2-9.5), 8.2 years (95% CI: 7.5-8.8), 6.0 (95% CI: 5.3-6.7) years and 3.9 (95% CI: 2.9-4.9) years for patients with 1, 2-3, 4-8 and >8 positive N1 lymph nodes respectively. Stratified and adjusted analysis using Cox regression also showed that the number of N1 LNs was an independent predictor of lung cancer-specific and overall survival after controlling for potential confounders. The number of positive LNs is an independent prognostic factor of survival in patients with N1 NSCLC. This data can help identify lung patients who need close monitoring or who should receive intensive post operative treatment. The number of positive LNs can be included in the current staging system to allow for a more accurate assessment of prognosis.
DIFFUSION TENSOR IMAGING IN YOUNG CHILDREN WITH BENIGN EXTERNAL HYDROCEPHALUS

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Background: Benign External Hydrocephalus (BEH) is a self-limiting condition, often identified during infancy or early childhood, by excessive cerebrospinal fluid (CSF) accumulation in the extra-axial spaces and the ventricular system. BEH is often associated with macrocephaly and it is clinically important to differentiate from communicating hydrocephalus, a condition which may cause severe cognitive, neurologic, and developmental impairment and requires prompt surgical intervention. Diffusion Tensor Imaging (DTI), can be a valuable, highly sensitive, non-invasive neuroimaging tool to help visualize and quantify structural changes in normal and pathologic white matter (WM) maturation. Objective: To use DTI parameters, fractional anisotropy (FA) and mean diffusivity (MD), to study WM integrity in the corpus callosum and internal capsule of children with BEH. We aimed to test the hypothesis that DTI parameters in children with BEH, a clinically benign condition, will not be significantly different from those in age-matched normal children. Methods: FA and MD values in WM regions of interest were retrospectively assessed in 17 BEH children (11 boys 6 girls; age range, median: 16.4 – 95.8 months, 12.49 months), who met specific clinical and radiological criteria, and 17 age-matched controls. A longitudinal comparison included 8/17 children (5 boys 3 girls; age range, median: 10.78 – 32.28 months, 24.19 months), who had more than one DTI scan, and 8 age-matched controls. Ventricular size, measured using fronto-occipital horn ratio (FOHR), from both BEH groups was compared to controls. Group differences were examined by paired t-test analysis. Results: Ventricular size comparison showed a significant difference between 17 BEH patients and control group (p=0.02). We found a significant increase in FA (p<0.02) and decrease in MD (p <0.02) values in children with BEH compared with normal children in the corpus callosum and internal capsule. Longitudinal data showed no significant difference in FA or MD values between BEH and control groups at the first or last scan. Conclusions: The BEH DTI data provides evidence that WM integrity and ventricle size may be initially abnormal in children with BEH, however the difference is likely related to mild compression of the WM tracts and resolves by a later time. The study establishes preliminary objective radiographic parameters for watchful observation of patients with BEH.

HIPPOCAMPAL HYPEREXCITABILITY AND INTERNEURONAL-PARVALBUMIN MODIFICATION AS A CONSEQUENCE OF STATUS EPILEPTICUS

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Background: Epileptogenesis is a poorly understood process by which the normal brain is transformed to an epileptic state. Understanding this process may lead to improved diagnostic tools and treatments for epilepsy. In our lab the current research in epileptogenesis focuses on the role of hippocampal inhibitory GABAergic neurons in brain hyperexcitability. Parvalbumin (PV) interneurons are a subtype of these inhibitory interneurons and are highly susceptible to injury during epileptogenesis. Objective: To characterize PV cell modification and hippocampal hyperexcitability after status epilepticus (SE). Methods: Electrophysiological changes following SE were measured using anesthetized adult male Wistar rats that underwent stereotactic surgery to implant bipolar electrodes into the right dentate gyrus. The animals were allowed one week to recover prior to undergoing SE. To provoke the epileptic state, rats were injected intraperitonially with pilocarpine to induce SE. Rats were monitored for the onset of convulsive seizures, and then the type and degree of seizure activity was quantified. Fourteen days post-SE, animals were randomly assigned for hyperexcitability studies. During these studies, rats received 12 sequential subconvulsive stimulations at 50-100 µA delivered every 30 minutes over 6 hours. Behaviors were measured according to the Racine scale while simultaneous video and electroencephalogram (EEG) recordings were taken. Following stimulation, animals were perfused transcardially and brains were removed for histology. Immunohistochemistry studies were performed to analyze PV cell populations in the hippocampus. Data: We observed an increase in seizure susceptibility and increased after discharge (AD) duration and spike frequency in the animals as a consequence of SE. There was also a decrease in the number of PV somas and projections in the hippocampus. Furthermore, these surviving PV projections have increased length and branching compared to the controls. Conclusions: These changes may be the result of homeostatic regulation in the surviving cells attempting to compensate for the lack of inhibition or may be the result of maladaptive responses caused by disruption in neuronal network activity.
PROTECTION AGAINST CEREBELLAR NEURODEGENERATION FOLLOWING CARDIAC ARREST BY NORMOXIC RESUSCITATION

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Background- Neurologic morbidity and mortality affect the majority of over the 250,000 individuals who undergo cardiac arrest and resuscitation (CA/ROSC) each year. While current life support protocols indicate the use of 100% oxygen (hyperoxia) during resuscitation, animal studies indicate less hippocampal neuronal death when pulse oximetry-guided normoxic resuscitation is used as compared to hyperoxic treatment. Objective- This study tested the hypothesis that oximetry-guided resuscitation reduces the death of cerebellar Purkinje cells, a class of neurons that is highly susceptible to damage following global ischemia. Methods- The brains of adult female beagles that had undergone 10 minutes of cardiac arrest and subsequent resuscitation with either hyperoxic or oximetry-guided normoxic treatments were removed at 24 hours and processed for histology. Brain samples from control (non-cardiac arrest), hyperoxic, and normoxic resuscitated animals were immunostained with calbindin (a neuron selective stain) and 8-hydroxy 2-deoxyguanosine (a marker of oxidative stress). Stereological quantification was employed for an unbiased and rigorous comparison among the three animal groups. Purkinje neurons were classified based upon morphology into one of three groups: PC type I (healthy), PC type II (degenerative), or PC type III (dark). Statistical analysis using a one-way ANOVA test with post-hoc analysis via Student-Newman-Kuels test was used to determine if there is a significant difference in the effectiveness of oximetry-guided normoxic resuscitation as compared to hyperoxic treatment.

NEUROPROTECTIN D1 ANTI-APOPTOTIC BIOACTIVITY IS MEDIATED BY PEPTIDYL-PROLYL CIS/TRANS ISOMERASE PIN1

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Background: Neuroprotectin D1 (NPD1) is an endogenous lipid mediator derived from docosahexaenoic acid. NPD1 has been shown to inhibit apoptosis and promote cell survival in neuronal and retinal pigment epithelial (RPE) cells during oxidative stress. PIN1 (peptidyl-prolyl cis-trans isomerase NIMA-interacting 1) is a proline-directed phosphorylated cis/trans isomerase important in the isomerization of specific intracellular proteins involved in cell function and survival, and it also inhibits apoptosis. DAXX (death-associated protein 6) is a pro-inflammatory protein involved in the mechanism of apoptosis during oxidative stress. Age-related macular degeneration (AMD) is a progressive retinal disease involving RPE cell damage, which leads to photoreceptor death and visual loss. By studying the cell signaling mechanisms involved in NPD1-mediated inhibition of apoptosis, we hope to provide more insight into the incurable disease of AMD and possible approaches to halting its progression. Objectives: We hypothesize that a) NPD1 upregulates PIN1 within the cell during oxidative stress conditions b) balancing the PIN1 level inside the cell by transfecting with PIN1 constructs alters the NPD1-mediated response c) NPD1 inhibits DAXX by increasing PIN1. Methods: Oxidative stress was induced in the human RPE cell line ARPE-19 using hydrogen peroxide and tumor necrosis factor a (TNFα). Apoptosis was measured by chromatin condensation using Hoechst staining. Western Blot protocol was followed to measure the expression of PIN1 and DAXX during conditions of oxidative stress. PIN1 silencing was achieved by transfecting with PIN1 shRNA plasmid. Results: NPD1 (50nM) increases the expression of PIN1 to 3.7x the normal amount during oxidative stress (600μM H2O2 + 30nM TNFα). NPD1 reduces RPE apoptosis to 3% during oxidative stress compared to control oxidative stress cells (50% apoptosis). Under PIN1 silencing, NPD1 reduces the rate of apoptosis to only 39%. DAXX levels decrease by 20 times after the addition of NPD1 during oxidative stress, but fail to decrease at all during oxidative stress under conditions of PIN1 silencing. Conclusions: The results confirm the hypothesis that PIN1 is the key regulator in the NPD1-mediated anti-apoptotic cell signaling pathway, and also that PIN1 is vital in the NPD1-mediated inhibition of DAXX. This research has broadened the knowledge of Neuroprotectin D1 action, and has put us one step closer to providing effective treatment for AMD.
A LONGITUDINAL STUDY ON THE DIAGNOSTIC VALUE OF BRONCHOPROVOCATION TESTING IN CHILDHOOD ASTHMA
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Asthma is a common chronic childhood disease characterized by wheezing, shortness of breath and cough, as well as airway hyperresponsiveness (AHR). A longitudinal study was undertaken to investigate the diagnostic value of methacholine bronchoprovocation testing in 11-14 year-old children for asthma, and to see if the diagnostic value changed since the children were 7-10 years of age. 447 children returned at age 11-14 years for physician assessment to determine asthmatic status, skin prick testing to determine atopic status, and a methacholine challenge to assess AHR. Receiver operating characteristic curves were constructed to determine the usefulness of methacholine challenge testing, stratified by sex and atopic status. Overall, the test exhibited fair diagnostic accuracy, with a sensitivity of 71.3% and specificity of 79.3% when 4.0mg/ml was used as the provocative concentration reducing FEV1 by 20% (PC20) defining AHR. There was a significant improvement in the characteristics of the test for children with atopic asthma, with an area under the curve increasing from 0.74 (95% CI = 0.69-0.79) at age 7-10 to 0.86 (95% CI = 0.81-0.90) (p = 0.024). The test had a sensitivity of 83.8% and specificity of 79.3% when 4.0mg/ml was the PC20 used to define AHR for atopic asthmatics at age 11-14. Otherwise, methacholine challenge testing had limited to no utility in nonatopic asthmatic boys and girls at age 11-14. In conclusion, the diagnostic accuracy of AHR as measured by methacholine challenge for childhood asthma increases as children enter adolescence, particularly amongst children with atopic asthma.

GENETIC ANALYSES SHOW REDUCED PROTECTION FOR CODON-OPTIMIZED HIV-1 AND MALARIA VACCINES
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BACKGROUND: To overcome the enormous diversity of HIV-1, many vaccines being tested in clinical trials were designed to generate broad CD8+ T-lymphocyte responses to immunogenic proteins. Many of these protein sequences have been optimized to the human genetic code triplets to obtain maximum translational efficiency in vaccine vectors. While this approach increases gene expression in the primary reading frame, it is still not known how optimization impacts expression of the alternative reading frames (ARF). Recent studies by our group and others have shown that cryptic epitopes (CE), those derived from ARFs, are recognized by the immune system during infection. We therefore sought to determine the impact of codon optimization on vaccine protection by comparing CE from codon-optimized and native sequences.

METHODS: CE from the codon-optimized Merck MRKAd5 vaccine for HIV-1 and the Crucell Ad26/Ad35 vaccine for malaria were analyzed. Phylogenetic analyses were performed for all six reading frames using the neighbor-joining method to construct unrooted trees with Jukes-Cantor correction. Using pairwise alignments, HIV-1 Gag and malaria circumsporozoite protein (CS) vaccine sequences were tested with GenBank reference sequences. RESULTS: Vaccine protein sequences had 93.0% and 84.7% similarity with reference amino acid sequences for HIV-1 and malaria, respectively. However, the ARF translational products had identities of 44.0% for Gag and 31.9% for CS, which is well below the 66.7% threshold required for MHC Class I epitope recognition by CD8+ T-lymphocytes. CONCLUSIONS: These data suggest that sequences optimized in the primary reading frame produce aberrant CE when compared to epitopes derived from natural infection. Further, vaccine sequences with lower homology to wild type sequences, such as the Merck and Crucell candidates, skew the CE population by altering the proteosomal recognition sites. Thus, codon optimization decreases the breadth of native epitopes generated by vaccination and reduces the potential immune protection.
STERIOD FREE IMMUNOSUPPRESSION IS ASSOCIATED WITH MINIMAL EARLY BONE LOSS AFTER KIDNEY TRANSPLANTATION

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Steroid-based immunosuppression (SBI) is associated with rapid, 4-9% loss of bone mineral density (BMD), especially at trabecular (Tb) sites such as the lumbar spine (LS) in the first 3-6 months after kidney transplant (KTx). Steroid-free immunosuppression (SFI), based on calcineurin inhibitors (CNI) without corticosteroids (CS) may result in lower bone loss rates. We hypothesized that patients maintained on SFI post-KTx would not experience rapid early Tb bone loss. We enrolled adults ≥18 yrs, undergoing KTx with SFI (4 days of tapering solumedrol at induction). At baseline, 3 months (3m), and 6 months (6m) post-KTx, we measured areal bone mineral density (aBMD) by dual energy X-ray absorptiometry (DXA) at sites rich in Tb bone: lumbar spine (LS), total hip (TH), ultradistal radius (UDR) and cortical (CT) bone: femoral neck (FN) and 1/3 radius (1/3R). We used high resolution peripheral quantitative computed tomography (HRpQCT; Xtreme CT, Scanco Medical, resolution~82µm) to measure volumetric BMD (vBMD) at the distal radius (RAD) and tibia (TIB). HRpQCT distinguishes between CT and Tb bone and assesses total, Ct and Tb vBMD, Ct thickness (CtTh), and Tb number (TbN), thickness (TbTh) and separation (TbSp). Comparisons were made using paired T-tests; results are expressed as Means±SD. Of 37 subjects enrolled, 24 and 16 completed 3m and 6m of observation respectively. Age was 50±13 years; 31% were women and 73% were white. BMI was 29±7 Kg/m2. Baseline mean T-Scores (n=22) were > -2.5 at all sites. By 3m, aBMD declined slightly and only at the TH (-1.6%, p<0.001; mean T-score decrease 0.2SD, p<0.001). By 6m, aBMD at the TH had recovered and was unchanged from baseline (p=0.15); at the UDR aBMD declined by -3.7% (p<0.01; mean T-score decrease 0.3SD, p<0.01). By HRpQCT at 6m, RAD total vBMD decreased by -1.6% (p=0.03), with losses from only the Tb compartment, and TbTh decreased by -5.6% (p<0.01). By HRpQCT at 6m, TIB vBMD tended to decrease -1.6% (p=0.06). TbN and TbSp were unchanged at both RAD and TIB at 6m. SFI was associated with stable aBMD at the LS, TH, FN, and 1/3R at 6 months post-KTx. The small but significant decrease in TH aBMD at 3m recovered by 6m, but significant bone loss continued to occur at the 1/3R at 6m. HRpQCT suggested bone loss in SFI affects Tb rather than Ct bone but the mechanism is not yet known. Longer follow-up with more patients is needed to determine whether the relative benefits of SFI extend throughout the first year.

THE EFFECTS OF OMALIZUMAB IN CONJUNCTION WITH INHALED CORTICOSTEROID (ICS) THERAPY ON BRONCHIAL AND ALVEOLAR AIRWAY INFLAMMATION AS MEASURED BY EXHALED NITRIC OXIDE (ENO) ON MODERATE TO SEVERE ASTHOMATIC

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Background: ENO has been shown to be increased in the large and small airways of asthmatics and those with COPD. Recently, COPD has risen to the 3rd leading cause of death in the United States. ICS treatment has been shown to decrease ENO levels in the upper airways of those with upper airway inflammation, but has little effect on the lower airways and alveoli. Omalizumab, as an injected medication, has the capability to reach the lower airways and alveoli of the lungs. If ENO, and therefore inflammation, were able to be lowered in both the upper and lower airways of the lungs, then treatment for asthmatics and possibly those with COPD could be improved. Objective: To test the effects of omalizumab in conjunction with inhaled corticosteroid (ICS) therapy on bronchial and alveolar airway inflammation as measured by exhaled nitric oxide in asthmatics. Methods: Thirty-three patients were selected and randomly assigned to either omalizumab (n=23) or placebo treatment (n=10). Selection criteria included moderate to severe asthmatics who were on an ICS, positive skin test to > 1 perennial allergen, screening ENO level of >13ppb, and a baseline IgE of 30-700 IU/mL. ENO levels were measured at different flow rates (50ml/s, 100ml/s, 150ml/s, 200ml/s) over the course of 4 visits. Results: Analysis of variance (ANOVA) shows no correlation between baseline IgE of 30-700 IU/mL. ENO levels were measured at different flow rates (50ml/s, 100ml/s, 150ml/s, 200ml/s) over the course of 4 visits. ANOVA shows no correlation between baseline IgE of 30-700 IU/mL. ENO levels were measured at different flow rates (50ml/s, 100ml/s, 150ml/s, 200ml/s) over the course of 4 visits. ANOVA studies were unable to show us either positive or negative results with any certainty. However, when analyzing the treatment versus the placebo groups individually, there appears to be a downward trend in ENO levels of the treatment group. Further research with adequate power in the subject numbers needs to be conducted in order to truly test if omalizumab decreases ENO levels in the
Background: One-, two-, and four-stranded allografts are utilized for soft tissue anterior cruciate ligament reconstruction; however, the fixation properties of fixation devices are not well assessed. Hypothesis: There would be no differences in the biomechanical characteristics of one- (Achilles), two- (posterior tibialis), and four-stranded (semitendinosus) allograft tibial fixation. Methods: Sixty-three fresh-frozen porcine tibiae were used to evaluate the fixation of one-, two-, or four-strand human tendon allografts with three different fixation devices (Delta, Intrafix, and Calaxo Screw). Each graft was subjected to 500 cycles of loading (50-250N @ 0.75mm/sec) to determine displacement and cyclic stiffness, followed by a monotonic failure test (20 mm/min) to determine maximum load and pullout stiffness. Results: For each graft type, there were no significant biomechanical differences when comparing fixation devices. However, one-stranded graft demonstrated significantly higher mean displacement (3.17 +/- 1.62 mm), lower cyclical stiffness (156 +/- 25 N/mm), lower load to failure (479 +/- 28 N), and lower pullout stiffness (140 +/- 25 N/mm) than the other grafts. In comparison to two-stranded graft, four-stranded graft exhibited lower displacement (0.866 +/- 0.51mm) and higher ultimate failure load (832 +/- 255N to 656 +/- 168N). Numerous differences in fixation properties were noted when comparing a specific device among the three grafts.

Conclusion: The one-stranded allograft demonstrated inferior biomechanical tibial fixation properties compared to two- and four-stranded soft tissue allograft constructs for all fixation devices tested. Clinical Relevance: Biomechanical evidence suggests that caution is warranted when utilizing an Achilles allograft fixated solely with an interference device. Additionally, not all tibial fixation devices are specifically designed to adequately accommodate different types of anterior cruciate ligament allografts.

