7TH ANNUAL AUB BIOMEDICAL RESEARCH DAY

Saturday, February 18, 2017

West Hall

9:00 am - 2:00 pm

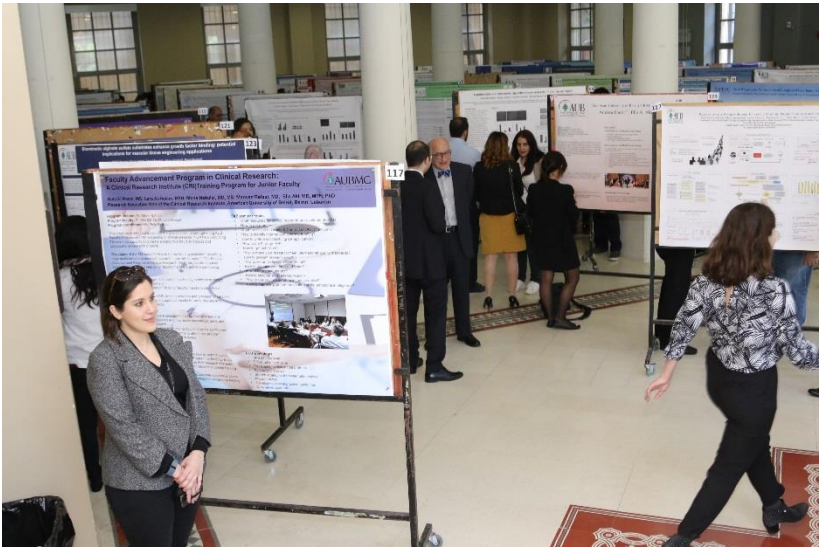
Organizing Committee

Chairperson

- Ayad Jaffa, Assistant Dean of Graduate Studies & Interdisciplinary Programs, FM, Department of Biochemistry and Molecular Genetics

Members

- Hala Muhtasib, FAS, Department of Biology
- Bilal Kaafarani, FAS, Department of Chemistry
- Marwan Sabban, FM, Department of Anatomy, Cell Biology and Physiological Sciences
- Lara Nasreddine, FAFS, Department of Nutrition and Food Sciences
- Rami Mhanna, FEA, Biomedical Engineering
- Nadine Darwiche, FM, Department of Biochemistry and Molecular Genetics
- Assaad Eid, FM, Department of Anatomy, Cell Biology and Physiological Sciences
- Miran Salameh Jaffa, FHS, Department of Epidemiology and Population Health
- Nathalie Zgheib, FM, Department of Pharmacology and Toxicology
- Hassan Zaraket, FM, Department of Experimental Pathology, Immunology and Microbiology
- Hala Darwish, HSON
- Samira Kaissi, FM, Basic Science Research
- Yumna Maalouf, FM, Medical Dean's Office
- Ali Nabbouh, FM, Graduate Student Affairs


Faculty Advancement Program in Clinical Research:
K Clinical Research Institute (CRI) Training Program for Junior Faculty
AUBMC
117

Student Awardees of the 2016 AUB Biomedical Research Day

- **Khalil Kreidieh**, FHS: *Clinical and Epidemiologic Characteristics of Norovirus Gastroenteritis in Lebanon among Hospitalized Children Less than Five Years Old*
- **Fatima Sleiman**, FM: *Short relative telomere length (RTL) in peripheral blood is associated with breast cancer risk in the Lebanese*
- **Mohammed Shahait**, FM: *Combined Multi-Parametric MRI & Targeted Biopsies Improve Detection of Clinically Significant Prostate Cancer*
- **Sally El-Sitt**, FM: *Exogenous Galactosylceramide (GalCer) as potential treatment for CLN3 disease*
- **Dima Diab El-Harakeh**, FAS: *Insights into the Deregulation of Caveolin-1 in Myopathic Laminopathies*
- **Leeanna El Houjeiri**, FM: *Antitumor Effect and Nanoparticle Drug Development of the Adamantyl Retinoid ST1926 in Acute Myeloid Leukemia*
- **Sarah Mantash**, FM: *Neural Stem Cells as a new cell-based therapy for Traumatic Brain Injury*
- **Nadia Soudani**, FM: *High Incidence of Respiratory Virus Co-infections among Pediatric Cancer Patients in Lebanon*
- **Hind Zahr**, FAS: *Proteomic Profiling of Nuclei from Lamin A/C-Deficient Mouse Embryo Fibroblasts by Differential Phage Display Screens*
- **Mohannad Khandakji**, FM: *Assessment of preventive and curative care in assessing the determinants of dental services utilization*
- **Rita Hleihel**, FM: Mutant *NPM-1*: a therapeutic target in Acute Myeloid Leukemia

2016 Farouk Jabre Award Recipients

- **Dr. Ramzi Alami**, FM and **Dr. Ali Tehrani**, FEA: *Novel Electrospun Surgical Meshes for Hernia Repair*

- **Dr. Issam El Rassi**, FM and **Dr. Ramsey Hamade**, FEA: *Building on a 3D printing Program for Congenital Heart Disease at AUB: A Model for Clinical Applications, Education and Research. The first initiative in Lebanon and the Region*