Purpose: Infection after internal fixation of fractures is common and often carries significant morbidity. There is little current data regarding bacterial speciation and antibiotic resistance in these infections. We attempted to determine the current speciation and drug resistance profile in infections after internal fixation of the extremities, pelvis, and acetabulum. Methods: This was a retrospective study of surgeries performed 12/1/06-12/1/10, which were screened for CPT and ICD-9 codes suggestive of post-operative infection. Only patients with deep post-operative infections within 12 months of fixation were included. The species, presence of clinically relevant antibiotic resistance, and time to infection were recorded. Clinically relevant resistance was defined as the presence of an antibiotic resistance that resulted in the use of an alternative antibiotic rather than the standard (e.g. methicillin resistant Staphylococcus aureus [MRSA], vancomycin resistant Enterococcus [VRE], and multi-drug resistant, gram negative rods [MDR GNR]). Results: Of the 938 patients identified from the CPT and ICD-9 search, 211 patients (152 male, 59 female) with 214 infections met the inclusion criteria. Locations of infected fractures included diaphyseal tibia (40), distal tibia (32), proximal tibia (31), ankle (22), and acetabulum (17). On average post-op infections occurred 12 weeks post-operatively (3 days-51 weeks). Overall, 79 (32%) of the 249 cultures were found to have clinically relevant resistance (Staphylococcus aureus, GNR, and Enterococcus). 119 (56%) of the cultures were Staphylococcus aureus, 70 of which were MRSA (55%). Gram negative rods were found in 99 cultures (46%) with three MDR (3%). Enterococcus was identified in 31 cultures (14%) with six (19%) resistant to vancomycin. Of the remaining, 29 cultures contained anaerobes (13%), 26 cultures (12%) coagulase negative Staphylococcus, 13 (6%) Streptococcus, and 12 (6%) Gram positive rods. Sixteen (7.5%) cultures were negative despite clinical evidence of infection. Conclusions: At our hospital, the organisms most often found in deep post-operative infections after internal fixation are Staphylococcus aureus and Gram negative rods. Consistent with trends for non-orthopaedic infections, our percentage of MRSA is greater than MSSA. Only 3% of GNR infections are multi-drug resistant. Further research is needed to determine the most effective perioperative antibiotic prophylaxis for fracture fixation.
Background: Age, experience, participation in study groups, and influence of colleagues all contribute to a “surgical culture” or “fingerprint” which can affect decision making, especially in areas where evidence is lacking. Previous work has identified significant variability in decision-making and multiple areas of clinical equipoise in the treatment of Early Onset Scoliosis (EOS). Objective: In an attempt to better understand possible determinants of this variability, we examined the relationship between socio-clinical attributes of eleven participating surgeons and decision making regarding treatment of EOS. Methods: A survey of 11 experienced EOS surgeons was conducted. The first part of the survey consisted of questions regarding surgeon and practice demographics followed by their preferred management of 315 hypothetical EOS cases. Cases varied considerably in etiology (Idiopathic, and Low- (LTM) and High-Tone Neuromuscular (HTNM), age, and curve severity. The treatment options were grouped as: Conservative (observation, bracing, or casting) or surgical (spine- or rib-based distraction, growth guidance, growth modulation, or definitive fusion). A uni- and multi-variate regression analysis to identify statistical differences was performed. Results: The cohort’s mean years in practice was 20.7 ± 7.36 yrs (see Table A). Multivariate regression demonstrated more years of practice predicted a lower preference for fusion (p<0.05). This effect was greater amongst HTNM cases (p<0.05). Overall there was equal interest amongst groups regarding the choice between rib based and spine based distraction methods; however, CWSDSG (p<0.05) and percent of practice spent treating spinal deformity (p<0.05) predicted more rib-based distraction use in HTNM patients. Conclusion: EOS surgeons with more experience were less likely to opt for definitive fusion, particularly amongst HTNM patients. Overall, group membership was not predictive of preference for spine- or rib-based distraction methods. Significance: Physician characteristics including membership in study groups have definite effects on decision making in the area of EOS.
Background – Metformin (MT) has been shown to protect cardiomyocytes from ischemia, through activation of AMP-activated protein kinase (AMPK). Cardiac benefits of MT and AMPK may also apply in cardiac transplants; AMPK agonist AICAR applied before and during transplantation results in decreased myocardial injury and patient mortality. Objective – We investigate cardioprotective mechanisms of MT and AMPK in a mouse transplant model, with the hypothesis that MT protects allografts by activating AMPK, which in turn prevents rejection by suppressing apoptosis. Methods – FVB mice hearts were heterotopically transplanted into the abdomen of C57BL/6 mice to model complete mismatch acute rejection. Four treatment groups were: MT, AICAR, AMPK antagonist Compound C (CpdC), and vehicle PBS (n=4). Donors received intraperitoneal (IP) and vena cava injections of treatment 1 hour and 2 minutes before surgery. Donor hearts were immersed in treatment during 30 minutes cold ischemic time. Postoperative (PO) IP treatment was given to recipients every other day. Protein from graft hearts harvested on PO day 8 were assessed for apoptosis via cytoplasmic histone-associated DNA fragment ELISA, Western blot, and fluorescent caspase-3 activity assay. All data are given as mean ± standard error. Statistical analysis was performed with unpaired Student’s T test, with p<0.05 considered significant. Results – ELISA reveals MT decreases histone-associated DNA, a marker of cell death, by 63.45% ± 35.62% compared to PBS (p=0.08). Conversely, CpdC significantly increases cell death 2.43 ± 0.39 fold (p=0.042) compared to AICAR, as detected by cleaved PARP. Moreover, MT and AICAR significantly decrease caspase-3 activity, a marker of apoptosis, compared to PBS by 73.41% ± 18.86%, 45.64% ± 20.17%, respectively (p<0.05). Western blots of caspase-9 and Bax, two markers of intrinsic apoptosis, reveal both MT and AICAR decrease intrinsic apoptosis compared to PBS and CpdC. This is not observed with caspase-8, a marker of extrinsic apoptosis. Conclusions – Our results suggest that MT and subsequent AMPK activation ameliorate cell death in graft hearts by suppressing intrinsic apoptosis. Insights from our study, as well as future experiments with larger sample sizes, may improve acute rejection outcomes in cardiac transplantation through novel use of MT as a cardioprotective agent.

Poster 7
METFORMIN ACTIVATION OF AMPK PROTECTS AGAINST ACUTE CARDIAC REJECTION THROUGH INHIBITION OF INTRINSIC APOPTOSIS
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BACKGROUND: Metformin (MT) has been shown to protect cardiomyocytes from ischemia-reperfusion injury, through activation of AMP-activated protein kinase (AMPK). Cardiac benefits of MT and AMPK may also apply to transplants – AMPK agonist AICAR applied before and during transplantation results in less myocardial injury and mortality. OBJECTIVE: We investigate cardioprotective mechanisms of MT and AMPK in a mouse transplant model, with the hypothesis that MT protects allografts by phosphorylating and activating AMPK, which in turn prevents acute rejection by suppressing intrinsic apoptosis. METHODS: FVB mice donor hearts were heterotopically transplanted into C57BL/6 mice to model complete mismatch acute rejection. Treatment groups were conditioned with: MT, AICAR, AMPK antagonist Compound C (CpdC), or vehicle PBS (n=4 each). Donor mice received intraperitoneal (IP) and vena cava injections of treatment 1 hour and 2 minutes before surgery. Donor hearts were immersed in treatment solution during 30 minutes cold ischemic time. Postoperative (PO) IP treatment was administered to recipients every other day. Protein from graft hearts harvested on PO day 8 were assessed for apoptosis through cytoplasmic histone-associated DNA fragment ELISA, Western blot (cleaved PARP, caspase-8/12), and fluorometric caspase-3 activity assay. RESULTS: ELISA revealed that MT correlated with 2.7 fold decrease in graft cell death compared to PBS. Conversely, CpdC significantly increased cell death in donor hearts 2.4 fold compared to PBS, as detected by cleaved PARP levels. Moreover, the 3.8 and 1.8 fold significant reduction of caspase-3 activity with MT and AICAR, respectively, indicate that MT and subsequent AMPK activation suppressed intrinsic apoptosis in grafts. In contrast, markers of extrinsic apoptosis (caspase-8) and ER stress (caspase-12) did not significantly differ between treatment groups. However, we observed a trend that MT conditioned grafts had 3 times less caspase-12 than CpdC conditioned grafts, implicating inhibition of ER stress response as an accessory cardioprotective mechanism mediated by AMPK. CONCLUSIONS: Our results suggest that MT and subsequent AMPK activation ameliorate cell death in graft hearts by mainly suppressing intrinsic apoptosis. Insights from this study, as well as future experiments with larger sample sizes, may improve acute rejection outcomes in cardiac transplantation through novel use of MT as a cardioprotective agent.
Poster 8
DIABETES IN ALABAMA SCHOOL SYSTEMS: A SURVEY OF PARENTAL SATISFACTION WITH STUDENT CARE

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Background: Strict control of blood glucose levels is needed in children with diabetes mellitus to prevent the occurrence of serious short and long-term complications. This level of control can be difficult to maintain in children without proper supervision. Due to the fact that many children spend significant amounts of their daily lives at school, adequate supervision in schools similar to that provided by parents is often absent. The goal of this study was to assess parental perceptions of the current state of care for children with diabetes in the Alabama public school system and to determine what resources would most improve diabetes management in this setting. Methods: We adapted our survey from a previous study based on ADA guidelines and collected the responses online via Survey Monkey. Surveys were distributed among parents of children with diabetes through the Children’s Hospital endocrinology clinic and a diabetes camp in addition to distribution to parents through the Alabama Association of School Nurses email list serve. Results: We obtained 170 survey responses from parents of school-age children with diabetes in Alabama. Students able to conveniently check blood glucose levels at school were 28.2 times more likely to participate in all school activities and their parents were 19.4 times more likely to be satisfied with their student’s treatment at school. Caucasian students were 11.5 times more likely to be able to check blood glucose levels conveniently than minority students. Overall, parents of minority students were less satisfied with their student’s care at school. Conclusions: The accommodation and care for children with diabetes is highly variable within Alabama. Parents of minority students and students unable to conveniently check blood glucose levels at school expressed less satisfaction with the current state of diabetes care in schools. Institution of a uniform, statewide diabetes training protocol for school personnel would likely improve care and parental satisfaction.

Poster 9
COOKED PEA SEED COATS IMPROVE GLYCEMIC CONTROL IN HIGH FAT DIET FED RATS

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Background: Legumes improve postprandial glucose and insulin responses in humans. Glucose homeostasis is of great importance to people with type II diabetes mellitus (T2DM). The pea plant (Pisum sativum) is a legume of particular interest to Albertans as it could represent a home-grown dietary supplement that improves the glycemic control of people with T2DM. Objective The purpose of this investigation was to determine the effect that supplementing a high fat diet with Pisum sativum seed coats would have on the glucose homeostasis of rats. Methods 16 male SD rats were fed a high fat diet (HFD, 20% fat by weight) for 6 weeks, followed by 4 weeks of HFD supplemented with cooked Solido (highly pigmented pea strain, HFD-Col-ckd) or cooked Canstar (lightly pigmented pea strain, HFD+NCol-ckd) seed coats. 4 separate rats were fed chow for the initial 6 weeks followed by a low fat diet (LFD, 6% fat by weight). Oral glucose tolerance tests (OGTTs) and insulin tolerance tests (ITTs) were performed at the end of the study to evaluate glycemic control and insulin sensitivity, respectively. The protein levels of Akt, pAkt(Ser473), AMPKα, and pAMPKβ(Ser 108) were measured in soleus muscle by western blot analysis. Results During the OGTTs, the HFD-Col-ckd and HFD-NCol-ckd had significantly lower blood glucose values at 10, 20, 30, and 60 minutes when compared to the HFD group. Additionally, the HFD-NCol-ckd had significantly higher plasma insulin concentrations during the OGTT at 20 and 30 minutes, when compared to the HFD. During the ITTs, there were no significant differences between the blood glucose concentrations of the different groups. Western blot analysis showed the HFD-NCol-ckd group had significantly higher amounts of Akt in the soleus muscle; but there was no change in the phosphorylation of Akt at Ser 473. Also, the AMPKα protein levels and AMPKβ phosphorylation at Ser 108 were not altered by diet supplementation. Conclusions Supplementing high fat diets with pea seed coats improved glucose homeostasis in diabetic rats. Although both pea-supplemented diets showed improved glycemic control, the cooked Canstar seed coats had measurable changes in plasma insulin and Akt protein levels. Considering the Canstar strain has less proanthocyanidins, relative to the Solido strain, it appears that the fibrous husk of the seed coat is likely the beneficial component that improves glycemic control. Future studies are needed to definitively identify the specific factor in pea seed coats that improves glucose homeostasis.
OUTCOMES OF REVISION ROTATOR CUFF REPAIR AFTER A FAILED ACROMIOPLASTY

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BACKGROUND: Shoulder impingement is one of the most common disorders affecting the upper limb. Its symptoms include pain, decreased range of motion and weakness. Acromioplasty is defined as shaving off the anterior hook of the acromion to relieve pressure on the rotator cuff during movement. The literature is unclear as to whether acromioplasty alone is sufficient for treatment of rotator cuff tears (RCT). Many patients who failed treatment with an acromioplasty are often identified as having a RCT. A RCT can be treated with an arthroscopic rotator cuff repair (RCR). Historically, the outcomes of primary RCR have been good compared to revision RCR. OBJECTIVE The aim of this study is to look at the outcomes of arthroscopic RCR after a failed acromioplasty for partial and small, full-thickness rotator cuff tears. Our hypothesis is that patients who had an arthroscopic rotator cuff repair after a failed acromioplasty will have improvement in pain levels and functional status compared to preoperative levels. We believe this revision surgery will produce outcomes consistent with primary rotator cuff repair surgery. METHODS A total of 18 consecutive patients were included in this study. Demographic information as well as dates of surgeries, pre- and postoperative range of motion, strength, pain levels, and functional assessments were collected from the patients’ charts. RESULTS We found statistically significant (p<.001) improvements from preoperation values in all of the measured shoulder outcome scores: Simple Shoulder Test, 4.41 to 9.00; UCLA Score, 14.69 to 27.17; Constant Score, 43.31 to 69.10; American Shoulder and Elbow Score (ASES), 40.63 to 72.84; and Pain Visual Analog Scale (VAS), 5.83 to 2.10. CONCLUSION Arthroscopic rotator cuff repair after a failed acromioplasty does produce statistically significant improvements in functional status and pain levels compared to preoperative levels. However, these gains are not as great as those reported for primary rotator cuff repairs.
Poster 13

CLINICAL FEATURES OF PATIENTS WITH RECURRENT INVASIVE STREPTOCOCCUS PNEUMONIAE DISEASE

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Background: Invasive Streptococcus pneumoniae (pneumococcal) disease (IPD), including pneumonia and meningitis, carries a high risk of death, about 15% in pneumonia and 40% in meningitis. The occurrence of two or more IPD (recurrent) in the same individual is unusual and raises the key question of whether these individuals possess risk factors that increase their likelihood of recurrent IPD. We investigated the clinical features among a group of individuals with recurrent IPD to examine this question. Methods: Between 1981 and 2010, we identified 27 patients with recurrent IPD during inpatient surveillance of IPD in Huntington. We isolated pneumococci from otherwise sterile sites, serotyped them by capsular swelling and determined their MIC to penicillin by E-strip. Clinical data were abstracted from hospital charts. The Marshall University IRB approved this research. Results: Of the 27 patients with recurrent IPD, 16 (59%) were 65 years of age and older at the first IPD, males predominated (67%), two-thirds had pneumonia and 21 (78%) had the same clinical diagnosis at both IPD. Four (80%) of 5 patients with the same serotype experienced their second IPD within 12 months (p=0.047), unlike patients with different serotypes at each IPD. Seventy-seven percent of serotypes were PPV23 vaccine types, occurring as often in the first IPD as the 2nd IPD, as did penicillin resistant (I/R) serotypes. Three (60%) of 5 patients who died had I/R strains (p=0.29). Four (36%) of all 11 patients with multiple myeloma in the entire IPD database acquired a 2nd IPD and one had a 3rd IPD and 8 patients had cancer or lymphoma. Discussion: Recurrent IPD, an infrequent event, occurs mainly in persons 65 years of age and older, caused by penicillin sensitive PPV23 vaccine serotypes, mostly as pneumonia, less often as meningitis, with multiple myeloma and cancer/lymphoma representing unique risk factors.

Poster 14

ASTHMA TEMPORAL VENTILATION MAPS FROM HYPERPOLARIZED 3HE MAGNETIC RESONANCE IMAGING

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Introduction: Asthma is a chronic inflammatory pulmonary disease characterized by acute intermittent attacks of airflow obstruction. Airflow obstruction in asthma occurs heterogeneously in distal airways and is caused by inflammation, smooth muscle constriction and airway remodeling. Despite our expanding knowledge of the pathophysiology of asthma, current pulmonary function tests measure global respiratory function, which cannot identify diseased lung regions from healthy ones. Hyperpolarized 3He magnetic resonance imaging (3He MRI) has emerged as a method that provides high temporal and spatial visualization of anatomical and functional changes associated with asthma. Here we describe the development of 3D temporal ventilation maps of the lung for asthma subjects that provide a way to visualize lung function in a single 3D volume allowing for clinical and therapeutic guidance of asthma therapy. Materials and Methods: Seven subjects with exercise-induced asthma were evaluated using 3He MRI (General Electric Health Care, Durham, NC), spirometry and plethysmography on three occasions, each within 7 ± 2 days. Four of these subjects were evaluated again at a fourth visit 770 ± 145 days later before and after methacholine challenge. For all subjects, 3D temporal ventilation maps were generated based on three visits using rigid registration and k-means cluster analysis. Results from k-means cluster analysis were also compared to manual segmentation to verify validity (Pearson correlation coefficient). For subjects who returned for a fourth visit, temporal ventilation maps were compared to 3He MRI scans before and after methacholine challenge to evaluate correlations (Pearson correlation coefficient). Results: K-means cluster analysis was well correlated with manual segmentation (p<0.001) and 3D temporal ventilation maps were able to identify lung regions consistently hypoventilated (7.6 ± 4.6%) and variably hypoventilated (2.9 ± 1.0%). These maps were predictive of lung regions prone to exacerbation after methacholine challenge (p<0.01). Conclusion: Pulmonary ventilation maps can be generated from hyperpolarized 3He MR ventilation images for asthmatic subjects across multiple visits reflecting temporal changes or persistence of ventilation defects over time. These maps provide a way to identify regions of the lung that are consistently hypoventilated in individual asthma patients and may be used to guide targeted treatment of diseased airways in asthma.
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AUGMENTATION OF CLOPIDOGREL EFFECTS BY CHOCOLATE  
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BACKGROUND: Chocolate have been proved to increase the effects of aspirin but the role of chocolate on the anti-platelet effects of clopidogrel has not been determined. AIM: With this study we aim to establish the augmenting effects of flavonoid rich food (chocolate) on the anti-platelets effects of clopidogrel. MATERIALS AND METHODS: A Quasi-experiment, consisting of 65 healthy adult volunteers selected through non-probability convenient sampling, was carried out in Karachi Medical and Dental College & Dow University of Health Sciences Karachi. Study design was approved by the colleges “Research and Ethical Board” and all the volunteers gave written informed consent prior to participation in the study. Those included in the study were healthy, non-smoking, not taking hormonal and Vitamin supplements. Subjects were divided into two groups Group 1 (consuming 75 mgs of oral clopidogrel), Group 2 (consuming 75 mgs of oral clopidogrel followed by consumption of chocolate after 24 hrs). Bleeding time was set as a measurement of anti-platelet effects and its measurements of all the groups were carried before and after the experiment utilizing Duke Method. Data analysis was carried out by using SPSS version 17.0. RESULTS: The pre-test bleeding time comparison showed a bleeding time of 45.97±11.47 seconds for group 1 and 64.41±28.73 seconds for group 2 (p = 0.30). A bivariate analysis was done by comparing the means of both the pre-test groups through independent t-test followed by a regression analysis. Bivariate analysis compared both the control and interventional groups. After comparing pre-test groups bleeding time we obtained a p-value of 0.30 and after comparing post test groups we obtained a bleeding time of 68.23±12.14 seconds for group 1, while for the group 2 the bleeding time was 124.85±44.73 seconds (p=0.01). Multiple regression analysis was also done for which multivariate regression models were used. In the regression models among the constant variables, sex, age, acute and systemic infections were used and for dependent variable, bleeding time for both the control and intervention were used. The model summary for the multivariate regression analysis reached an R-square of 0.467. CONCLUSION: Among the subjects who consumed clopidogrel & chocolate there was a significant increase in bleeding time compared to those who consumed clopidogrel only.

Poster 17  
PROGRESSION OF PRIMARY GEOGRAPHIC ATROPHY (GA) IN AGE-RELATED MACULAR DEGENERATION (AMD)  
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Background: Age-related macular degeneration (AMD) is the most common cause of irreversible blindness in industrialized countries. The end stages of AMD are choroidal neovascularization (CNV) and geographic atrophy (GA). Objective: This project examines GA progression using autofluorescence (AF) and infrared (IR) imaging. We hypothesize that initial GA size and patterns of GA influence progression rate. Methods: We retrospectively identified 36 subjects (52 eyes) with a diagnosis of primary GA who had ≥2 examinations with AF or IR imaging and were followed for ≥6 months. We classified baseline GA into two patterns: unilobular (one lesion) and multilobular (two or more lesions). Areas of atrophy and progression rates were calculated using custom interactive software. Results: The mean duration of follow up was 26.3 months (range 6 - 51 months). At baseline, 5 eyes (9.6%) had unilobular GA, and 47 eyes (90.4%) had multilobular GA. The mean GA size at baseline was 3.47 mm². The mean growth rate overall was 1.08 mm²/yr, and it was statistically significantly different between the unilobular (0.39 mm²/yr) and multilobular groups (1.17 mm²/yr, p<0.001). With respect to initial GA size, the lower 50th percentile had a lower progression rate than the upper 50th percentile (0.88 mm²/yr vs 1.44 mm²/yr, p=0.003). Age and gender did not influence GA progression. Conclusions: This study shows that multilobular GA represents the majority of primary GA cases, and it offers prognostic estimation of GA growth based on initial lesion size and pattern. Limitations include retrospective study design and small size of serial data.
Background: High-frequency neuronal activity (30-100Hz) contributes to several normal functions, including filtering input, and encoding and retrieving memory. High-frequency activity also occurs under pathological conditions (e.g. seizures). While the basic mechanisms underlying action potential generation are well known, the consequences of high-frequency activation on action potential generation have received relatively little experimental attention. In this study, we examined how activity at frequencies up to 100Hz affects the function of pyramidal neuron axons in the hippocampus, an area of the brain essential for normal memory function. Objective: To determine how high-frequency stimulation (HFS) affects action potential conduction in the Schaffer collateral axons of pyramidal neurons in area CA3 of the hippocampus. Methods: Sprague-Dawley rats were humanely euthanized, the brain rapidly removed, and horizontal slices of the hippocampus prepared. A stimulating electrode was placed in stratum radiatum at the CA3/CA1 border to activate Schaffer collateral axons. Whole cell patch clamp recordings were obtained from individual CA3 neurons, and antidromic action potentials were recorded in response to low-frequency stimulation (≤1Hz) and sustained (1.6s) HFS of Schaffer collateral axons. To ensure action potentials were not evoked by synaptic transmission, glutamate and GABA receptors were blocked by DNQX, D-AP5/MK801, bicuculline, and CGP-55845. Results: Action potential amplitude and latency were stable during low-frequency stimulation, but changed dramatically during sustained HFS. Amplitudes averaged 103.6 ± 3.0mV (mean ± 1 SEM) at the beginning of HFS, but decreased to 61.8 ± 7.7mV by the end of HFS. This decrease in amplitude reflected a combination of reduced spike height along with increased probability of complete action potential failure, which occurred on >90% of trials at the end of HFS. In addition to decreased amplitude, conduction latency increased by 0.51 ± 0.15ms, indicating decreased conduction velocity.
Poster 24
IMPACT OF RESTRICTED FLUID THERAPY ON THE PHYSIOLOGICAL CONDITION OF NEWBORNS DURING CESAREAN SECTIONS
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BACKGROUND: Currently, between 20 and 48 ml/kg of LR is administrated for an uncomplicated C-Section performed under spinal anesthesia. Studies have shown that fluid restriction, rather than the current “standard” fluid regimen, improves clinical outcome after intra-abdominal surgery. In this study we are evaluating the impact of different volumes of intraoperative fluid therapy to mother during the C-Section on the physiological conditions of newborns. OBJECTIVE: We hypothesize that restricting IV fluid for mothers during C-Sections will not adversely affect the physiological condition of newborns. METHODS: Patients scheduled for a C-Section are randomly assigned to one of two treatment groups, a restricted fluid group (RFV) and a standard fluid group (SFV). These groups are treated with two levels of fluid therapy with LR: 10 ml/kg (n=35) and 35 ml/kg (n=27). LR is administrated at a constant rate to patients over a period of 70min. Newborn APGAR scores, and both venous and arterial blood gas reports are collected for analytical comparison. RESULTS: The APGAR scores for RFV and SFV groups are 7.97± 0.23 vs 7.96 ± 0.27 at 1 minute and 8.97 ± 0.03 vs 8.88 ± 0.09 at 5 minutes, respectively. The profiles of umbilical cord blood pH and acid-base balance of both cord venous and arterial blood gases from RFV and SFV groups are comparable to each other without significant difference. The pHs of venous blood are 7.30 ± 0.05 vs 7.31 ± 0.06 in RFV vs SFV groups, respectively. DISCUSSION: The impact of restricted fluid infusion to mothers during C-Sections on newborns general condition is analyzed by APGAR scores at 1 and 5 min. The APGAR scores in our study from both treatment groups are almost identical, which suggests that restricted fluid therapy during C-Sections has no detrimental effects on the newborn's physical condition after delivery. Comparison of cord blood gases and pH show that restricted fluid therapy during C-Sections does not compromise fetal perfusion and general physiologic status. This study shows that there are no detrimental effects of restricted fluid infusion to the mother on newborns. We also understand that giving the mother different volumes of fluid for only 30-40 minutes may not be long enough to have an impact on the fetus. On the other hand, while studying the beneficial effects of restricted fluid infusion for the mother, we are pleased to find that it is safe to continue this study without a negative impact on the fetus or newborn.

Poster 25
PRALATREXATE SELECTIVELY INDUCES APOPTOSIS AND SYNERGIZES WITH BEXAROTENE THROUGH UP-REGULATION OF P53/BAX/PUMA IN CUTANEOUS T-CELL LYMPHOMA CELLS
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Background: Pralatrexate (PDX), a targeted antifolate, was designed for preferential uptake and accumulation in tumor cells based on its high affinity for reduced folate carrier-1 and efficient polyglutamation by folypolyglutamyl synthetase. PDX is approved by the FDA for relapsed or refractory peripheral T-cell lymphoma, and clinical studies are ongoing in cutaneous T-cell lymphoma (CTCL). Bexarotene (BEX) is an RXR-selective retinoid approved for treatment of CTCL. Objective: Here we investigated the therapeutic mechanisms of PDX and whether PDX combined with BEX has synergistic anti-tumor effects in CTCL. Methods: Cell viability was examined by MTS assay, apoptosis by FACS analysis, and expression of apoptosis-associated proteins by Western blotting. Results: PDX (1-5 nM for 24 and 48 hrs) decreased cell viability and induced apoptosis in a time- and dose-dependent manner in 4 CTCL cell lines (MJ, Hut78, HH, and HH/VOR). PDX (1-5 nM for 48 hrs) also caused significantly more apoptosis of CD4+ T cells from 4 Sézary Syndrome (SS) patients with high percentages (74-96%) of circulating CD4+CD26- T cells compared to CD4+ T cells from 3 healthy donors (p < 0.05). Moreover, PDX at a low dose (2 nM) combined with BEX (10 μM) induced up to 12-fold increase in apoptosis compared to either drug alone in all 4 CTCL cell lines and in a SS patient’s CD4+ T cells. Additionally, PDX combined with BEX synergistically increased the tumor suppressor p53, and the p53-regulated pro-apoptosis proteins, Bax and PUMA. Conclusions: In conclusion, our results show that PDX at low nanomolar concentrations selectively induces apoptosis in CTCL cell lines and SS patients’ CD4+ T cells, and PDX combined with BEX exerts a synergistic pro-apoptosis effect through up-regulation of p53/Bax/PUMA in CTCL. These findings support the ongoing phase 1 clinical trial of PDX/BEX and provide the rationale for future studies of this combination in CTCL patients.
OBJECTIVE: Both, obesity and preeclampsia, are associated with long term cardiovascular morbidity. We hypothesize that this effect is the result of altered vascular dysfunction. Our objective was to determine vascular function 6 months after delivery in mice with prepregnancy obesity and/or preeclampsia-like syndrome induced by over-expression of sFlt-1. STUDY DESIGN: CD-1 female mice were placed on either standard fat (SF) or high fat diet (HF) for 3 months before they were mated. On day 8 of pregnancy, mice in both groups were injected with either adenovirus carrying sFlt1 (HF sFlt1 n=6, SF sFlt1 n=4) or adenovirus carrying mFc as virus control (HF mFc n=4, SF mFc n=7). Following the weaning, all dams were placed on standard fat diet. Six months after delivery, the animals were sacrificed and their right carotid arteries were extracted for in vitro contractility experiments. Responses to single doses of potassium chloride (KCL, 60 mmol/l), phenylephrine (PE, 10-4 M) and acetylcholine (Ach 10-5 M, after precontraction with PE) were obtained. One-way ANOVA with appropriate post-hoc tests were used (significance: P<0.05). RESULTS: Contractile responses to KCL were significantly increased in the HF sFlt1 group compared to the other three groups (figure). Addition of PE induced significantly higher responses in HF groups compared with SF dams with no differences within HF and SF diets groups. Relaxation to acetylcholine was lowest in both HF groups, followed by SF sFlt1 group, but the differences were not statistically significant. CONCLUSION: Prepregnancy obesity and sFlt1-induced preeclampsia result in long-term impairment of vascular function, with the combination having the biggest effect.

Poster 27
THE ROLE OF KIF3A IN PROSTATE CANCER PROGRESSION AND METASTASIS
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Background: Kif3a is part of the motor protein complex forming the kinesin motor family. Along with Kif3b and Kap3, Kif3a is required for the function of primary cilia. Recently, it is this role in ciliogenesis that has been associated with cancer progression. However, the role of Kif3a in cancer development independent of ciliogenesis is still largely unknown. Objective: Here, we show that Kif3a is expressed in the epithelium of prostatic tissue. We try to elucidate its role in prostate cancer cell growth and oncogenesis. Methods: All cell lines were obtained from American Type Culture Collection (ATCC). Primary tumor samples were obtained from the Louisiana Cancer Research Consortium (LCRC). Infection of cells was done via a Lentiviral packaging system using the pPACKH1-XL Packaging Mix (System Biosciences: Mountain View, CA) and FuGENE Transfection Reagent (Roche, Indianapolis IN) using pLKO and pCDH vectors. Immunohistochemical studies were done using the PR483 tissue array (US Biomax; Rockville, MD). Western blot and immunohistochemical analysis were done with Kif3a primary antibody (Sigma; St. Louis, MO). An MTT assay (Sigma, St. Louis, MO) was used for cell proliferation studies. Results: In cell line analysis, levels of Kif3a are higher in 100% of prostate cancer cell lines compared to normal prostate cell lines. Furthermore, 4/5 prostate tumor samples showed higher expression of Kif3a than their matched normal samples shown by western blot. These findings suggest that Kif3a elevation is associated with prostate cancer. In an effort to elucidate this role, we reduced the level of Kif3a in LNCaP prostate cancer cell line with shRNA specifically against Kif3a. In these cells, growth rate was greatly inhibited as evidenced by a high level of cell death. Moreover, we ectopically expressed Kif3a in the normal prostate epithelial cell line, BPH1. We found that overexpression of Kif3a in this cell line enhanced the cell growth rate. Conclusions: Our results suggest that Kif3a may play an important role in prostate cancer cell proliferation and tumorigenesis.
CROSSTALK BETWEEN PKA AND EPAC REGULATES THE PHENOTYPIC MATURATION AND FUNCTION OF HUMAN DENDRITIC CELLS
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The cAMP-dependent signaling pathways involved in dendritic cell (DC) maturation not been defined in detail. While cAMP was previously thought to signal exclusively through PKA, it is now clear that cAMP also activates Epac, a second major cAMP effector. Whether cAMP signaling via PKA is sufficient to drive DC maturation or whether Epac plays a role has not been examined. We used cAMP analogs to selectively activate PKA (analog 6-8nz-cAMP) or Epac (analog O-Me-cAMP) in human monocyte-derived DCs and examined the effect of these signaling pathways on several hallmarks of DC maturation. We show that PKA activation induced DC maturation as evident by the increased cell surface expression of MHC class II, co-stimulatory molecules and the maturation marker CD83. We further show that PKA activation enhances DC activation of allogeneic T cells. In contrast to the stimulatory effects of PKA, Epac signaling had no effect on DC maturation or function. Rather, Epac suppresses the effects of PKA when both pathways are activated simultaneously. These data reveal a previously unrecognized crosstalk between the PKA and Epac signaling pathways in DCs and raise the possibility that therapeutics targeting PKA may generate immunogenic DCs while those that activate Epac may produce tolerogenic DCs capable of attenuating allergic or autoimmune disease.

ANGIOTENSIN II DECREASES ANGIOTENSIN CONVERTING ENZYME 2 LEVELS BY INCREASING THE ACTIVITY OF TNF(ALPHA)-CONVERTING ENZYME IN THE HEART
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Background: Angiotensin converting enzyme (ACE) 2 is a key negative regulator of the renin-angiotensin system where it metabolizes angiotensin (Ang) II into Ang 1-7, an endogenous antagonist of Ang II. Loss of ACE2 is detrimental to heart diseases as it leads to impaired contractility. We have previously shown that while Ang II upregulates cardiac ACE2 mRNA, it reduces ACE2 protein levels, possibly due to TNF(alpha)-converting enzyme (TACE) mediated proteolytic cleavage of the ACE2 ectodomain. This reduction of ACE2 is in fact associated with ventricular hypertrophy and a phenotype resembling heart failure. As well, recent findings revealed that Ang II regulates TACE activity via differential cellular compartmentalization, positing a mechanism for Ang II induced downregulation of ACE2 protein. Hypothesis: We postulate that Ang II suppresses ACE2 by increasing TACE activity and ACE2 cleavage, thereby exacerbating Ang II’s harmful effects via positive feedback. Methods: We used cardiomyocytes isolated from adult wildtype (WT) and TIMP3 knockout (TIMP3KO) mice as TIMP3 is the endogenous inhibitor of TACE. Cells were treated with Ang II (10μM) alone, or with one of two TACE inhibitors, TAPI-1 (10μM) or GW280264X (10μM), for 2 or 24hrs. ACE2 protein and mRNA were assessed using Western blotting and real-time PCR respectively. TACE activity was measured using a specific fluorogenic assay. Results: Shedding of ACE2 was increased 1.8-folds in WT cells and 1.4-folds in TIMP3KO cells after 2hrs of Ang II treatment, which was blocked by pre-treatment with TAPI-1. TIMP3KO cells showed a 2-fold increase after 24hrs, but WT cells reverted to baseline levels in all treatment groups. TACE activity was reduced by half only by TAPI pre-treatment after 2hrs and was unchanged after 24hrs in WT myocytes; whereas, Ang II elevated TACE activity 1.3-folds in TIMP3KO cells, which was reversed by TAPI-1 pre-treatment, at both time points. Conclusion: Our data illustrate that Ang II induces ACE2 shedding by promoting TACE activity. Loss of TIMP3 and resultant loss of TACE inhibition reduce cellular resistance to this effect. This supports the idea of positive feedback where Ang II degrades its negative regulator ACE2. Since heart failure is associated with high Ang II levels and ACE2 downregulation, our data may explain the disease progression. To pursue this, further studies will be conducted to examine Ang II, TACE, and ACE2 levels in plasma samples of patients with heart failure.
MOLECULAR MECHANISMS CONTROLLING GLIOBLASTOMA TUMOR GROWTH AND SURVIVAL

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Glioblastoma multiforme (GBM) is the most common type of malignant primary brain tumor. GBMs are characterized by a rapid cell growth and relentless invasion of the Central Nervous System (CNS). They develop from glial cells in the CNS and are extremely resistant to anticancer regimens. Nearly 12,000 people are diagnosed with GBM annually in the U.S. and all diagnosed patients die within 3 years. One of the possible mechanisms which make Glioblastoma cells resistant to treatment is their exceptional ability to escape apoptosis. Our group hypothesized that these cells can survive the treatment by withdrawing from the cell cycle, entering autophagy. After the treatment is completed, we believe that the surviving tumor cells can reenter the cell cycle and thrive. Our research is aimed to determine if Glioblastoma cells are, in fact, utilizing autophagy to escape the treatment and if conventional anticancer regimens could benefit from supplemental agents known to inhibit autophagy. In our experiments, cisplatin (DNA damaging agent), fenofibrate (glycolysis inhibitor) and chloroquine (autophagy inhibitor) were used to determine if human Glioblastoma cell line, LN-229, can be sensitized to the anticancer agents when the treatment is accompanied by the inhibition of autophagy. The effectiveness of autophagy inhibition was documented by detecting accumulation of LC3-positive autophagosomes by Western blot and immunocytofluorescence; and flowcytometry was used to evaluate cell cycle distribution and apoptotic cell death in Glioblastoma cultures treated with the combination of cisplatin, fenofibrate and chloroquine. Our results show that the cisplatin treatment resulted in G2/M cell cycle arrest accompanied by a low level of apoptotic cell death (1%). In a similar manner, fenofibrate treatment resulted in G1 cell cycle arrest predomination and very low levels of apoptosis (3%). Importantly, we have observed over 25% of apoptotic cells with cisplatin/chloroquine treatment, and 35% of apoptotic cells with fenofibrate/chloroquine treatment. In summary, these experiments have shown positive results in sensitizing Glioblastoma cells to other treatments. Chloroquine was shown to effectively inhibit autophagy, while follow-up treatment with fenofibrate or cisplatin increased the amount of apoptotic cells. These promising results will be followed up to further determine the effect of this combined treatment in sensitizing Glioblastoma to current treatments.

ATTENTIONAL TASK

TEST-RETEST RELIABILITY OF FMRI SIGNALS DURING AN INTEGRATED EMOTIONAL-ATTENTIONAL TASK

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Functional MRI (fMRI) is now frequently used to assess how brain activity patterns change with development, progression of neuropsychiatric disorders, and pharmacological treatments. In order to interpret changes in imaging signals with targeted interventions, it is necessary to establish the long-term test-retest reliability of blood oxygenation level dependent (BOLD) signals. The aim of the present study was to determine which brain regions elicited highly reliable activation to attentional and emotional stimuli between fMRI scanning sessions performed by the same subjects over 3 visits spaced approximately four months apart. 59 subjects healthy subjects were recruited for the initial scan, 39 participated in the second scan, and 31 subjects participated in the third scan. All subjects were physically and neurologically healthy. After providing written informed consent, all subjects participated in all fMRI sessions on a 4.0 T Varian Unity INOVA MRI/MRS system while performing an integrated visual oddball task, termed the Continuous Performance Test with Emotional and Neutral Distracters (CPT-END). Visual cues consisted of 70% colored squares, 10% colored circles, 10% emotionally neutral pictures, and 10% emotionally unpleasant pictures. fMRI analysis included motion correction, normalization, conversion to percent signal change, and event-related modeling for responses to circles, emotional pictures, and neutral pictures in AFNI (http://afni.nimh.nih.gov/). Test re-test reliability was assessed using intraclass correlation (ICC) which assesses within-subject reliability. There were no significant differences on any performance measure on the CPT-END task between the three scanning sessions. A number of brain regions were reliability (ICC(2,1)>0.5) activated between scan sessions in response to the three events of interest. While attentional stimuli (circles) reliably activated the precuneus and middle temporal gyrus, distracter images elicited a wider network of activation including the middle frontal gyrus, precuneus, and lingual gyrus. In conclusion, this study suggests that the BOLD signal effects for the CPT-END related to the dissociation of attentional and emotional functions in the prefrontal and parietal cortices show high test-retest reliability over a period of eight months. These results suggest that the CPT-END is a stable fMRI paradigm that can be used for the long-term investigation of changes due to psychiatric and neurological diseases.
Poster 33
INTEGRATIVE GENOMIC, GENETIC, AND EPigenetic APPROACHES TO THE ANALYSIS OF GENES AND PATHWAYS RESPONSIBLE FOR THE DEVELOPMENT OF SEXUALLY DIMORPHIC EXTERNAL GENITALIA
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Androgens are responsible for the development of male genitalia during embryogenesis. Malfunction of androgen receptors (AR), as seen in androgen insensitivity syndrome (AIS), can result in female external genitalia despite normal XY karyotype. The aim of this study was to identify AR genomic targets that may be implicated in penile development. We hypothesized that genes which are syn-expressed with AR in male genitalia and also exhibit nearby AR binding sites (ChIP-seq analyses) can be implicated in development of male external genitalia. Using the Human Body Map (GEO: GSE7307), we identified 74 genes exhibiting robust expression and syn-expression with AR in the male reproductive tract. These 74 probe sets were cross-referenced with AR ChIP-seq data from androgen-dependent prostate cancer cells (LNCaP; Myles Brown laboratory) to identify genes with androgen response elements (ARE). Twelve AR-binding sequences were identified from this data set and were confirmed to contain ARE motifs by Multiple EM for Motif Elicitation (MEME). Through functional enrichment of this gene set, TBX3 surfaced as a strong candidate for AR interaction. For further analysis, we microdissected and performed microarray gene expression analysis on eight e14 murine genital tubercles (4 female, 4 male). This microarray analysis was combined with TBX3 ChIP-seq data from murine induced pluripotent stem cells (Bing Lim laboratory) to investigate TBX3 genomic targets and their possible roles in dimorphic genital development. We were able to identify 555 genes that are both bound by TBX3 and dimorphically expressed in male vs. female murine genital tubercles (GT) by embryonic day 14. Of these 555 genes, 349 were found to be downregulated 2-fold in the male GT. Further analysis highlighted that many of these 349 genes have pro-apoptotic and transcriptional repressor activities. The remaining 206 genes were upregulated 2-fold in male GT, and have been implicated in anti-apoptotic activities. In conclusion, our analysis has suggested that TBX3 may be transcriptionally regulated by ligand-bound androgen receptor. Our data and analysis also suggests that TBX3 downregulates pro-apoptotic genes and transcriptional repressors in developing male external genitalia. In the absence of TBX3, these genes are upregulated, which may lead to the regression of the genital tubercle during formation of female external genitalia.