List of jury members for the 6th Annual Biomedical Research Day

Faculty of Medicine

1. Hiba El-Hajj
2. Marwan Refaat
3. Nathalie Zgheib
4. Elias Rahal
5. Lama Fawwaz
6. Assaad Eid
7. Fouad Zouein
8. Margret Shirinian
9. Elie Akl
10. Hassan Zaraket
11. Mazen Kurban
12. Souha Fares (Hariri School of Nursing)

Faculty of Arts and Sciences

1. Youssef Mouneimne
2. Diana Jaalouk
3. Malek Tabbal
4. Digambara Patra

Faculty of Agricultural and Food Sciences

1. Ammar Olabi
2. Omar Obeid
3. Lara Nasreddin

Faculty of Engineering and Architecture

1. Ramsey Hamade
2. Rami Mhanna

7TH ANNUAL AUB BIOMEDICAL RESEARCH DAY

Schedule of events

9:00 am - 9:45 am	Welcome note **Dr. Ayad Jaffa**, Assistant Dean for Graduate Studies and Interdisciplinary Programs **Dr. Ziyad Ghazzal**, Deputy Executive Vice President and Founding Director of the Heart and Vascular Clinical Center of Excellence ***Title:*** *The sesquicentennial of AUB Faculty of Medicine* 2017 Farouk Jabre Award Presentation *Dean Sayegh, Trustee Jabre*
9:45 am - 10:30 am	Keynote speaker to be introduced by Dr. Samia Khoury, Associate Dean for Clinical and Translational Research **Dr. Ziad Mallat**, Professor of Cardiovascular Medicine, University of Cambridge, UK ***Title:*** *Targeting the Immune Response in Cardiovascular Disease*
10:30 am – 11:15 am	Speaker to be introduced by Dr. Zaher Dawy, Professor, Department of Electrical and Computer Engineering **Dr. Thomas Heldt,** Helmholtz Career Development Professor, Department of Electrical Engineering & Computer Science, Massachusetts Institute of Technology ***Title:*** *Cardiovascular parameter estimation: from microgravity to the intensive care unit*
11:15 am – 2:00 pm	Poster viewing followed by lunch, award presentation for the top 10 posters and closing

Objectives

- serve as a platform to bring together the research community of different AUB faculties and to showcase the biomedical research performed at AUB
- provide an intellectual environment for scientific exchange among the various researchers at AUB
- provide a platform for students, postdoctoral fellows and junior investigators to present their scientific findings and to foster collaboration within the AUB family of investigators

Eligibility

- Students
- Trainees
- Residents
- Research Assistants
- Fellows
- Post docs

Keynote Speaker

Ziad Mallat, MD, PhD

Dr. Mallat received his MD and qualification in Cardiovascular Diseases from University of Pierre et Marie Curie in 1996, and his Ph.D. in Cardiovascular Physiology from University of Paris-Diderot in 1999. He joined INSERM, Paris in 1998 as Assistant Research Professor, and then became Associate Professor in 2002 and Research Professor in 2007. He is currently BHF Professor of Cardiovascular Medicine at the University of Cambridge, UK. He is on the Editorial Board of Circulation Research and Journal of Molecular Medicine, and is Associate Editor of Arteriosclerosis Thrombosis and Vascular Biology, Atherosclerosis and British Journal of Pharmacology. He served from 2004 to 2008 as a scientific advisor to the General Director of INSERM, France. He is co-founder and consultant for ATEROVAX, a biopharmaceutical company. Current research activities address the relation between autoimmune diseases and atherosclerosis, and the role of the regulatory immune response in the prevention and/or treatment of plaque vulnerability.

Speakers

Thomas Heldt, PhD

Thomas Heldt studied physics at Johannes Gutenberg University, Germany, at Yale University, and at MIT. He received the PhD degree in Medical Physics from MIT's Division of Health Sciences and Technology and undertook postdoctoral training at MIT's Laboratory for Electromagnetic and Electronic Systems and the Research Laboratory of Electronics. He currently holds the W.M. Keck Career Development Chair in Biomedical Engineering at MIT. He is a member of MIT's Institute for Medical Engineering and Science and on the faculty of the Department of Electrical Engineering and Computer Science.

Dr. Heldt's research interests focus on signal processing, mathematical modeling and model identification in support of real-time clinical decision making, monitoring of disease progression, and titration of therapy, primarily in neurocritical and neonatal critical care. In particular, Dr. Heldt is interested in developing a mechanistic understanding of physiologic systems, and in formulating appropriately chosen computational physiologic models for improved patient care. His research is conducted in close collaboration with clinicians from Boston-area hospitals, where he is integrally involved in designing and deploying high-quality data-acquisition systems and collecting clinical data.

Ziyad Ghazzal, MD

Dr. Ziyad Ghazzal earned his MD at AUB Faculty of Medicine and completed his residency in internal medicine at AUBMC in 1984. Dr. Ghazzal has upheld an academic rigor in all his professional life, becoming an internationally renowned interventional cardiologist who has excelled as a highly accomplished clinician, researcher, and teacher/ mentor. He was promoted to Professor of Medicine at Emory University, Atlanta, GA, where he has been a full-time faculty member since 1990, after completing his fellowship training at the same institution from 1985 to 1990.