Poster 34
EPIDEMIOLOGY AND SURGICAL RESECTION OF ATRIAL MYXOMAS: EXPERIENCE IN SOUTH ASIAN POPULATION
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Background: Myxomas are the most common benign tumors of the heart. Their presence causes obstruction, valvular damage and can even lead to death which is why prompt surgical resection is of utmost importance. Objective: The aim of this study is to discuss the epidemiology of myxoma, its surgical importance, the various approaches used for myxoma resection and post operative outcomes. Material and Methods: Twenty-four patients who underwent echocardiography were diagnosed with atrial myxomas between the years 2000 and 2006. Their files and surgical notes were obtained and evaluated. SPSS for Windows was used to analyze the data. Results: Out of these twenty-four patients, there were 11 males (45.8%) and 13 females (54.2%). The mean age of diagnosis was 32.7 years, the median being 38 years and the mode stood at 14 years. Twenty-one (87.5%) of the myxomas were located in the left atrium and three (12.5%) in the right atrium, no ventricular myxomas were observed. Twenty-three of these patients underwent myxomectomy and one died prior to surgery. Conclusion: Pedunculated myxomas which are gelatinous in nature were the more common type. Surgical resection is definitive treatment. Myxomectomy should be employed as soon as possible to prevent embolism, valvular injury and even mortality. Non resection of the tumor margins did not increase chances of tumor recurrence and most importantly we concluded that myxoma resection had low surgical mortality and an excellent prognosis.
Genomics of Isolated Congenital Heart Disease: Using Pecoenpi to Identify Putative Developmental Regulators of Cardiac Genes.

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Congenital heart defects (CHD) are the most common human birth defects, affecting up to 1 out of every 100 births. Defects are seen as a component of multiple syndromes as well as in isolation. The molecular etiologies of many syndromic forms have been elucidated. Logically, if a gene harbors a mutation, it will be present in all cells of the body, thus affecting all tissues in which that gene is expressed resulting in a syndromic phenotype. The genetic etiology of the more common isolated forms of CHDs has remained much more elusive. We hypothesized that mutations in regulators (that “switch-on/off” genes in a temporal-spatial fashion) of syndromic cardiac genes will be responsible for isolated CHDs when disrupted. DNA from probands with CHDs was genotyped with SNP arrays, raw data analyzed with BeadStudio, copy number variations (CNV) identified with PennCNV software, PECONPI software was used to rank these deletions according to pathogenicity parameters including: increased non-coding sequence conservation across species, within 1 Mb of a known/putative syndromic heart gene and decreased overlap with literature or control CNVs. Out of 408 probands, 3878 total CNV deletions were identified. Of these, 156 novel CNV deletions encompassed a conserved non-coding element (CNE) and 30 encompassed a CNE and were also within 1 Mb of a CHD gene (novel CNVs contained no control or literature overlap). A small CNV upstream of Transforming Growth Factor Alpha (TGFα) was identified in 7 probands with ventricular outflow tract anomalies (4 with transposition of the great arteries (TGA)). The CNV encompasses a CNE, with no control or literature overlap. Further studies performed in the mouse demonstrate this element's ability to drive expression of a trans gene in the heart. The data to date suggests that deletion of this regulatory CNE is a potential cause of the CHDs in these probands. Further work is needed to identify the gene(s) regulated by this CNE and to fully elucidate the role that it plays in heart development. This suite of analytic software, using CNV deletions to localize CNEs that regulate cardiac genes, could be used to find genotype-phenotype correlations between other enhancers and correlated CHDs, as well as applied to other diagnoses.

Impact of Preventive Health Measures on Men Having Sex with Men (MSM).

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Background: First case of HIV in Pakistan was identified in the year 1988. Data from the national AIDS control program indicates that HIV/AIDS cases have been increasing over the past decade. Among other risk factors, males having sex with males (MSM) has also been identified. Recent study in Karachi showed prevalence of HIV among Intravenous drug users was 23% and 4% among male sex workers MSWs were HIV positive. Unprotected commercial sex activity with men and women was high. Objective: To assess the impact of preventive health measures taken on men having sex with men (MSM). Materials & Method: This is a prospective study conducted in Karachi, Pakistan from period of April 2009 to September 2010. First 50 male homosexuals encountered and who gave consent to participate were included in the study. Target population was first identified through pre mapping of their location. Informed consent was taken from each individual. VDRL and HIV antibody tests were conducted once at the beginning of intervention and after one year. Other activities were also done twice with the interval of one year in between, they included raising awareness, education, behavior change communication, provision of Primary Health Care and syndromic management of STIs, provision of condom and water based lubricants and referral for other related services including anti retro viral therapy. SPSS 12.0 is used to carry out the Statistical analyses. Results: Knowledge regarding STIs/HIV was improved from 20% to 53%, behavior 9% to 37%, communication skills 13% to 51% and provision of syndromic management of STIs 4% to 48%. Practice of Condom use increased from 23% to 72%. For better understanding and in bringing positive response towards sexual practice interpersonal communication was of great importance. Conclusion: Significant reduction in the rate of STIs among homosexual males noted along with all other factors. Implementation of well structured models regarding prevention of STIs/HIV especially in high risk groups is needed.
EUTHANASIA: PERCEPTIONS AND ETHICAL CONSIDERATIONS OF DOCTORS IN PAKISTAN.
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BACKGROUND: The present era has witnessed tremendous improvement in palliative care which has intensified the debate of euthanasia. Being Islamic republic, its practice is not legalized here but it is the necessity of time that the perspective of doctors in Pakistan should be evaluated. OBJECTIVE: The purpose of this study is to know the perception and the ethical concerns of doctors towards euthanasia in Pakistan. METHODS: It was a cross-sectional study conducted from August 2008 to February 2009 in three major government hospitals of Karachi. Ethical review board approval was taken prior to the commencement of the study and only those doctors who consented to participate were interviewed through a pre tested interviewer administered questionnaire. To carry out data entry and statistical analysis SPSS-12.0 was used. RESULTS: Out of 248 doctors approached 153 consented to participate in the study. The male to female ratio was 90:63 and the mean age was 30.90 with ± 6.580. It was quite interesting that only 89 doctors knew about euthanasia therefore the remaining results were out of them: Regarding different types of euthanasia used 69.66% of the respondents were aware of voluntary euthanasia. Law of Pakistan about the euthanasia was known to 53.93%. About the ethical considerations only 25.84% of the doctors believed that it is ethical to practice euthanasia on a patient. During practice 22% of doctors were encountered in a situation where their opinion was taken about the practice of euthanasia and 60% of them had advised it. CONCLUSION: It is quite astonishing that more than a third of the doctors in Pakistan did not even know about euthanasia and only one fourth of those who knew about it believed that it is ethical to practice. However, since it is an important issue in the care of terminally ill patients, our health professionals are in favor of further research of this controversial, yet debatable issue for the benefit of our society.

SACCADIC EYE MOVEMENT TASKS ASSES CNS DYSFUNCTION IN CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS
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The central nervous system (CNS) dysfunction resulting from prenatal alcohol exposure is the most debilitating aspect of fetal alcohol spectrum disorders (FASDs). Affected children exhibit numerous cognitive and behavioral deficits, which often contribute to the development of secondary disabilities that include difficulty in school, drug and alcohol addiction, and trouble with the law. Early and accurate diagnosis of an FASD is an important protective factor against the development of these secondary disabilities, and therefore for improving quality of life. The complex nature of this disorder, and the lack of specially trained physicians, creates a need for novel objective screening tools in order to assess CNS dysfunction in the FASD population. As saccadic eye movement behaviors reflect the integrity of multiple brain structures, a battery of oculomotor tasks may serve this function. This study sought to test the hypothesis that oculomotor performance in FASD would differ from typically developing children. A cohort of 31 children with FASDs, and 31 age- and sex-matched controls completed prosaccade, antisaccade, and delayed memory-guided sequential (DMS) tasks. Compared to controls, children with FASDs elicited increased direction and anticipatory errors in the antisaccade task, and increased timing and sequence errors in the DMS task. The FASD group also exhibited an increase in the error of saccade trajectories in the pro- and antisaccade tasks. This study indicates that frontostriatal and cerebellar dysfunction may be assessed in children with FASDs using a battery of eye movement tasks. These findings suggest that select eye movement tasks may be useful to identify CNS dysfunction in the FASD population, and could therefore be incorporated as a screening tool to improve the diagnostic process. Future studies will aim to expand group size, and to compare oculomotor performance of the FASD population to that of other neurodevelopmental disorders with similar clinical presentations.
The PTEN-/-, P53-/- mouse model of prostate cancer holds promise as a model of metastatic prostate cancer because of the human-like histological characteristics of cell lines derived from this model. Two cell lines derived from the PTEN-/-, P53-/- model, Clone-2 (Cl-2) and the Tamoxifen Clone (TC), were infected with viral vectors that contain constructs which constitutively activate the Ras, WNT (B-catenin), Smoothened and NF-kB (IKBKB) pathways. These four pathways were chosen because they have been found to be overexpressed in metastatic human prostate lines and are thought to play a role in prostate cancer metastasis. The Cl-2 and TC lines were chosen from the model because they show human-like epithelial characteristics histologically and do not display significant extra-pulmonary metastatic activity upon orthotopic injection into the prostate of nu/nu mice. Thus, any metastatic activity induced would be related to transfection with one of the chosen constructs. Intracardiac injections of tumor cells were done with the infected cell lines on nu/nu mice to evaluate for potential to extravasate from the vasculature and survive in a metastatic site. The results of these studies showed a significant increase in mortality in the Cl-2 Ras line. The average survival decreased from 12 weeks in a non-infected Cl-2 line to 4 weeks in the Cl-2 Ras line (p < 0.05). Additionally, mice injected with Cl-2 Ras showed significantly more aggressive tumors on histology and 5/9 of them demonstrated brain metastasis compared to 0/7 from the uninfected line. Further, the B-catenin lines from both the Cl-2 and TC lines both demonstrated 1/5 mice with skull metastases by bioluminescent imaging compared to 0/7 mice in the uninfected Cl-2 and TC lines. This is suggestive of a possible role of B-catenin in bone metastasis. It is clear that the Ras pathway and the WNT pathway are important in extrapulmonary metastasis of prostate cancer in the PTEN-/-, P53-/- model, while the roles of Smoothened and IKBKB are not supported by this study. Ongoing studies include orthotopic prostate injections of the Ras and B-catenin lines in order to evaluate for increased metastatic potential from the primary tissue site and future studies include knockdown studies to further localize downstream pathways essential to metastasis in the Ras and B-catenin lines.

The study of etiological and demographic characteristics of acute household accidental poisoning in children-- A consecutive case control series from Pakistan.

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BACKGROUND: To determine the agents of poisoning and demographic distribution of children brought to Civil Hospital Karachi (CHK) with a history of accidental poison intake and to examine the factors associated with it. METHODS: This hospital based descriptive study of first 100 patients from both sexes who presented to Pediatric department, CHK from 1st January 2006 till 31st December 2008 with exposure to a known poisonous agent and fulfilling other inclusion criteria were included in the study. Data regarding their demographic profile and potential risk factors was collected on a well structured proforma, cases were followed until discharge or expiry. Data was analyzed using frequencies, proportions, group means, median and standard deviations. RESULTS: The male to female ratio in our study was 1.2:1, with kerosene (50%) being the most common household agent followed by medicines (38%), insecticides (7%) and bathroom cleaners (5%). Factors such as mother's education level, number of siblings and storage place of poison correlated significantly with the cases of accidental poisoning. Most of the children (70%) presented within 3 hours of ingestion. Dyspnea was the most common symptom observed. The mortality rate in our study was 3%. CONCLUSIONS: Children belonging to age group 2-3 years are the most susceptible both in terms of morbidity and mortality. Preventive strategies need to be adopted at a national level to spread awareness among parents.
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FROM THE HEART TO THE BRAIN: BRIDGING THE INFLAMMATORY GAP
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Upregulation of the cytokine Tumor Necrosis Factor-α (TNF-α) is a major component of many pathological states including cardiovascular disease, asthma, rheumatoid arthritis, Crohn’s disease, type 2 Diabetes, and neuropsychiatric diseases such as depression. TNF-α signaling induces genes such as ICAM-1 and VCAM-1, which are promoters of inflammation. Therefore, blocking TNF-α pro-inflammatory signaling holds great potential for the development of anti-inflammatory medications. Unfortunately, there are currently no small molecule, bio-available, cost effective treatments for TNF-α induced inflammation available on the market. Dr. Charles Nichols at LSU-HSC has recently discovered that activation of serotonin 5-HT2A receptors by certain hallucinogenic drugs including lysergic acid diethylamide (LSD) potently activate anti-inflammatory pathways to block the effects of TNF-α. The 5-HT2A agonist (R)-2,5-dimethoxy-4-iodoamphetamine [(R)-DOI] blocks TNF-α induced inflammation with an EC50 of 10 picomolar. Work in the lab to date has primarily focused on the repression of inflammation in cardiovascular tissues including rat aortic smooth muscle cells (RASM), vascular endothelial cells, and macrophages. The major goals of my project were to identify more effective markers of inflammation that would translate into the neuroinflammation model, as well as to investigate the effects of our most effective 5-HT2A agonists in this system. For example, ICAM-1 is not a very effective marker for inflammation in neuronally derived C6 glioma cells. This project identified a collection of potential new inflammatory markers to test (MCP-1, CX3CL1, CCL5, and IL-1β), and then designed QRT-PCR to examine respective expression in RASM cells. RASM cells show a marked increase in ICAM-1, CCL-5, CX3CL1, and MCP-1 expression, but no increase in IL-1β expression upon TNF-α induction [10 ng/ml]. Dose response studies indicated DOI provided extremely potent repression of these additional markers, consistent with earlier results. Significantly, the fold increase of CCL5, and MCP-1 markers were 60x and 150,000x respectively, which are much higher than for ICAM, indicating that these may be suitable genes to model in the CNS. Future studies will include examining the effects of (R)-DOI in neuronally related tissues, as well as evaluation of novel drugs for anti-inflammatory activity.

Poster 44
SURVEY ON TOBACCO-CESSATION POLICIES AND PRACTICES (STOPP) AMONG OTOLARYNGOLOGISTS
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Background: Tobacco use is the leading cause of preventable death in the United States, claiming over 435,000 lives annually. There are an estimated 46 million adult smokers in the United States, with 10.7% of 8th grade and 26.7% of 12th grade students having used tobacco products over the last 12 months. Over 70% of tobacco users are seen by medical providers each year, while an estimated 51.6% of tobacco users are counseled on tobacco-cessation by their physician. Particularly, as tobacco use is the number one risk factor for most head and neck cancers, Otolaryngologists have a distinct obligation to their patients to counsel on tobacco-cessation. Objectives: 1. Analyze current practices and policies of Otolaryngologists on tobacco-cessation counseling. 2. Analyze the relationship between formal training in tobacco-cessation and confidence in counseling and prescription therapy behavior for Otolaryngologists. Methods: This survey was launched at the American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) and the American Academy of Facial Plastics and Reconstructive Surgery (AAFPFRS) meetings in September 2010. Surveys were distributed in person. Regression analysis was performed to assess the effects of training on Otolaryngologists’ confidence in counseling. Results: 207 surveys were collected; 202 respondents indicating training in otolaryngology. 88.5% of otolaryngologists ask most or all of their patients about tobacco use at an initial encounter; 83.7% advise most to all of their patients to quit at this encounter; 64.5% assess most to all of their patients’ interest to quit, 49.7% assess most to all of their reasons to quit; 22.3% arrange support between visits for most to all of their patients. Regression analysis showed that training during medical school and after residency were independently associated with higher levels of confidence and higher rates of prescribed therapy for patients (all p<.025). Conclusion: Otolaryngologists counsel their patients on tobacco at a low rate, and fewer provide patients with the support necessary to assist them in quitting. Formal training in tobacco-cessation was associated with higher levels of confidence. Further research is indicated to assess the utility and cost-effectiveness of tobacco-cessation training programs for otolaryngologists.
Poster 45
INTERMITTENT CATHETERIZATION AND RECURRENT URINARY TRACT INFECTION IN SPINAL CORD INJURY PATIENTS
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Background – Alteration in the function of the lower urinary tract following spinal cord injury (SCI) leads to neurogenic voiding dysfunction. Clean intermittent catheterization (CIC) is widely believed to be associated with fewer complications compared to other neurogenic bladder management methods. However most SCI patients on CIC will develop urinary tract infections (UTI) often necessitating the use of antimicrobial prophylaxis. Objective – We studied the association of recurrent symptomatic UTI with the long-term use of CIC for neurogenic bladder management in our population of SCI patients. Methods - Retrospective study of 61 SCI patients with neurogenic bladder managed by CIC. Subjects were selected from 210 SCI patients seen at our urology group between 2000 and 2010. Subjects with a minimum of 1 year follow-up were included. Patients with urinary diversion or those not using CIC were excluded. Recurrent symptomatic UTI was recorded as use of medical UTI prophylaxis (PRx) with either oral antibiotics or methanamine/vitamin C. Results - 61 subjects (51 male and 10 female) were managed with CIC. 41 (67%) subjects required medical PRx for symptomatic recurrent UTI (8 (80%) females and 33 (65%) males). There was no statistical difference (P = .47) between the percentage of males and females requiring PRx. The date of initial PRx use was noted in 39 of 41 subjects and the results demonstrate 28 (72%) required PRx within 2 years after initiation of CIC. Conclusion - Recurrent symptomatic UTI remain a major complication of long-term neurogenic bladder management in SCI patients. Although CIC is generally believed to have the fewest number of complications compared with other bladder management methods, most SCI patients managed with long-term CIC will require medical PRx for prevention of symptomatic UTI within 2 years after its initiation.

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CAN INFECTION FOLLOWING SCOLIOSIS INSTRUMENTATION SURGERY BE A ‘NEVER EVENT’?: DRAMATIC REDUCTION IN INFECTION RATES AT ONE INSTITUTION AFTER IMPLEMENTATION OF A MULTIMODAL PREVENTION PROTOCOL
Williams, Brendan, Dr. Michael G Vitale, Ms. Hiroko Matsumoto, Dr. Michael P Horan, Mr. Stuart Mackenzie, Ms. Lisa Covington, Ms. Lisa Saiman, Dr. Joshua E Hyman, Dr. David P Roye, Dr. Benjamin D Roye
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Background: During the 3rd quarter of 2008 an increased rate of scoliosis surgical site infection (SSI) was encountered at our institution. An interdisciplinary review of our infection-prevention protocol was performed with implementation of a new standardized SSI prevention protocol including: an antibiotic prophylaxis educational program for correct timing and dosage with dual prophylaxis of cefazolin and tobramycin, pre-operative chlorhexadine gluconate bathing, a room traffic reduction program, and pre-closure high volume lavage. Objective: This purpose of this study was to evaluate SSI rates and etiology-specific case volumes before and after prevention protocol implementation. Methods: A retrospective chart review was performed of children undergoing posterior or combined scoliosis instrumentation at our institution from January 2006 to December 2009. SSI rates were calculated for idiopathic and non-idiopathic scoliosis. Overall and etiology-specific quarterly case volume was calculated Results: 424 procedures for the correction of scoliosis were performed on 268 patients (36.1% idiopathic and 63.9% non-idiopathic). Cases performed per quarter increased throughout the study period (17.25 cases/quarter in 2006 to 34.75 cases/quarter in 2009). The proportion of non-idiopathic scoliosis before and after implementation of the SSI prevention protocol was similar (62.1% vs. 67.6%, p= 0.283). The average quarterly infection rate prior to the new protocol was 7.03%, peaking in the 3rd quarter of 2008 at 23.1%. In the 12 months post-implementation, no cases of infection were observed (p = .004, 95% CI = 2.7-11.3). Conclusion: Quarterly SSI rates for pediatric scoliosis instrumentation surgery showed a sustained reduction for one year following implementation of a multimodal SSI prevention protocol at our institution. There was no change in the etiology of scoliosis operated on during this period. Significance: The study shows institution of a standardized multimodal SSI prevention program can dramatically reduce SSI rates in pediatric scoliosis instrumentation surgery. Longer periods of follow up across multiple centers are necessary to examine whether this effect is sustainable and generalizable.
HOW MUCH IS TOO MUCH? : UNINTENDED CHANGE OF PHYSIOLOGIC LUMBAR LORDOSIS AND PELVIC TILT AFTER POSTERIOR SPINAL INSTRUMENTATION AND FUSION FOR ADOLESCENT IDIOPATHIC SCOLIOSIS

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BACKGROUND: The relationship between the spine and pelvis highly influences sagittal balance. In adults, correlation between HRQOL and adequate lumbar lordosis (LL), defined as lordosis proportional to a patient specific pelvic incidence (PI), has been established. Although spinal balance in adolescent idiopathic scoliosis (AIS) has been well studied, its relation to pelvic configuration is poorly defined in the literature. The possible implications of poor sagittal balance warrant further examination of sagittal alignment of the spine and pelvis in AIS. OBJECTIVE: This study investigates the effect of decreased LL after PSIF on the change in pelvic tilt (PT). Furthermore, this study examines the patient-specific relationship between LL and PI, testing the hypothesis that lumbar spinal fusion resulting in "mismatched LL" is associated with increased PT. METHODS: Query of a prospective multicenter database identified 155 AIS patients at least 2 years after PSIF with lowest instrumented vertebra between L2-L5. LL (T12-S1), LL within fusion (LLIF), LL below fusion (LLBF), sagittal balance (SB), PT, and PI at preop and 2 years postop were measured. Change in PT was compared between patients with "appropriate" or "inappropriate" LL as defined by the relationship between LL and PI. Appropriate LL was defined by both the relationship commonly used in clinical practice (LL = PI+10), and a research driven model from the literature (LL = 0.56PI + 33.43). Health related quality of life measures (HRQOL) were also examined. RESULTS: 38% of patients had loss of LL 2 years after PSIF. Patients with loss of LL had a significantly higher rate of increased PT than patients without loss of LL (73% vs. 40%, p<0.0001). In multiple regression, change in LL, LLIF and change in SB all had significant predictive effect on PT (p<0.001, R2=0.21). Using either the clinical practice definition or the research driven model, patients with LL < 2SD (12°) from predicted were more likely to have increased PT (p=0.046 and p=0.027, respectively). There were no significant associations between changes in TK or LL and HRQOL. CONCLUSION: Iatrogenic loss of LL commonly occurs in lumbar fusion for AIS. This loss of LL is strongly associated with a reciprocal increase in PT. As such, spinal fusion can have unintended effects on sagittal alignment which may have unknown consequences in the future.

FLATBACK REVISITED? : RECIPROCAL LOSS OF LUMBAR LORDOSIS FOLLOWING SELECTIVE THORACIC FUSION

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BACKGROUND: Segmental instrumentation using pedicle screws is the standard of care for treating adolescent idiopathic scoliosis (AIS). A common outcome of this intervention is loss of physiological thoracic kyphosis (TK). OBJECTIVE: This investigates the relationship between iatrogenic loss of TK after selective spinal fusion for AIS with straightening of lumbar lordosis (LL) and increase in pelvic tilt (PT). This study tests the hypothesis that loss of TK will result in a compensatory and reciprocal loss of LL. METHODS: Query of a prospective multicenter database identified 123 AIS patients (Lenke 1,2,3) at least 2 years following selective thoracic posterior spinal instrumentation and fusion (PSIF) with lowest instrumented vertebra equal or cephalad to L1. TK (T5-T12), LL (T12-S1), sagittal balance (SB) and PT at preop and 2 years postop were measured. Health related quality of life measures (HRQOL) were also examined. RESULTS: 31% of patients undergoing a selective fusion had a net loss of TK at 2 years postoperatively (2yearTK–PreopTK<0). Patients who had decreased TK had a significantly higher rate of loss of LL than patients without loss of TK (68% vs. 32%, p<0.0001). Change in LL was positively correlated to change in TK (p=0.0001) and negatively correlated to both change in SB (p=0.002) and change in weight (p=0.04). Change in PT was negatively correlated to both change in TK (p=0.03) and change in LL (p<0.0001), and positively correlated to change in weight (p=0.01). Multiple regression analysis revealed that both TK and SB had significant predictive effect on LL (p<0.001, R2=0.31), and LL had significant predictive effect on PT (p=0.0045, R2=0.12). There were no significant associations between changes in TK or LL and HRQOL. CONCLUSION: Iatrogenic loss of TK occurs commonly in selective fusion for AIS. This loss of kyphosis is strongly associated with a compensatory and reciprocal loss of LL in the unfused segments, as well as an increase in PT. Although a significant difference in HRQOL at 2 years postoperatively was not appreciated in this study, the experience of adults with “flatback syndrome” suggests that loss of physiologic sagittal alignment in surgical correction of AIS may increase the risk for suboptimal clinical outcomes for these patients in the future.
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MORE EXPERIENCED SURGEONS LESS LIKELY TO FUSE: A FOCUS GROUP REVIEW OF 315 HYPOTHETICAL EARLY ONSET SCOLIOSIS CASES
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Background: Age, experience, participation in study groups, and influence of colleagues all contribute to a "surgical culture" or "fingerprint" which can affect decision making, especially in areas where evidence is lacking. Previous work has identified significant variability in decision-making and multiple areas of clinical equipoise in the treatment of Early Onset Scoliosis (EOS). Objective: In an attempt to better understand possible determinants of this variability, we examined the relationship between socio-clinical attributes of eleven participating surgeons and decision making regarding treatment of EOS. Methods: A survey of 11 experienced EOS surgeons was conducted. The first part of the survey consisted of questions regarding surgeon and practice demographics followed by their preferred management of 315 hypothetical EOS cases. Cases varied considerably in etiology (Idiopathic, and Low- (LTNM) and High-Tone Neuromuscular (HTNM), age, and curve severity. The treatment options were grouped as: Conservative (observation, bracing, or casting) or surgical (spine- or rib-based distraction, growth guidance, growth modulation, or definitive fusion). A uni- and multi-variate regression analysis to identify statistical differences was performed. Results: The cohort's mean years in practice was 20.7 ± 7.36 yrs (see Table A). Multivariate regression demonstrated more years of practice predicted a lower preference for fusion (p<0.05). This effect was greater amongst HTNM cases (p<0.05). Overall there was equal interest amongst groups regarding the choice between rib based and spine based distraction methods; however, CWSDSG (p<0.05) and percent of practice spent treating spinal deformity (p<0.05) predicted more rib-based distraction use in HTNM patients. Conclusion: EOS surgeons with more experience were less likely to opt for definitive fusion, particularly amongst HTNM patients. Overall, group membership was not predictive of preference for spine- or rib-based distraction methods. Significance: Physician characteristics including membership in study groups have definite effects on decision making in the area of EOS.

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FRONTAL OR SAGITTAL SPINAL IMBALANCE DOES NOT AFFECT QUALITY OF LIFE TWO YEARS AFTER POSTERIOR SPINAL INSTRUMENTATION AND FUSION FOR ADOLESCENT IDIOPATHIC SCOLIOSIS
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BACKGROUND: Literature suggests that curve correction by PSIF for AIS is correlated with improved self-image and QOL. Despite segmental fixation with modern techniques, ~20% of patients have significant spinal imbalance after PSIF.
OBJECTIVE: This study aims to investigate the influence of sagittal and coronal balance on QOL and self-perception 2 years following PSIF for AIS.
METHODS: Review of a multicenter database identified 761 patients who underwent PSIF with minimum 2 years follow-up. Scoliosis Research Society-30 (SRS-30) and Spinal Appearance Questionnaire (SAQ) scores were compared in patients with and without imbalance. Coronal imbalance was defined as > ±2cm deviation of the C7-plumbline from the central sacral vertical line. Sagittal imbalance was defined as > ±2cm deviation of the C7-plumbline from the posterior-superior corner of the S1 vertebra.
RESULTS: Major preop Cobb angle was positively correlated with both an improvement in self-perception and QOL. Body Mass Index (BMI) was positively correlated with increased pain and improved QOL. While statistically significant, the relationships with Cobb angle and BMI were quite small and potentially clinically insignificant. In contrast, spinal imbalance at 2 years postop did not correlate with change or absolute magnitude of either SRS-30 or SAQ scores.
CONCLUSION Moderate spinal imbalance is currently considered to be >2cm deviation in either the coronal or sagittal planes, and the presence of coronal or sagittal imbalance at 2 years does not negatively affect self-perception or quality of life. Care must be taken interpreting this data, as although AIS patients did not report issues with QOL or self-perception 2 years following PSIF, our definition of imbalance may not be fully correct and spinal imbalance may have long-term implications beyond two years. However, if these findings persist with longer follow-up, surgical strategies including the choice of more extensive levels of fusion may need to be revisited.
CHARACTERISTICS OF PATIENTS WITH ADOLESCENT IDIOPATHIC SCOLIOSIS WHO EXPERIENCE CORONAL DECOMPENSATION FOLLOWING POSTERIOR SPINAL INSTRUMENTATION AND FUSION

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BACKGROUND: Coronal decompensation is a potential complication of spinal instrumentation for AIS. This can result in problems requiring revision surgery. OBJECTIVE: The purpose of this study is to investigate risk factors for coronal decompensation 2 years after PSIF for AIS. METHODS: Retrospective review of a large, multicenter dataset identified 890 patients with AIS and at least 2 years of follow up after PSIF. Demographic, clinical and radiographic measures were reviewed. Coronal decompensation was defined as a change further away from midline (or horizontal) from 6 weeks to 2 years in any one of the following radiographic parameters: change in LIV Tilt Angle > 10°; change in Coronal Position of the LIV > 2 cm; change in Thoracic Trunk Shift > 2 cm; or change in Coronal Balance > 2 cm. Patients with decompensation were compared to those without. The relationship between the lowest instrumented vertebrae (LIV) and lowest end vertebra (LEV) was examined as an independent variable. RESULTS: 6.4% (57/890) of patients exhibited coronal decompensation at 2 years postop. Univariate analysis demonstrated that decompensated patients were more likely to be males, have lower preop Risser scores, a more cephalad LIV, and lower percent major curve correction (56.7 vs. 64%). Multivariate regression revealed that decompensated patients were twice as likely to be male, to have lower preop Risser score, and lower percent major curve correction. The relationship between the LIV and LEV was not significant. CONCLUSION: AIS patients with male gender, low preoperative Risser score and smaller percent major curve correction following PSIF are more likely to exhibit coronal decompensation at 2 years postoperatively. 6.4% of patients with AIS exhibit radiographic decompensation 2 years after PSIF. While this study did not demonstrate a significant association between the relationship of LIV and LEV and decompensation 2 years postoperatively, results of this study indicate that skeletal immaturity, male gender and less correction of the major curve may be related to higher rates of decompensation.

HIGHER DEGREES OF CURVE CORRECTION CORRELATE WITH WORSENED SAGITTAL BALANCE

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BACKGROUND: Modern day techniques for the management of spinal deformities allow dramatic correction in both the frontal and axial plane, however, these methods can have unintended negative effects on sagittal balance. Investigation into the correlation between coronal correction and sagittal is lacking in the literature. OBJECTIVE: The purpose of this study is to investigate the correlation between coronal correction and sagittal balance at 2 years postoperatively after posterior spinal instrumentation and fusion (PSIF) for adolescent idiopathic scoliosis (AIS). METHODS: Review of a prospective multicenter dataset was performed to identify patients with AIS following PSIF. Demographic, clinical and radiographic measures were reviewed for 1053 patients with 2 year follow up. Patients were grouped in two cohorts according to coronal correction >50% and <=50%. RESULTS: Sagittal balance averaged -14.3mm preoperatively and -23.4mm postoperatively. 46.5% (490/1053) of patients demonstrated worsening sagittal balance at 2 years. The two groups had equal sagittal balance score at baseline (14.5 vs 13.6 mm; p=0.74). Patients with >50% major curve correction had significantly worse negative sagittal balance at 2 years when compared to those who had <50% curve correction (-24.5 vs -19.9mm; p=0.04). Only Lenke 1 curves showed a trend toward significant difference (p=0.068). When looking at lumbar modifiers only Lenke 1A curve’s sagittal balance remained significantly affected after >50% correction was performed (p=0.03). Patients with sagittal modifier “N” with >50% correction had worsened sagittal balance at 2 years (p=0.03), and those with “+” (>40) curves showed a trend (p=0.08). CONCLUSION: 46% of patients treated for AIS experience significant worsening of sagittal balance at 2 years postoperatively, an effect that seems to be correlated with >50% of coronal correction. This association should be considered especially in Lenke 1 curves and in curves that have neutral or positive sagittal balance preoperatively.
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TROPHIC EFFECT OF AMNIOTIC FLUID ON FETAL INTESTINAL EPITHELIAL CELLS
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Background - Necrotizing enterocolitis (NEC) is a gastrointestinal (GI) condition that mostly affects premature infants. NEC is an acute inflammatory disease for which the pathogenesis is not yet fully understood. LPS has been shown to contribute to the cell apoptosis seen in NEC. Hypothesis - We hypothesized that growth factors (EGF, HGF, IGF) present in amniotic fluid (AF) will increase proliferation of GI epithelial cells and will be protective against the cytokines that are responsible for cell apoptosis associated with NEC. As cells proliferate and form a confluent layer, they act as an insulator and thus constrain the electrical current causing an increase in resistance measured as transepithelial resistance (TER). Methods - The barrier function of fetal GI epithelial cells was measured using electric cell-substrate impedance sensing (ECIS). IEC-6 cells were plated on 8W10e electrode array and treated with LPS (1ug/ml) and either 30% whole rat AF or 30% cell growth medium (with 1%fetal bovine serum). TER was measured at 0, 4, 8, 16, and 24 hours. Results - LPS treatment produced concentration and time-dependent decreases in IEC-6 TER. The AF (30%) protected fetal epithelial cells and increased proliferation shown as increased TER. Conclusion - Amniotic fluid protects GI epithelial cells from LPS exposure. Future study - Further studies will be done to demonstrate the proliferative affect of amniotic fluid on the GI epithelial cells in the presence of LPS and TNF alpha alone and in combination.

Poster 55

GENOME-WIDE AMINO ACID COVARIANCE IN HEPATITIS B VIRUS
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Background: Hepatitis B virus (HBV) chronically infects over 350 million people in the world and causes 600,000 to 1 million deaths annually. Past HBV genetic studies have focused on individual genetic variations and thus have been unable to assess intragenomic interactions. One method to reveal such interactions is through analysis of amino acid covariation, which is coordinated variations at two or more residues in the genome due to selective pressures simultaneously affecting more than one site. Objective: The objective was to examine the amino acid covariation pattern in the HBV genome to gain insights into the evolution of the virus and into how the virus’ unusual genetic organization may have influenced intragenomic interactions. Methods: 100 random sequences for each HBV genotypes B, C, and D were collected, the predicted protein sequences for all genes were extracted from their overlapping reading frames, the sequences were concatenated into a single string of ~1600 residues for each sequence, and all possible covariances were identified and scored using the Observed Minus Expected Squared algorithm. Results: About 5% of the residues covaried with one or more residues at a false-discovery rate of < 1%. 89% of the covariances involved the polymerase gene, in part due to its size and variability profile. In contrast, the core gene had almost no covariances despite sufficient genetic variability, indicating that it evolved with little coordinate pressure from the rest of the genome. The covariances linked into a single interconnected network in which the hubs are covarying positions and the edges are the covariances, indicating that the genomes largely evolved as a coordinated unit. The networks had a very tightly interconnected cluster of residue positions surrounded by less-connected positions that was unlike any architecture seen before in a biological network. The networks for each of the genotypes were topologically similar, indicating that the selective pressures on each genotype are similar. The unusual network architecture indicates that the extensive overlap of HBV’s coding regions constrains the mutational freedom of HBV sequences even beyond the overlaps. Mapping the covariant positions between the terminal protein and reverse transcriptase domains within the polymerase onto the predicted reverse transcriptase domain molecular structure allowed us to predict that the interdomain interface on the reverse transcriptase domain is located at the end of the nucleic acid binding groove. Conclusions: Genome-wide covariance network analysis is a promising new avenue of research that could be used to assist structural analysis, improve understanding of viral evolution (including evolution of drug resistance), and identify novel genetic biomarkers for complex phenotypes.
Background: Keloids are dense fibrous scars that result from pathologic healing of cutaneous injuries. Unlike other scars, they grow beyond the site of trauma and do not regress. Affected individuals may suffer from pain, and itching, thus it is a common reason for presentation in a dermatological setting. Despite its prevalence, the pathophysiological mechanism of keloid formation remains unclear which results in a lack of consensus on treatment. As medical and surgical interventions are unable to prevent recurrence of keloids, affected individuals may encounter life-long frustrations due to the chronicity of the disease. As numerous investigations have revealed that patients with other chronic dermatologic conditions, such as psoriasis, experience reduced quality of life and increased psychiatric dysfunction, it is possible that individuals with keloids may suffer similarly. Objective: To elucidate that patients with keloids suffer from psychiatric dysfunction at increased levels similar to patients with psoriasis and emphasize the importance of psychiatric evaluation in patients with this condition. To determine if there is a correlation between keloid severity and level of psychiatric dysfunction. Methods: This is cross sectional study that uses the General Health Questionnaire-12 to measure and evaluate psychiatric dysfunction. Subjects recruited from online psoriasis and keloid support groups participate in an online anonymous GHQ-12 survey and are divided into one of three groups: psoriasis, keloid, or control group. Mean GHQ-12 score of the keloid group is calculated and compared to the normal and psoriasis group using a two sample t-test. Keloid group is further stratified into mild, moderate and severe group according to size and number of lesion and mean GHQ-12 score of each group is compared. Prelim Results: Subjects with keloids have increased levels of psychiatric dysfunction compared to normal subjects (p < 0.001). There is no difference in the level of psychiatric dysfunction between the keloid and psoriasis groups (p = 0.78). There is insufficient data to determine the correlation between the severity of keloids and level of psychiatric dysfunction. Conclusion: Individuals with keloids suffer from increased levels of psychiatric dysfunction than the normal population and at levels similar to those with psoriasis. Affected individuals should undergo psychiatric evaluation which may result in improved quality of life.

Background: HPV, or Human Papillomavirus, is the most common sexually transmitted virus and is etiologically linked to cervical cancer. Other factors are necessary for the development of cervical dysplasia since most HPV+ women never get this cancer. This is likely due to an individual's immune system. However, when HPV remains in the body for many years, cancer may develop. EBV is also linked to Burkitt’s lymphoma, Hodgkin’s Disease, and central nervous system lymphomas associated with HIV. Previous cross-sectional studies have demonstrated a significantly increased risk of cervical dysplasia in HIV+ women shedding EBV and high-oncogenic-risk HPV. To better understand the mechanism of this interaction, a longitudinal study was conducted in which cervical specimens from HIV+ and HIV- women were tested for the presence of HPV and EBV and compared to concurrently obtained Pap smears. Objective: Chronic co-shedding of EBV and HPV will lead to a further increase in cervical dysplasia. Methods: HIV+ women (n=76) and HIV- women (n=29) were enrolled. After informed consent a Pap smear was collected followed by a cervical swab for HPV DNA detection. Women were seen at 3-month intervals for up to 3 years. Cellular DNA was isolated and HPV was detected and genotyped using the Roche reverse line blot assay. EBV was detected using the highly-sensitive PCR assay targeting the BamHI repeat. Chronic viral shedding was defined as being positive for at least 2 consecutive study visits. Pap smears were classified using the Bethesda criteria. Results: Of the 105 HIV+ and HIV- women enrolled in the study, 35 exhibited only chronic HPV shedding, 19 only chronic EBV shedding, 11 both HPV and EBV shedding, and 40 were negative for both. The group that chronically shed both HPV and EBV had the largest percentage of abnormal pap smears at 81.8% as compared to only 57.9% of those chronically shedding only HPV (chi-square, p=.13) and 67% of those shedding both viruses at the first study visit. A significant relationship would be found if the sample size was doubled (p=.036). Conclusions: Previous cross-sectional studies have demonstrated a role for EBV in HPV-related carcinogenesis. This study further supports this hypothesis by showing that chronically shedding both of these viruses provides an even further increase in risk of dysplasia as compared to co-shedding on a single visit. Larger cohorts need to be studied to confirm these findings.
Background: Previous studies in our laboratory have indicated that the lymphovascular embolus is not simply a cellular fragment that detaches from the main tumor passively, but represents an active clonal selection for a stem cell phenotype exhibiting enhanced stem cell signaling and survival pathways. Lymphovascular emboli exhibit increased resistance to chemotherapy and patients with large numbers of lymphovascular emboli exhibit decreased disease-free survival and poorer prognosis. Florid lymphovascular emboli are the diagnostic signature of inflammatory breast cancer (IBC) and other aggressive metastasizing cancers. The emboli have been presumed to form as a result of lymphovascular invasion, but this event is thought to be rare, and therefore would not be sufficient to explain the large number of emboli observed in IBC and other highly metastatic carcinomas. Objective: The reasons why some patients exhibit large numbers of lymphovascular emboli whereas others exhibit only rare numbers remain unknown. We wanted to specifically address this anomaly, and thus (Methods:) carried out both animal and in vitro imaging studies with our human xenograft model of inflammatory breast cancer, MARY-X, which exhibits florid emboli in mice and gives rise to high density spheroids in vitro. We also carried out morphometric studies on the density of human lymphovascular emboli in 25 IBC and 250 non-IBC cases and subsequent laser capture microdissection. Results: Animal and in vitro multicolor imaging studies using anti-E-cadherin and anti-podoplanin showed evidence of self-budding histogenesis within the lymphovascular spaces with one parent embolus giving rise to daughter emboli. Correspondingly, budding spheroidgenesis was observed in vitro. Density studies of tumoral emboli in the human cases showed their numbers distributed over an exponential rather than linear range. By both RT-PCR and IHC, emboli compared to their non-embolic invasive carcinoma areas exhibited five to ten fold higher stem cell markers including Stellar, H19, Rex-1, Nestin, CD133 and Aldehyde Dehydrogenase 1 (ALDH1), stem cell transcriptional determinants including OCT4, SOX2 and Nanog, and stem cell signaling pathways, e.g. Bmi-1, Hedgehog and Notch3. Conclusions: These studies, though not explaining the genesis of the initial embolus, demonstrate conclusively that emboli beget emboli through stem cell initiated self-budding histogenesis. This latter process is of paramount importance as it accounts for the exponential numbers of emboli seen in the human cases, which exhibit aggressive behavior.

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GENETIC MANIPULATION OF THE SMALL GTPASE RAC1 INFLUENCES DENDRITE DEVELOPMENT AND HIPPOCAMPAL-DEPENDENT LEARNING
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Dendrites and dendritic spines are the major recipients of excitatory synaptic transmission in the brain and their abnormalities have been implicated in several diseases of mental retardation and cognitive impairment such as such as Down syndrome, Fragile X mental retardation, Autism and Alzheimer’s disease. Their formation and maintenance are therefore very critical for synaptic development and plasticity, and require a very dynamic actin cytoskeleton. Rac1 (Ras related C3 botulinum toxin substrate 1) is a member of the Rho subfamily of small GTPases, largely known for its involvement in actin cytoskeleton remodeling. In neurons, Rac1 is associated with neuronal development, participating in the morphological changes required for migration of newborn neurons to characteristic locations, extension of axons and dendrites into proper target regions, and formation of synapses with appropriate partners. Our laboratory and others have recently revealed that Rac1 might have a role in plasticity, bringing us to hypothesize that Rac1 is involved in the morphological changes observed at neuronal synapses during hippocampal learning and memory as well as long-term plasticity. To investigate our hypothesis, we developed mice with conditional inactivation of rac1 gene in the CA1 area of the hippocampus using the Cre/Lox-P system (by crossing Rac1flox mice with Cre transgenic mice), driven under the CaMKIlo promoter. We observed that Rac1 mutant mice developed normally displaying no gross physical or behavioral abnormalities. Nissl staining of hippocampal slices showed that these mutant mice presented normal hippocampal architecture. In situ hybridization analysis showed that, in the Racflox/flox-Cre+ mice, Cre recombinase significantly deleted the floxed rac1 allele in the hippocampal CA1 area at 3 months of age. To demonstrate loss of protein, western blot analysis of hippocampal lysates as well as other brain regions was performed. In the CA1, Rac1 levels were slightly decreased at 1 and 2 months, and those levels became significantly decreased at 3 months and older. Additionally, loss of Rac1 in the hippocampal CA1 area was not compensated for by any other small GTPase of the Rho family. Imaging analysis of CA1 pyramidal neurons by Golgi-Cox impregnation revealed an aberrant morphology in Rac1 deficient mice as compared to control mice, with less dendrites, deficient branching and a significant reduction in spine density. Through electrophysiological measurements, we demonstrated that Rac1 is necessary for long-term synaptic plasticity. Behaviorally, using the Morris water maze and fear conditioning tests we further showed that Rac1 is also critical for hippocampus-dependent learning and memory functions. Our results indicate that regulation of Rac1 may provide a functional link between deficient neuronal morphology, aberrant synaptic plasticity and cognition impairment, phenotypes often associated with certain autistic disorders.
A SINGLE CENTRE EXPERIENCE OF GESTATIONAL TROPHOBLASTIC TUMOURS
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Background: Variable incidence and clinical course of Gestational Trophoblastic Tumours (GTT) has been reported in few published studies from different parts of Pakistan and none has mentioned the magnitude of Persistent Trophoblastic Tumour. Objective: To study the natural course, outcome and treatment experience of GTT in a diverse cohort of patients referred to a Tertiary Care Centre. Methods: Data was collected from 1998 to 2009 for 54 patients with gestational Trophoblastic tumour presented to Aga Khan University Hospital. It was analyzed for 48 patients for different clinical variables and outcome using SPSS version 16.0. Results: The incidence of GTT was 1.3 in 1000 pregnancies while it was 29% for PTD. The mean age of patients was 29 years. The initial diagnosis was established on the basis of ultrasound and Beta subunit of Human Chorionic Gonadotrophins (βhCG) levels. The diagnosis of Hydatidiform mole, Invasive mole and Choriocarcinoma was found in 27(56%), 4(8%), and 14(29%) patients respectively while for 3 patients no specific histology had been mentioned. The uterine size was more than 5 cm for 24 patients (46%) which had linear co-relation with the level of the βhCG at presentation. The highest level of βhCG noted was 4,831,356IU/ milliliter. Among 25 patients who received chemotherapy, 16 were categorized to be in low risk while 9 in high risk group based on their prognostic scoring. The multidrug chemotherapy regimen was used in 17 patients; 7 being in high risk and 10 patients in low risk group. 15 patients were lost to follow but none died among the remaining 33 patients as per last follow up. Conclusion: In contrast to local data, our study showed an incidence of GTT comparable to western figures but with higher incidence of persistent Trophoblastic disease. There was a trend towards use of multidrug regimen even in low risk GTT. Further studies with long term follow up are needed for exploring the pattern of resistance to single agent chemotherapy and rationalizing multidrug regimen for low risk GTT group.

A SURVEY STUDY OF PRIMARY HEALTH CARE USAGE AND EXPERIENCE IN THE GAY MALE POPULATION OF WINNIPEG
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Purpose: To explore primary health care experiences, realities and preferences of Winnipeg’s gay male population and to determine whether gay men’s health care needs would be better met through access to a gay male physician. Method: Gay male survey participants were recruited through healthcare clinics, social venues serving the gay population and personal social networks. Responses were compared with those from heterosexual men. Results: Among 133 (98 gay and 35 heterosexual) respondents to the survey, 93.2% have access to a regular primary care physician. Among the gay respondents, 36.7% have a gay male doctor, 51% have attempted to find, and 64.3% would have preferred to have a gay male doctor. A total of 78.6% of gay men have told their present doctor about their sexual orientation. Among gay men having a gay male doctor 97.2% have disclosed their sexual orientation compared with 71.9% of who do not have a gay male doctor (P-value: <.000). 76.5% of gay men reported they would feel more comfortable discussing sexual issues with a gay male doctor. Physician-initiated communication about sexual orientation is often lacking. (50% gay/bi men vs. 14.3% heterosexual men) Approximately half of gay male respondents who do not have a gay male doctor would like to have one. (50.9%) Conclusion: Although the gay male population does not seem marginalized with regard to primary health care services, it is likely that for a subset health care needs may be better met through access to gay male physician.
Background: Glioblastoma multiforme (GBM) is the most common malignant primary brain tumour encountered in clinical practice. Despite therapy survival remains poor. Methods: All GBM patients at CancerCare Manitoba from 2002-2009 were assessed. Inclusion criteria: histologically confirmed GBM, age 18-70 years, receipt of CRT, and intent to treat with adjuvant TMZ and concomitant CRA. Patients received up to 30 cycles of TMZ (150-200 mg/m2 days 1-5/28 day cycle) concurrent with cis-retinoic acid (CRA) (50 mg/m2 BID) days 1-21. BNIP3 and AIF expression was determined on FFPE section slides of patient tumours using immunohistochemistry. Relationships between BNIP3 and AIF expression and survival outcomes were examined. Results: 80 patients met inclusion criteria. Median overall survival (OS) for the cohort initiating adjuvant therapy was 18.9 months and median progression free survival (PFS) on TMZ was 9.6 months. Nuclear BNIP3 expression highly correlated with low AIF expression. Median survival for patients with nuclear BNIP3 expression was 13.5 months while median survival for patients with mixed or cytoplasmic BNIP3 expression was 15.1 months; median survival for patients with low AIF expression patients was 14.8 months and for intermediate AIF expression patients was 16.8 months. The survival differences for patients stratified by BNIP3 and AIF expression were not significant. Conclusions: TMZ and CRA are well tolerated as long-term adjuvant treatment for GBM. Nuclear BNIP3 expression and low AIF expression appear to be associated with decreased overall survival, however, analysis of a larger cohort is necessary to properly evaluate this relationship. The effects of CRA on survival are unclear from this study and require further investigation.

Gentamicin is an aminoglycoside antibiotic commonly used to treat severe gram negative infections. Its use has been limited due to its potential to induce ototoxicity. Mouse inner ear organs are immature at birth and continue to develop during the postnatal period. The mouse cochlea consists of three separate turns that vary in their progression of development. Immature inner ear organs are more susceptible to aminoglycoside-induced ototoxicity than are mature inner ear organs. The present study was undertaken to assess gentamicin-induced hair cell loss at the differing turns of the cochlea in developing mouse pups. Mouse cochlear tissue at ages postnatal day 1 or 5 (P1, P5) was dissected, attached to a cover glass, and incubated in standard culture medium in 5% CO2 for 24 hours. Culture medium was replaced with culture medium with or without 0.03% gentamicin and harvested at 24 or 48 hours. The tissue was labeled with markers for stereocilia and nuclei. Explants were visualized under fluorescent microscopy. The cochlear inner and outer hair cells were counted at each turn along the cochlear duct. The number of intact hair cells was averaged. In one day old mice, gentamicin exposure resulted in both inner and outer hair cell loss, while five day old mouse inner ear organs exposed to gentamicin resulted in selective inner hair cell loss. The hair cell loss was more extensive in the 48 hour exposed group versus the 24 hour exposed group. The basal turn was most resistant to gentamicin-induced hair cell loss. The middle turn was most susceptible to gentamicin-induced hair cell loss. The apical turn had intermediate hair cell loss due to gentamicin exposure. The difference observed between nonselective hair cell loss in P1 mice and selective inner hair cell loss observed in P5 mice suggests that the outer hair cells mature in a different manner than inner hair cells. Outer hair cells undergo critical developmental changes between P1 and postnatal day 5 that help protect them against gentamicin-induced ototoxicity. The varying degrees of ototoxicity expressed at each turn of the cochlea suggest that the cochlear turns have differing temporal development. Understanding of these differences in developmental sequences in inner and outer cochlear hair cells may aid in the characterization of maturational differences which confer susceptibility or protection against aminoglycoside-induced ototoxicity.
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THE STUDY OF ETIOLOGICAL AND DEMOGRAPHIC CHARACTERISTICS OF INTRACRANIAL BRAIN ABSCESS - A CONSECUTIVE CASE SERIES STUDY FROM PAKISTAN
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Background: To determine the demographics, management, bacteriological spectrum and outcome of brain abscesses of patients brought to Aga Khan University Hospital Karachi (AKUH) with a history of neurological symptoms and to examine the factors associated with it. Methods: This hospital based descriptive study of fifty-three patients from both sexes who presented to section of Neurosurgery, AKUH from 1st January 2000 till 31st December 2008 with neurological symptomatology and fulfilling other inclusion criteria were included in the study. Data regarding their demographic profile and other factors were collected on a well structured proforma. Data were analyzed using frequencies, proportions, group means and standard deviations. Results: The male to female ratio in our study was 3.4:1 with S. milleri (20.7%) being the most common etiological agent followed by anaerobic bacteria (15.1%). The triad of headache, fever and vomiting was present in 62.7% patients at the time of presentation. The most important factors influencing mortality was the neurological condition of the patient at the time of admission. Chronic Suppurative Otitis Media was the most common predisposing factor for temporal lobe infections while frontal lobe was the most common site of involvement in majority of the patients (67.8%). The mortality rate in our study was 11.3%. Conclusion: The result of the study suggests that patients aged between the second and the fourth decades of life are the most susceptible both in terms of morbidity and mortality. Early diagnosis, appropriate management with rapid access to tertiary care centers will lead to a better prognosis.

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THE ETHICAL DILEMMA OF EMBRYONIC STEM CELL RESEARCH
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Objective: To determine the knowledge, attitude, and ethical concerns of medical students as regards to Embryonic Stem Cell (ESC) research. Subjects and Methods: This questionnaire based descriptive study was conducted in Civil Hospital Karachi (CHK), Pakistan from February to July 2008. A well-structured questionnaire was administered to medical students and graduate doctors, which included their demographic profile as well as questions in line with the study objective. Informed consent was taken and full confidentiality was assured to the participants. Data was entered in Statistical Package for Social Sciences (SPSS version.15) and analyzed. Results: A total of 204 male and 216 female medical students and doctors were administered questionnaires out of which 105 males (51.4%) and 108 females (50%) were aware of embryonic stem cell research and its ethical implications. 40% males and 47% of females were of the opinion that life begins at conception. 46% males and 39% females were in favor of stem cell research with only 31% males and 28% females supporting ES cell research. Less than 1/3 of students supported using frozen embryos for research purpose while more than 2/3 indicated that they were unlikely to support abortion for stem cell research purpose. Conclusion: The majority of the students were in favor of stem cell research with some reservations regarding ES cell research. A sizeable amount of students abstained their views reflecting their incoherent moral and religious views. The finding of the study indicates a need for incorporating bioethics in medical student's curriculum.
Pancreatic cancer is a common cancer in the US, and due to its aggressive nature, it accounts for six percent of all cancer associated deaths. The mortality rate seen in patients with pancreatic cancer is nearly equal to its rate of incidence, accounting for approximately 32,000 cases each year. As compared to other gastrointestinal cancers, pancreatic cancer is one of the most drug resistant tumors [1]. Treatment of pancreatic cancer is greatly hindered by a multidrug resistance (MDR) phenotype often exhibited by tumor cells even before their exposure to chemotherapy [2]. A mechanism responsible for this inherent resistance seen in pancreatic cancer may occur due to decreased intracellular accumulation of chemotherapeutic agents as a result of their active efflux via the ATP binding cassette (ABC) transporters. A broad range of anticancer drugs are effluxed by the ABCC family of transporters [a.k.a. multidrug resistance associated proteins (MRPs)] especially via the MRP-1 and MRP-2 pumps. Several of the MRPs are overexpressed in pancreatic cancer cells and are implicated in their intrinsic MDR-phenotype [3]. Thus, inhibiting the MRP-mediated drug-efflux function may prove clinically beneficial. However, currently there are no drugs approved for the specific inhibition of MRP transporters in pancreatic cancer. Since leukotrienes are natural substrates of MRPs, we wanted to investigate whether leukotriene receptor antagonists (LTRAs), often used as anti-asthmatic medications, may be used as competitive inhibitors of MRPs. Using an MRP-2 overexpressing cell line, we have previously published that several LTRAs, including the widely prescribed LTRA, montelukast (SingulairTM), can inhibit MRP function and increase intracellular levels of paclitaxel [4]. In the pancreatic cancer cell line PANC-1, our preliminary experiments also demonstrated that pre-exposure to montelukast produced a dose dependent increase in intracellular retention of the fluorescent MRP substrate calcein. A significantly (p<0.05) higher calcein retention occurred in PANC-1 cells which were pre-exposed to high concentrations (100-150 µM) of montelukast. Thus, we propose that concurrent administration of montelukast and anticancer drugs (substrates of MRPs, e.g. doxorubicin, paclitaxel) may lead to better therapeutic outcomes. Ultimately, this adjunct therapy approach may be highly beneficial in treating patients suffering from the lethal disease of drug-resistant pancreatic cancer.

Background: High prevalence of depression in individuals with type 2 diabetes mellitus (DM2) has been highlighted by different studies; however, the definite reasons for this association are yet to be established. This prospective case control study was carried out to assess the frequency and severity of depression in DM2 patients and to investigate the associated factors. Methods: This hospital based prospective case control study of 411 participants, who presented to the diabetic outpatient department from January 2007 till December 2009 with established diagnosis of type-2 diabetes mellitus (T2DM) and fulfilling other inclusion criteria were enrolled in the study. They were compared with an age matched control of 411 individuals. Both groups were screened for depression and were subsequently interviewed by a psychiatrist for a formal diagnosis using the Aga Khan University Anxiety and Depression Scale (AKUAD). Age, gender, socio-demographics, BMI, smoking and exercise status of both groups were recorded. Family history, complications and control of blood glucose using HbA1c levels of diabetics were assessed. Data were analyzed using proportion, group means, standard deviations and Pearson Chi Square test. Results: The overall yield from AKUAD in detecting depression from the T2DM group was 66.2% as compared to 33.5% in the control group (P= <0.001, Pearson Chi Square test). Diabetic females had a higher prevalence of depression than diabetic males (60% vs. 40%; p <0.01). Increased HbA1c level coupled with a family history of depression correlated significantly with depression in T2DM group. Nephropathy was the most frequent complication associated with depression in the T2DM group. Conclusion: Prevention of diabetic complications by glycemic control can limit the prevalence and severity of depression. Regular screening of diabetics for depression should be made mandatory in order to identify and
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THE STUDY OF ETIOLOGICAL AND DEMOGRAPHIC CHARACTERISTICS OF ACUTE HOUSEHOLD ACCIDENTAL POISONING IN CHILDREN - A CONSECUTIVE CASE SERIES STUDY FROM PAKISTAN
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Background: To determine the agents of poisoning and demographic distribution of children brought to Civil Hospital Karachi (CHK) with a history of accidental poison intake and to examine the factors associated with it. Methods: This hospital based descriptive study of first 100 patients from both sexes who presented to Pediatric department, CHK from 1st January 2006 till 31st December 2008 with exposure to a known poisonous agent and fulfilling other inclusion criteria were included in the study. Data regarding their demographic profile and potential risk factors was collected on a well structured proforma, cases were followed until discharge or expiry. Data was analyzed using frequencies, proportions, group means, median and standard deviations. Results: The male to female ratio in our study was 1.2:1, with kerosene (50%) being the most common household agent followed by medicines (38%), insecticides (7%) and bathroom cleaners (5%). Factors such as mother’s education level, number of siblings and storage place of poison correlated significantly with the cases of accidental poisoning. Most of the children (70%) presented within 3 hours of ingestion. Dyspnea was the most common symptom observed. The mortality rate in our study was 3%. Conclusions: Children belonging to age group 2-3 years are the most susceptible both in terms of morbidity and mortality. Preventive strategies need to be adopted at a national level to spread awareness among parents.

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IDENTIFICATION OF NOVEL THERAPEUTICS FOR NEUROFIBROMATOSIS TYPE 1
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Background: Neurofibromatosis type 1 (NF1) is an autosomal dominant disease that affects 1 in 3000 people. NF1 patients have defects in the neural-crest-derived tissues, leading to a wide spectrum of clinical presentations, including developmental, pigmented, or neoplastic aberrations of the skin, nervous system, bones, endocrine organs, blood vessels, and eyes. Neurofibromas, the most frequent tumour in NF1, and malignant peripheral nerve sheath tumours (MPNSTs) are serious complications of NF1. Since surgery is currently the only option for MPNSTs, there is an urgent need for new chemotherapy. Objective: The purpose of this research is to identify novel chemotherapeutic compounds using high-throughput, small-molecule screening. The efficacy of candidate compounds will be validated in vitro and in vivo. Furthermore, we seek to identify the pathways that are perturbed upon the introduction of these compounds to MPNST cells. Methods: Our lab developed a mouse model, in which adult stem cells called skin-derived precursors (SKPs) that are deficient for NF1 and p53 can produce MPNSTs upon autologous transplantation and xenotransplantation into nude mice. In this project, I used these murine MPNST cells to screen a library of 4480 small molecules in order to find compounds that can inhibit the growth of MPNST cells. Next, I performed a control, counter screen on Schwann cells, which are believed to be the cell-of-origin for MPNSTs. Our goal is to identify molecules that can inhibit the growth of MPNST cancer cells but spare the survival of Schwann cells. Hits are defined as compounds with an RZ Score less than or equal to -3. Data from a previous screen on MEF cells were also used to filter the hits. Results: 1515 hits were discovered to be effective against MPNST cell survival. Counter-screening data on Schwann cells and MEF cells were used to filter the data, and a finalized list of 50 compounds that reduce MPNST cell survival were identified. Conclusions: The identification of novel drugs and the discovery of pathways that these compounds inhibit will vastly increase the potential for cures. Studying the 50 compounds that were identified by our screening protocol in vitro and in vivo will also lead to advances in cancer biology.
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**POST-TRANSPLANT FIBROSING CHOLESTATIC HEPATITIS C IS ASSOCIATED WITH EARLY ACUTE REJECTION AND POOR LONG TERM PROGNOSIS**  
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Fibrosing cholestatic hepatitis C (FCH) is a rare form of recurrent hepatitis C virus (HCV) in liver transplant (LT) recipients, characterized by rapidly progressive graft dysfunction. Greater understanding of factors that lead to this HCV variant could provide pivotal insight into beneficial treatments. We aimed to evaluate outcomes in patients with FCH in our center. Methods: All patients with HCV who underwent LT between 2/02-12/09 were retrospectively divided into 3 groups: stage 0, stage ≥ 2 (of 4) fibrosis on biopsy at 1-year, and FCH (defined as serum bilirubin ≥ 3 mg/dl, imaging without biliary obstruction, and ≥ 3 of 4 pathological criteria including ductular proliferation, canalicular ± intracellular cholestasis, hepatocyte swelling ± lobular disarray, and sinusoidal/pericellular fibrosis. Results: 365 patients with HCV underwent LT, 15 (4%) developed FCH, 86 (23%) had stage 0 and 58 (16%) had ≥ stage 2 fibrosis at 1-year post-LT. There were no baseline differences in age at LT, gender, living donor grafts, cold or warm ischemia times, donor HCV status or CNI. Calculated MELD (21.8 v. 18.1), donor age (47.7 v. 41.9), and HCC (32% v. 57%) were significantly different in stage ≥ 2 v. stage 0, but statistically similar to the FCH group (MELD 21.8, donor age 43.8, HCC 40%). Rejection with Banff ≥ 5 prior to the study biopsy was more common in the FCH group (47%) compared to stage ≥ 2 (21%) and stage 0 (18%). 13 (87%) FCH patients underwent antiviral therapy at any time post-LT (3 remain on therapy, 1 achieved SVR), compared to 36 (62%) stage ≥ 2 patients (8 on therapy, 4 SVR) and 18 (21%) stage 0 patients (6 on therapy, 2 SVR). Overall (13% v. 57% v. 84%) and median (2.0 v. 4.6 v. >6.4 years) survival was significantly different between FCH, stage ≥ 2 and stage 0 groups with median follow-up of 2.0, 3.0, 3.6 years, respectively. In the final multivariable models, FCH (HR 14.5, p<0.001), stage ≥ 2 fibrosis (HR 2.75, p=0.004) and donor age (1.03 per year, p<0.001) independently predicted mortality as well as graft failure (FCH HR 9.45, p<.0.001; stage 2 HR 2.23, p=0.012; donor age 1.04 per year, p<0.001). Conclusions: FCH portends a very poor prognosis compared to patients with minimal disease as well as those with more standard rapid fibrosis. Early rejection was more common in our FCH patients and thus future studies should evaluate this finding to determine if it is a risk factor for FCH. Improved antiviral therapy is greatly needed in this group.

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**PEDIATRIC HIGH GRADE GLIOMA OF THE SPINAL CORD**  
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Object. Pediatric spinal cord high grade glioma (SCHGG) still have a dismal prognosis. This is in part due to low incidence and few studies reporting these tumors. This paper presents the currently largest group of pediatric spinal high grade glioma. Methods. 28 patients (13 boys, 15 girls, mean age at diagnosis 10.9y) with primary SCHGG are reported in the pediatric HIT-GBM database, which documents 310 pediatric patients with high grade glioma. Eligibility criteria were based on astrocytic histology, WHO Grade III or IV, age < 18 years at diagnosis and tumors with spinal cord location. Results. The tumor sizes varied greatly with a range of up to 19 vertebrae (median of 4.00). Larger tumors spanning over >8 vertebrae were correlated to younger age <5 years (p=0.027). The initial surgery was a complete resection (GTR) (n=6), subtotal resection (n=6), partial resection (n=12) or biopsy (n=3). Five of the patients received secondary surgery, two of which were GTR. Adjuvant therapy was chemo plus radiation (n= 22). The median overall survival was 2.5 years, with the mean follow up time of 3.0 years. After 1 year, 2 years and 11 years overall survival was 78.2%, 50.6% and 32.7% respectively. The positive prognostic indicators for OS were: age at diagnosis below 5 years (p=0.047), WHO grade III (p=0.056) and gross total resection for the first (p=0.046) and second surgery (p=0.013). WHO grade was confirmed as prognostic factor in EFS (p=0.044) Conclusions. These initial data of SCHGG describe the starting point for future treatment studies. Larger tumors were more common in the younger children who had the best OS, so there seem to be biological differences related to age, which need to be taken into account.
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CYTOGENETIC DIFFERENCES BETWEEN SECONDARY AND DE NOVO LEUKEMIA
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Background: Late effects of cancer treatment are the occurrence of myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). The communication of potential risk will influence a patient’s decisions for treatment. However, a specific risk tailored to the individual is unavailable. Leukemia patients with a prior history of chemotherapy or radiation leads to attribution of cause to prior treatments received. The incidence of MDS and unfavorable AML cytogenetics increases with age. Objective: We sought to determine if adverse cytogenetics occurs more commonly in patients with a prior malignancy. Methods: We conducted a retrospective review of patients with MDS or AML between 2002 and 2009. Excluded were a prior hematologic malignancy; no cytogenetics; acute promyelocytic leukemia; and age less than 18 years old. Patients identified with a history of malignancy prior to MDS/AML were our study population, and those with MDS/AML without a preceding malignancy were controls. Cytogenetics, age, and gender were collected. The available records of prior therapy (radiation and chemotherapy) were limited. Results: 447 patients met study criteria: 88 in the prior malignancy group and 359 controls. The mean age was 64.7 years in the group with a prior malignancy and 57.7 years in the control group. The occurrence of abnormal cytogenetics was more common in the prior malignancy group. The 5q abnormality occurred 22.6% vs 13.9% (p=0.07), 7q abnormality occurred 20.5% vs 10.6% (p=0.01), chromosome 16 abnormalities occurred 9.5% vs 4.6% (p=0.14), and complex cytogenetics occurred 5.8% vs. 3.4% (p=0.36). In contrast normal cytogenetics occurred more frequently in the group without a prior malignancy 45.4% vs 36.4% (p=0.13). There were only 3 cases of 11q23 abnormalities. Conclusions: From a single institution review we found that patients with a diagnosis of MDS/AML and a history of a prior solid malignancy are significantly older and are more likely to have abnormal cytogenetics. The relative contribution of age and prior malignancy to cytogenetics cannot be determined. The occurrence of 7q abnormalities was significantly more common in those patients who develop MDS or AML with a prior solid malignancy.

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GENOMIC PROFILING IN DOWN SYNDROME ACUTE LYMPHOBLASTIC LEUKEMIA IDENTIFIES HISTONE GENE DELETIONS ASSOCIATED WITH ALTERED METHYLATION PROFILES
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Patients with Down syndrome (DS) and acute lymphoblastic leukemia (ALL) have distinct clinical and biological features. DS-ALL cases both lack the sentinel cytogenetic lesions that guide risk assignment and treatment planning in childhood ALL as well as represent a subset of patients that have greater susceptibility to treatment related toxicities such as infections and fatal sepsis. We sought to identify additional recurrent molecular abnormalities specific to DS-ALL. Such findings could provide prognostic information and guide the development of targeted therapies lacking the toxicities that conventional chemotherapeutic agents impose in this particularly vulnerable subset of patients. We performed genome-wide profiling using DNA copy number, loss of heterozygosity, gene expression, and methylation analyses of 58 DS-ALL and 68 non-Down syndrome (NDS) ALL cases with their paired germline DNA when available. We report a novel deletion within the 6p22 histone gene cluster as significantly more frequent in DS-ALL, occurring in 11 DS (22%) and only two NDS cases (3.1%) (Fisher's exact p = 0.002). Homozygous deletions yielded significantly lower histone expression levels and were associated with higher methylation levels, distinct spatial localization of methylated promoters, and enrichment of highly methylated genes for specific pathways and transcription factor binding motifs. Altered gene methylation patterns have been shown to play a part in tumorigenesis through gene silencing. In conclusion, we believe that further characterization of the etiology of these genetic alterations, and characterization of their functional effects may identify opportunities for novel targeted interventions.
The presence of lymphovascular invasion (LVI) is known to be an independent predictor of disease-related mortality in patients undergoing radical cystectomy (RC) for transitional cell carcinoma (TCC) of the bladder. This study sought to determine whether the presence of LVI on precystectomy TURBT was associated with pathological upstaging and node-positive disease. The Columbia University Urologic Oncology database was queried for patients who had data from their transurethral resection of bladder tumor (TURBT) prior to RC from 1990-2010. Patients were divided based on the presence or absence of LVI on precystectomy TURBT. Specimens were deemed LVI positive if any single TURBT prior to RC yielded evidence of this feature. Clinical and pathological variables were assessed between groups and the rate of upstaging and node positive disease determined for each respective cohort. The groups were compared using chi-square and cox regression analysis. Within a cohort of 564 patients, who had TURBT data prior to cystectomy, 423 had no evidence of LVI at the time of biopsy and 141 had LVI. The mean follow-up period was 43.9+/-48.7 mo. The groups did not differ with respect to demographic variables; however, the LVI group had a significantly lower proportion of patients with nonmuscle invasive disease as compared to their counterparts (46/95 (48.4%) vs. 177/246 (71.9%); p<0.001). The LVI group had a significantly lower proportion treated with intravesical therapy prior to cystectomy (14/141 (9.9%) vs. 83/423 (19.6%); p=0.008). Furthermore, although the groups did not differ with respect to adjuvant chemotherapy exposure, there was a greater number of patients in the LVI group who had adjuvant chemotherapy 26/141 (18.4%) vs. 36/423 (8.5%); p<0.001. The positive surgical margin rate was higher in the non-LVI group, but not significantly (27/423 (6.4%) vs 16/141 (11.3%); p=0.054). On final pathology the groups did not differ with respect to the presence of CIS or high grade disease. The presence of LVI on precystectomy TURBT did not correlate with an increased upstaging risk on univariable analysis (OR 0.98, CI0.90-1.07; p=0.744). However, the presence of LVI was a significant predictor of positive nodal status (OR 1.17, CI 1.09-1.26; p<0.001). On multivariable analysis, the presence of LVI correlated with pathological node positive disease when controlling for high grade disease and stage (OR 1.13, CI 1.05-1.22; p=0.002).

The heart is a plastic organ which undergoes pathological or physiological remodeling in response to a variety of stimuli to meet the demands of the body. Chronic exercise training promotes a physiological remodeling response in which the heart increases in size and function to match loading demands. Recent reports have implicated microRNAs as key mediators of pathological cardiac remodeling, yet the role of microRNAs in physiological cardiac remodeling has not been explored. The aim of the current study was to identify microRNAs regulated in the heart after voluntary exercise training. We found miR-499, previously identified as a member of a family of microRNAs which are encoded by myosin genes and are required for pathological remodeling, was down-regulated in the heart following 2 weeks of voluntary running. To examine the function of miR-499 in response to exercise training, we over-expressed miR-499 in the heart and found diminished physiological cardiac growth, whereas genetic and anti-miR mediated knockdown of miR-499 showed enhanced physiological growth. We also show that miR-499 represses multiple components of the IGF-1/PI3K/Akt and beta-catenin signaling pathways, which drive physiological growth of the heart. Finally, we have identified several direct targets of miR-499 including PurB, Ptpb2, Fzd4 and Lin7c, which may contribute to the physiological cardiac remodeling response. Thus miR-499 functions as an important negative regulator of exercise-induced physiological cardiac hypertrophy.
LIVER HYPODENSITIES: A COMPARISON OF AUTOPSY AND CT FINDINGS FROM THE UTMB COMpendium OF Radiological-Anatomical Correlation

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BACKGROUND: Radiologic-Pathologic correlative research has vastly improved the clinical impact of diagnostic radiology imaging and our omnibus understanding of disease presentation. The primary aim of the UTMB Compendium of Radiological-Anatomical Correlation (CRAC) is to provide a rich understanding of human pathology through the juxtaposition of antemortem radiological imaging and associated postmortem autopsy findings for students, residents, and practicing physicians. A further benefit may be to familiarize users with common, yet discipline-specific jargon. In this pilot study, we sought to demonstrate the utility of the CRAC in investigating the pathology underlying the radiological finding of liver hypodensities.

METHODS: We queried the UTMB CRAC, currently consisting of the 215 autopsy cases performed at UTMB during 2010, for the terms “hypodense” and “hypodensity” as they pertained to antemortem radiology of the liver and identified 15 cases. These cases were evaluated for corresponding postmortem autopsy gross and microscopic findings. One case was excluded due to restrictions associated with a limited autopsy. RESULTS: Of the 14 cases identified, average age was 55.9 (±12.8) years, 13 were male, 5 were African American, 5 were Caucasian, and 2 were Hispanic. With one exception, all lesions were identified at autopsy as neoplastic. The exception was a case in which no lesion was identified on autopsy and a single, small lesion was noted on imaging. 64% of lesions were primary liver neoplasias with the remainder being metastases from lung, colon, and cervix. The most common finding on histology was necrosis (71%), followed by fibrosis (41%) and hemorrhage (21%). In all cases where an antemortem diagnosis was made, there was consensus with the autopsy findings. CONCLUSION: The UTMB CRAC is an educational tool that allows retrospective linear review of cases from death to initial diagnosis. In this study, we sought to illuminate the spectrum of findings that contribute to the frequently-used radiology term “hypodensity,” as applied to the liver. From these data, it seems that tumors that appear hypodense on CT imaging tend to be necrotic and hemorrhagic and are frequently accompanied by fibrosis (underlying cirrhosis or desmoplastic reaction).

COMPARISON OF ISOTROPIC AND HIGH TEMPORAL RESOLUTION, DYNAMIC (TWIST) AND NON-DYNAMIC HIGH SPATIAL RESOLUTION 3D CONTRAST ENHANCED MRA AT 3 T, USING DSA AS A REFERENCE STANDARD, IN A PORCINE MODEL CAROTID ANEURYSM

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PURPOSE: Time resolved contrast enhanced 3D MRA (TWIST), optimized for either spatial or temporal resolution, was compared to conventional non-dynamic contrast enhanced MRA (CE-MRA) with DSA performed as the reference standard. METHOD AND MATERIALS: In 8 domestic swine, bilateral aneurysms were surgically created of the common carotid artery, in this IACUC approved study, using a pouch derived from a segment of the left external jugular vein (modeling an intracranial aneurysm). CE-MRA was performed at 3 T (Verio, Siemens Medical Systems, Erlangen, Germany) employing gadobutrol (Gadovist, Bayer Healthcare, Berlin, Germany). CE-MRA sequences optimized for temporal (TWISTt) vs spatial (TWISTs) resolution, were performed (0.5 sec scan acquisition with a 1.4 x 1.1 x 3.0 mm3 voxel size vs 2.2 sec with 1.2 x 1.2 x 1.2 mm3) and compared to non-dynamic high spatial resolution CE-MRA (0.9 x 0.9 x 0.9 mm3). Biplane DSA was performed for further quantitation. The dimensions of the aneurysm (n=16), as well as the aneurysm neck, were measured independently on all images, in three dimensions, by two viewers. The scan sequences were also ranked in a consensus read assessing 4 qualitative measures.

RESULTS: The mean absolute difference in size from DSA to TWISTt, TWISTs and conventional CE-MRA was as follows: AP 7.2, 1.5 and 1.5 mm; CC 1.7, 1.1 and 1.0 mm; RL 1.1, 1.0 and 0.6 mm and neck 2.6, 1.5 and 1.4 mm respectively. CE-MRA was more accurate than TWISTt in all measurements and showed no statistical difference with TWISTs in all but one measurement, CE-MRA was marginally superior to TWISTs in measuring the RL diameter. The CE-MRA and TWISTs ranked similarly on the qualitative assessment, with the exception of venous overlay where CE-MRA ranked the worst and depiction of aneurysm boundaries where CE-MRA was marginally superior to TWISTs. CONCLUSION: Dynamic CE-MRA using TWIST, applied in combination with a 1 M gadolinium chelate formulation, is capable of depicting fine vascular anatomical detail and is likely suitable to replace in some applications more conventional non-dynamic imaging, allowing as well a reduction in administered contrast dose.
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EFFECTS OF A WOOD-STOVE MODEL INTERVENTION IN RURAL NICARAGUA: A PILOT STUDY
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Indoor air pollution affects people across the world, especially women and children living in rural areas of developing countries. The smoke from these stoves exposes the women using them to a variety of pollutants including high levels of particulate matter. These pollutants have been associated with several adverse outcomes, including chronic obstructive pulmonary disease and low birth weights in infants born to exposed mothers. Areas for intervention exist via stove change out programs which exchange the traditional, high pollution stoves for models that either remove the smoke from the indoor environment or rely on more cleanly burning fuels to decrease smoke exposure. A cross-sectional pilot study was employed to assess the effects of an improved stove model on lung function and particulate matter levels in rural Nicaragua. We determined that there is no association between stove-model and lung function (percent predicted value) in a population of women who were the primary cook in the home (Wilcoxon Rank Sum; p=0.36). This study demonstrates no correlation between reported symptoms of wheezing or shortness of breath and stove type (Fisher’s Exact Test; p=1 and p=0.18, respectively). Particulate matter concentration sample sizes differed amongst stove models but were too small to measure statistical correlations (n = 10, improved stove = 26.06 μg/m3, traditional stoves = 64.61 μg/m3, outdoor stoves 29.09 μg/m3). From this pilot, the feasibility of a larger, more comprehensive study is assessed and several qualitative factors that can influence the benefits of smoke-reducing stoves are elucidated.

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INTERFERON GAMMA VERSUS AMANTADINE IN COMBINATION WITH INTERFERON ALPHA-2B AND RIBAVIRIN IN CHRONIC HEPATITIS C GENOTYPE 3 NON-RESPONDERS AND RELAPSERS
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Background: When administered simultaneously, interferon-alpha 2b + interferon-gamma result in dramatic antiviral synergy. Ribavirin has shown to enhance interferon-gamma levels in patients with chronic hepatitis C treated with interferon-alpha. Considering the antiviral effects of gamma interferon and favorable effects with interferon alpha and ribavirin, it seems logical to use a regimen combing gamma interferon with interferon alpha plus ribavirin in patients who have not responded to the combination of last two drugs.

Objective: The aim of the present study was to evaluate the efficacy and safety of triple combination regimens comprising of interferon alfa-2b and ribavirin plus either interferon gamma or amantadine in HCV genotype 3 infected patients who have not previously responded or relapsed to interferon alpha (standard or pegylated) in combination of ribavirin.

Methods: Patients were randomized to receive interferon alpha 2b 3MU thrice a week, ribavirin 800-1200 mg per day with either interferon gamma 2 MU thrice a week or amantadine 100 mg twice daily. Treatment was continued for 48 weeks in patients showing complete or partial (2 log reduction) early virological response (EVR) at 12 weeks and negative PCR at 24 weeks.

Results: Total enrollments were 44. Mean age 44.1 years (28-60) ; 25 were previously non-responders out of them 12 were in the gamma arm. Nineteen were relapsers, out of them 10 received Gamma interferon. F3 or F4 fibrosis was seen in 14 (34%) and 9 (23%) were diabetic. By intention-to-treat analysis, the overall early virological response (EVR) with triple regimens was 61.4% (27/44). The EVR for interferon gamma arm was 72.7% (16/22) and for amantadine arm 50% (11/22) (p = 0.089). Sustained virological response (SVR) with both triple regimens was seen in 38.6% (17/44). SVR was 50% (11/22) in the gamma arm and 27.27% (6/22) in the amantadine arm (p=0.122). In the subgroup analysis, this figure was 60% (6/10) and 44% (5/9) for relapers (p=0.645), and 41.6% (5/12) and 7.69% (1/13) for non-responders in both arms respectively (p=0.047). Treatment was well tolerated in both arms. Conclusions: About one third of genotype 3 patients who had not previously responded well to the interferon and ribavirin responded to the triple regimens. However addition of interferon gamma was a better option with an acceptable safety profile. Its combination with pegylated interferon and ribavirin needs further evaluation.
Poster 125
VARIATIONS IN PRESENTATION OF CELIAC DISEASE IN ADULTS AND ITS ASSOCIATION WITH OTHER CONDITIONS.
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Background: Celiac disease (CD) is an autoimmune enteropathy triggered by ingestion of gluten in genetically susceptible individuals. It has extremely varied clinical presentations. Though the disease is well described in children, it is often missed in adults by treating physicians due to lack of awareness. Objective: To evaluate the variations in presentation of celiac disease in adults and its association with various conditions. Methods: This retrospective study was conducted by reviewing the file records of the patients admitted during the last 10 years at the Aga Khan University Hospital. Patients diagnosed with celiac disease greater than 15 years of age were included in the study. Diagnosis was established by detecting raised tissue transglutaminase antibodies in serological tests and supportive biopsy findings. Results: A total of 31 patients were included in the study consisting of 61.3% males and 38.7% females ranging from 15 to 51 years of age (mean 27.55 ±9.93). Of the total patients 32% of the patients were underweight (BMI<18.5). Typical presentation with gastrointestinal (GI) symptoms was seen in 71% of the patients, atypical presentation with extra intestinal manifestations in 12.9% and silent presentation with no symptoms was seen in 10.3%. Predominant GI symptoms included diarrhea (in 71% patients), vomiting (in 41.9%), anorexia (in 22.6%) and abdominal pain (in 26%). Predominant extra intestinal manifestations include iron deficiency anemia in 29% of the individuals, vitamin B12 deficiency anemia in 16%, folic acid deficiency anemia in 10%, vitamin D deficiency in 12.9%, osteoporosis and osteomalacia in 3.2% each, renal calculi in 6.4%, arthritis in 3.2%, myopathy in 3.2% and 16% had raised ALT levels. Endoscopies revealed duodenal ulcer in 12.8% patients and gastritis in 35%. Biopsy findings revealed partial villous atrophy in 46.4% of the patients, complete villous atrophy in 35.5%, cryptal hyperplasia in 9.7% and intraepithelial lymphocytosis in 6.5%. H.pylori infection was seen in 48.4% of the patients with CD, irritable bowel syndrome (IBS) in 6.5% and giardiasis in 3.2%. Conclusion: Celiac disease in less common in adults but does exist and may present at any age. It should be looked for in underweight patients and patients with IBS, anemia, vitamin D, B12 and folic acid deficiency, arthritis and other related conditions.

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PREVALENCE OF MALNUTRITION(WASTING,STUNTING,UNDERWEIGHT AND OVERWEIGHT) AMONG SQUATTER SETTLEMENTS OF A METROPOLITAN
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OBJECTIVE: To determine the Prevalence of Malnutrition (Wasting, Stunting Underweight & Overweight) among Children of squatter settlement in the metropolitan city of Karachi (Arafat Town, Lyari & mehmoodabad). METHODS: Descriptive cross-sectional study. The sample size of 350 children aged between 6 and 59 months was calculated with a WHO software. The sample and target population size allowed a correction factor leading to a smaller sample size of 300 children. Main outcome measures are Present Weight in Kg, Present Height in cm, Mid Arm Circumference in inches. RESULT: Z scores for height for age, weight for age, and weight for height were applied on data. According to this, the prevalence of stunting was estimated up to 32%, underweight were 27%, Wasting was estimated up to 27% and the frequency of overweight was estimated 5%. Out of 300 children 19% were severely stunted, 9% severely underweight and 5% were severely wasted. CONCLUSION: The study revealed that stunting was most prevalent followed by underweight, wasting and obesity. Wasting and Underweight is more common in Females, while Stunting is more common in Males. Lower Age group is more affected than higher Age group. Early and aggressive nutritional intervention is required, if long-term outcomes are to be improved in the metropolitan city of Karachi. KEYWORDS: Prevalence, stunting, wasting, underweight, overweight, Z-score.
Poster 131
THE EFFECTS OF RELIGIOUS ATTENDANCE AND OBESITY
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The objectives of this paper are to examine the effects of religion and obesity on health and determine how the relationship varies by racial/ethnic groups with data from the Panel Study of American Race and Ethnicity (PS-ARE). Using ordinal logistic regression, the effects of religion and obesity on self-rated health and how the relationship varies by racial/ethnic groups are investigated. Additionally, to determine whether certain ethnic groups are more impacted by the frequency of religious attendance and obesity, whites, blacks, and Hispanics are analyzed separately with ordinal logistic regression. Adding obesity in focal relationship between religious services attendance and self-rated health strengthened this focal relationship which is a suppression effect between religious services attending and self-rated health adding obesity. In only white subjects, less attendance at religious services is more associated with self-rated health than attending religious services more frequently. The frequency of religious services attendance of blacks and Hispanics are not associated with self-rated health. For BMI, being white is more positively associated with increased odds of reporting better health than black and Hispanic subjects. Although white subjects are less likely to attend religious services more frequently than black and Hispanic subjects, the influence on self-rated health in white subjects is more evidenced than other racial/ethnic groups.

Poster 134
SELECTIVE STIMULATION OF THE 5-HT2CR SIGNALOSOME IS ASSOCIATED WITH INCREASED BASAL AND REDUCED 5-HT2CR-EVOKED LEVELS OF NOVELTY INDUCED MOTILITY
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Dysregulation in limbic-corticostriatal serotonin (5-HT) 2C receptor (5-HT2CR) function is implicated in a variety of neuropsychiatric conditions. However, little is known about 5-HT2CR regulation in vivo or how disruption of 5-HT2CR regulation may contribute to neuropsychiatric illness. To gain a better understanding of 5-HT2CR regulation, we tested the hypothesis that stimulation of the 5-HT2CR signalosome following repeated, intermittent pretreatment with the selective 5-HT2CR agonist WAY 163909 will result in a pattern of behavioral tolerance and associated molecular adaptations. Male Sprague-Dawley rats were pretreated once daily for 7 days with saline (1 ml/kg, i.p.) or WAY 163909 (10 mg/kg, i.p.). Weights were recorded daily. On day 8, rats received either a challenge injection of saline or WAY 163909 (10 mg/kg, i.p.), and motility induced upon exposure to a novel environment was measured (90 min). Brain tissue was immediately collected and frozen for future biochemical analysis of 5-HT2CR mRNA and protein expression. Interestingly, upon injection with saline, rats exposed to repeated WAY 163909 pretreatment exhibited elevated ambulations compared to saline-treated controls (p<0.05). As expected, acute challenge with WAY 163909 suppressed motility relative to vehicle controls, while repeated pretreatment with WAY 163909 blunted the WAY 163909-evoked hypomotility (p<0.05). Thus, repeated WAY 163909 pretreatment increases motility in response to a novel environment, suggesting desensitization of both tonic and agonist-induced 5-HT2CR signaling. Quantitative RT-PCR analyses revealed that repeated WAY 163909 administration did not alter 5-HT2CR mRNA levels in the nucleus accumbens, dorsal striatum, or hippocampus, indicating that alterations in 5-HT2CR transcription in these brain regions do not underlie the increase in novelty-induced motility associated with repeated WAY 163909. Studies are underway to examine WAY 163909-induced alterations in expression of the 5-HT2CR protein and protein complexes through Western blot and co-immunoprecipitation assays.
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MET SIGNALING PROMOTES PANCREATIC TUMORIGENESIS

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Background: Pancreatic Ductal Adenocarcinoma (PDAC) is the 4th leading cause of cancer deaths in the United States. In the past thirty years there has been no significant improvement in the 5-year survival rates for PDAC patients. These statistics underlie the importance of investigating the molecular mechanisms that drive PDAC tumorigenesis in order to develop effective therapies to treat this disease. The Met receptor tyrosine kinase and its ligand Hepatocyte Growth Factor (HGF) are often over expressed in PDAC. Increased Met signaling has been implicated in PDAC tumorigenesis given its role in increasing cell proliferation, survival and motility. However it remains unclear whether increased pancreatic Met expression drives tumorigenesis and is therefore a potential therapeutic target to treating disease progression.

Objective: To test the hypothesis that Met signaling drives PDAC tumorigenesis.

Methods: RNA interference was used to stably knock down Met expression in two human PDAC cell lines. The effect of Met knock down on cell proliferation, growth in soft agar and motility was measured in vitro. The role of Met signaling in PDAC tumorigenicity was assessed following the orthotopic injection of control or Met knock down cells into the pancreas of nude mice. The effect of Met knock down on cell proliferation, growth in soft agar and motility was measured in vitro. The role of Met signaling in PDAC tumorigenicity was assessed following the orthotopic injection of control or Met knock down cells into the pancreas of nude mice.

Results: In control PDAC cells, HGF treatment increased cell proliferation, growth in soft agar and cell migration in a scratch assay. Conversely, PDAC Met knock down cells did not show increased growth or cell migration in response to HGF. The effects of reduced Met expression on cell growth and migration were similar using two different PDAC cell lines tested indicating that the role of Met signaling in pancreatic cancer is not cell line specific. Using an orthotopic animal xenograft model of pancreatic cancer, implantation of Met expressing control cells and Met knock down cells resulted in primary tumor growth in vivo. However tumors initiated by Met knock down cells were significantly smaller then those initiated using control cells. Additionally animals inoculated with Met knock down cells displayed reduced peritoneal metastases as well as distal metastasis in the liver and lung.

Conclusion: This data supports the conclusion that increased Met signaling is important for PDAC tumorigenesis. Thus the HGF-Met signaling axis represents a potential target for therapeutic intervention in PDAC.

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DEVELOPMENT OF A NOVEL GELATIN-FIBRONECTIN CRYOGEL AS A SUPPORTING MATERIAL FOR STEM CELLS

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The isolation and description of mesenchymal stem cells (MSCs) from human umbilical cords has recently been reported (K. Kita et al. (2010) Stem Cells Dev., 19, 491-502). In order to use MSCs as a part of wound coverage, a supporting material must be developed. Here we describe a bio-degradable, easily prepared and inexpensive sponge-like gel that supports the growth of human cells. The material was developed using gelatin and fibronectin (FN). FN provides the added advantage of promoting wound healing. Gelatin (4.3%) was mixed with a minimum amount of FN (0.03%) on ice. Addition of varying concentrations of glutaraldehyde initiated the cross-linking of the matrix. The mixture was then frozen at -20°C overnight. The pore size of the sponge-like structure was approximately 80-200μm. Both light and electron microscopic images indicate that higher concentrations (0.3-0.5%) of glutaraldehyde resulted in the formation of denser mesh structures. The use of lower concentrations of glutaraldehyde produced a less dense mesh material that was softer in nature. Nuclear staining showed that both MSCs and human foreskin fibroblasts migrated into the gels and survived for up to 1 month with no apparent cytotoxicity. Although the softer gels were sensitive to trypsin digestion when gels were incubated in a 0.005% trypsin solution, highly cross-linked gels took longer to degrade (16 hours). Also, the gelatin-FN gels were less sensitive against trypsin digestion in comparison to gelatin-fibrinogen gels. The gelatin-FN gels are stable for a minimum of one week in cell culture, implying slow degradation/absorption during in vivo applications. We also prepared a sheet-like prototype of this gel for future animal trials and clinical applications. In conclusion, we successfully developed gelatin-FN cryogels for use with MSCs. The healthy growth of cells in the materials suggests negligible cytotoxicity by this new material. Our material may be useful as a carrier to build up artificial tissues/organs.
Increased oxidative stress has been linked to the development of insulin resistance and its progression to diabetes. Studies in skeletal muscle and adipose cells suggest a role for reactive oxygen species (ROS) in impairment of the insulin signaling pathway. However, the exact mechanism by which ROS lead to impairment of insulin signaling is not well understood. Furthermore, cellular mechanisms for hepatic insulin resistance are still lacking. Studies have shown increased basal activation of the stress-signaling kinase p38 MAPK in obese and/or diabetic subjects, while other studies show an association between oxidative stress and activation of the stress-response pathway. Therefore, our research focused on primary mouse hepatocytes to demonstrate whether (1) ROS production from the mitochondrial electron transport chain complex I (ETC CI), using the complex I inhibitor Rotenone, inactivates the insulin signaling pathway; and (2) p38 stress-response pathway is involved in the mechanism of ROS-induced impairment of the insulin signaling pathway. Young C57BL/6 mice are used for liver perfusion and the primary hepatocytes are treated with insulin, Rotenone, N-acetylcysteine, or the p38 inhibitors SB203580 and SB202190; cells were harvested and the cytoplasmic proteins subjected to western blot analysis. Our results show that (a) Rotenone induces IRS-1 Ser307 phosphorylation, that is inhibited by NAC treatment or by either of the p38 MAPK inhibitors, SB203580 and SB202190, indicating that Rotenone-induced generation of ROS inactivates the IRS1 in a p38 MAPK-dependent manner; (b) Both basal and insulin-stimulated AKT Ser473 phosphorylation, as well as GSK3 Ser9 phosphorylation are inhibited with Rotenone treatment, indicating hepatic insulin resistance; and (c) The Rotenone-induced inhibition of basal and insulin-stimulated AKT Ser473 as well as GSK3β Ser9 phosphorylations is not affected by the use of p38 MAPK inhibitors, indicating that Rotenone-induced insulin resistance may have more than one mechanism; p38 MAPK-dependent mechanism for the inhibition of the proximal end of insulin signaling, and a p38 MAPK-independent mechanism for the inhibition of the distal end. Our results indicate that in vitro oxidative stress in primary mouse hepatocytes leads to substantial insulin resistance both in the proximal as well as the distal ends of the insulin signaling in part due to a p38 MAPK-dependent mechanism. Furthermore, this study is a novel one to show that the

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POINT MUTATIONS IN THE inc ANTISENSE RNA GENE ARE ASSOCIATED WITH INCREASED PLASMID COPY NUMBER, EXPRESSION OF blaCMY-2, AND RESISTANCE TO PIPERACILLIN-TAZOBACTAM IN E. COLI.

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Background: High-level expression of plasmid-encoded AmpC β-lactamases is associated with resistance to almost all β-lactam antibiotics, including β-lactam/β-lactamase inhibitor combinations such as piperacillin-tazobactam, but the mechanisms that promote high-level expression are largely unknown. blaCMY-2 is the most prevalent plasmid-encoded AmpC β-lactamase gene found in E. coli worldwide, and IncI plasmids are a common framework for blaCMY-2. Replication and copy number of IncI1 plasmids are controlled by antisense RNA from the plasmid gene inc, and point mutations in the hairpin loop region of inc have been shown to increase copy number of IncI1 mini-plasmid models. Objective: This study sought to determine if inc point mutations and plasmid copy number changes were responsible for increased blaCMY-2 expression in three piperacillin-tazobactam selected E. coli mutant strains with blaCMY-2 encoded on a 100 kb IncI1 plasmid. Methods: The mutant strains were selected by exposing their parent strain to super-inhibitory concentrations of piperacillin-tazobactam. Relative blaCMY-2 transcript level, gene copy number, and plasmid copy number were measured for parent and mutant strains by real-time PCR. The DNA sequence of inc and its promoter region were examined for all strains. Results: Mutant strains had 3- to 13-fold higher blaCMY-2 transcript levels, and 8- to 100-fold higher piperacillin-tazobactam minimal inhibitory concentration levels than their parent strain. blaCMY-2 copy number and IncI1 plasmid copy number were found to be increased in correlation with the blaCMY-2 transcript level. Two mutant strains with 8- and 13-fold higher IncI1 copy number had single point mutations located within the hairpin loop region of inc. Conclusions: This is the first report of inc point mutations being associated with increased copy number of a full-sized clinical IncI1 plasmid. This is also the first report of increased IncI1 plasmid copy number being associated with increased blaCMY-2 expression and piperacillin-tazobactam resistance. inc point mutations such as those seen in this study may occur clinically and result in the increased expression of other IncI1-encoded resistance mechanisms by increasing plasmid copy number.
Head and neck cancers are the sixth most common cancers worldwide and more than 90% are squamous cell carcinomas. Even with extensive research and advancements, the patient survival rate remains at 5 years. Since HER2/ErbB2 receptor tyrosine kinase is over-expressed in many head and neck cancers, and because these kinases are implicated in tumor progression by means of upregulating proteases, we hypothesize that HER2 induction of disintegrin and metalloprotease (ADAM) protease increases cell migration and invasion. Using a panel of 11 oral SCC cell lines and modulation of HER2 by transfection or siRNA knockdown, we found that expression of the metalloprotease ADAM12 was increased by HER2. UM-SCC74A, having lower HER2 levels, was derived from a HNSCC tongue tumor. UM-SCC74B, having elevated HER2 levels, was obtained from tumor recurrence at the base of the tongue one year after the initial biopsy. ADAM12 expression was approximately six-fold higher in UM-SCC74B cells compared to UM-SCC74A. The higher ADAM12-expressing UM-SCC74B migrated approximately 50% faster than UM-SCC74A according to a cell culture scratch migration assay (P ≤ 0.001). ADAM12-targeted siRNA significantly decreased ADAM12 transcripts, as well as the migration of UM-SCC74B cells also by a scratch assay (P ≤ 0.05). In addition, higher ADAM12-expressing UM-SCC74B cells invaded through a matrigel in a Fluorblok transwell plate assay to a greater extent than the lower expressing UM-SCC74A (P ≤ 0.05). Furthermore, upregulation of ADAM12 in UM-SCC74A cells increased both ADAM12 transcripts and invasion (P ≤ 0.05). From these data, we conclude that ADAM12 increased tumor cell migration and invasion, suggesting that ADAM12 may also contribute to oral SCC progression in vivo.

The multifocal electroretinogram (mERG) is a useful test for evaluating retinal function, particularly of the outer retina, while frequency-domain optical coherence tomography (fdOCT) is an important clinical tool for visualizing retinal structure in vivo. Although the two testing modalities often agree in demonstrating retinal abnormalities, disagreements can occur. In this study, eyes with abnormal visual fields (VFs) and mERGs but normal appearing fdOCT scans were analyzed by measuring the thicknesses of the outer retinal layers. Testing for all patients included static automated perimetry (Zeiss Meditec), mERG (103 scaled hexagons, Veris, EDI), and fdOCT imaging (OCT 2000, Topcon) with 3D and line scans of the macula (central 10°). All patients had reliable VFs (indices < 33%) showing macular defects and good quality mERG and fdOCT results. The mERG results were classified as abnormal based on decreased amplitudes and/or increased latencies in the region of the abnormal VF. Based on visual inspection, three experienced observers graded the fdOCT scans as normal or inconclusive, as opposed to clearly abnormal. Retinal layers of the fdOCT scans were then manually segmented with the aid of a computer program and compared to mean thicknesses from 20 controls. The thicknesses of the outer segment plus RPE layer (OS+: Bruch’s membrane to inner-outter segment line), total receptor (REC: Bruch’s membrane to outer plexiform-inner nuclear layer (INL) border), and the INL were measured. One or more of the outer retinal layers was significantly thinner in 11 of the 25 eyes. The REC layer was significantly thinner in 10 eyes and OS+ layer in 8. These results suggest that (1) in some scans, quantitative analysis of fdOCT scans can demonstrate significant thinning of the outer retina that is not readily apparent on visual inspection, emphasizing the need for quantitative measures, and (2) in other cases, functional loss measured by VFs and mERGs can precede clear structural changes on fdOCT scans.
Debridement is one of the crucial steps for successful wound care. In addition to removing necrotic tissue, debridement has been shown to reduce wound-associated bacteria that delays healing. Two debridement methods recently developed are tangential hydrosurgery (TH) and coblation technology (CT). A controlled in-vivo study was conducted using a porcine wound model to compare the effectiveness of these two modalities in the removal of devitalized tissue and reduction of bacterial load. Partial thickness wounds were dyed black and photographed immediately before and after debridement to assess the ability to remove surface tissue. After treatment with CT and TH, the percentage of dye remaining was 6.27% and 6.72%, respectively. Additional wounds were inoculated with methicillin-sensitive Staphylococcus aureus (MSSA) and debrided with either CT or TH at 20 minutes (planktonic bacteria) or 24 hours (biofilm) and compared to non-debrided controls. At 20 minutes, both CT and TH treated wounds showed a statistically significant reduction of MSSA compared to No Debridement (2.14±0.01 and 1.24±0.38 Log CFU/g, respectively) with CT resulting in a greater reduction than TH (p<0.05). At 24 hours, only CT treated wounds showed a statistically significant reduction of MSSA when compared to No Debridement (2.40±0.12 Log CFU/g) (p<0.05). This study demonstrates that while both CT and TH were effective in removing devitalized tissue and wound associated bacteria, CT was superior to TH in the reduction of planktonic bacteria, and was the only modality effective against biofilm-associated organisms. Further studies are warranted to assess the effect of these novel debridement modalities on wound healing.

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A PTSD MOUSE MODEL: PHARMACOLOGIC VALIDATION AND MEASURES OF ETHANOL CONSUMPTION IN THE PREDATOR EXPOSURE PARADIGM
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Abstract
Post-Traumatic Stress Disorder (PTSD) is classified by the Diagnostic and Statistical Manual of Mental Disorders 4th ed. (DSM-IV) as an anxiety disorder that can develop after exposure to a terrifying event or ordeal in which grave physical harm occurred or was threatened. Traumatic events that may trigger PTSD include violent personal assaults, natural or human-caused disasters, accidents, or military combat. Diagnostic symptoms include re-experiences, such as flashbacks and nightmares, avoidance of stimuli associated with the trauma, increased arousal, such as difficulty falling or staying asleep, anger and hypervigilance. PTSD is defined by the coexistence of three clusters of symptoms: re-experiencing, avoidance and hyperarousal, which persist for at least 6 months in survivors of the event. In the general U.S. population, the lifetime prevalence rate for PTSD is estimated to be 8-9%, with the rate for women being as much as two-times that for men. Up to 25% of patients diagnosed with PTSD may also have alcohol use disorder. Unique behavioral characteristics associated with PTSD have a counterpart in rodent behavior. Of the available rodent models of PTSD, the predator exposure paradigm employs a life-threatening experience, which is one of the distinguishing characteristics of traumatic events, rather than simply stressful or painful ones. This study aimed to identify distinguishing features of mice displaying PTSD-like behaviors and mice displaying PTSD-like symptoms accompanied by depressive symptoms. Following behavioral testing and classification, ethanol (EtOH) consumption was measured in mice expressing depressive like symptoms following predator exposure in an effort to evaluate if there is a disparity between PTSD-like mice with depressive characteristics and control in ethanol consumption.