Dr. Ghazzal has published extensively in the cardiology literature, including high-quality original papers and many other reviews, editorials, book chapters, and video seminars. He is regularly sought after by international organizations for clinical lectures, tutorials, and other CME activities in the area of interventional cardiology. As a director of the Interventional Fellowship Program at Emory, Dr. Ghazzal has played an instrumental role in the success of the training program there, one of the premier programs in the United States. He has been a member of a large number of prospective multicenter clinical trials, including being the local principal investigator at Emory. He was an associate editor of the popular 'Cardiosource', the official teaching website of the American College of Cardiology. He was also the co-chair of the international distant learning program of the College. He is an editorial consultant for JACC Cardiovascular Interventions and the American Journal of Cardiology.

Dr. Ghazzal is an Alpha Omega Alpha member and has received many honors, including the Medical Leadership Award from the National Association of North America, and the Excellence in Teaching Award from Emory University. In 2008 Dr. Ghazzal joined AUB where he currently functions as the Deputy to the Executive Vice President/Dean of the Faculty of Medicine and Medical Center in addition to his duties as an interventional cardiologist. He is the Founding Director of the Heart & Vascular Center of Excellence.


BIOTECKNO
RESEARCH & QUALITY SOLUTIONS
S.A.L


IBRA HADAD
ET FILS


KGT


numelab
Delivering solutions on the cutting edge of science


RAINBOW
s.a.r.l
The Second Generation Laboratory Supplier


SARAMED


Technoline
s.a.l
LABORATORY SOLUTION PROVIDER

ABSTRACTS

Abstract # 1

Novel Role for Sphingolipid Metabolism in Radiation Nephropathy

Tatiana El Jalkh[1], Batoul Dia[1], Anis Ahmad[5], Alla Mitrofanova[2,3,4], Brian Marples[5], Alessia Fornoni[2,4,6] , Assaad Eid[1], Youssef H. Zeidan[1,7]

[1]Department of Anatomy Cell biology and Physiological Sciences, American University Beirut, Lebanon .[2]Peggy and Harold Katz Family Drug Discovery Center, University of Miami, Miami, Florida, USA .[3]Department of Surgery, University of Miami, Miami, Florida, USA. [4]Department of Medicine, University of Miami, Miami, Florida, USA. [5]Department of Radiation Oncology, Miller School of Medicine/Sylvester Cancer Center, University of Miami, Miami, Florida, USA; [6]Division of Nephrology, Department of Medicine, University of Miami, Miami, Florida, USA; and. [7] Department of Radiation Oncology, American University of Beirut, Beirut, Lebanon

Corresponding author: Yousef H. Zeidan - M.D, PhD - E-mail: yz09@aub.edu.lb.

Funding source: Faculty of Medicine SEED Grant Funding.

Keywords: SMPDL3b, lipids, radioprotection, ceramide, cancer.

Descriptive Statement: The current study uncovers a central role for a membrane bound lipid enzyme, SMPDL3b, in mediating radiation induced damage of renal podocytes.

Introduction: The specific mechanisms and mediators involved in the development of radiation induced nephropathies are still largely unidentified. The role of renal podocytes in the pathogenesis of proteinuria in glomerular diseases is well established. Sphingomyelin phosphodiesterase acid like 3B SMPDL3b, a known off target of the anti CD20 antibody rituximab (RTX), is a lipid modulating enzyme that plays a major role in podocyte injury. The current study investigates the role of bioactive sphingolipids in radiation induced podocytopathy.

Methods: Immortalized human podocytes were propagated at 33ºC then thermoshifted at 37ºC for differentiation on collagen coated T75 flasks. A single dose of irradiation was delivered using a 250 KV radiation source. Podocytes were pretreated with rituximab (100µg/ml) for 30 minutes before irradiation. The metabolic activity and viability of the podocytes was assessed using the MTT assay and flow cytometry. Transcriptional and translational levels of SMPDL3b were measured by RT-PCR and Western Blot respectively. Cytoskeletal remodeling and morphological changes were detected using immunofluorescence microscopy. In vivo experiments were performed using C57BL6 mice subjected to bilateral kidney irradiation via a single dose of 14 Gy.

Results: The viability and metabolic activity of podocytes decreased after a single dose radiation injury. Cytoskeletal remodeling was observed post radiation; manifesting as loss of lamellipodia and remodeling of cortical actin. Moreover, ezrin, an actin binding protein, relocated from the plasma membrane to the cytosol as early as 2h post radiation. SMPDL3b protein was also downregulated in the irradiated murine kidneys. Post radiation, ceramide levels increased while S1P and sphingosine levels decreased. In contrast, overexpression of SMPDL3b and exogenous S1P rescued the podocytes from radiation induced cytoskeletal changes. RTX pretreatment served as a protective factor by rescuing podocytes from SMPDL3b loss and caspase-3 cleavage after radiation injury.

Conclusion: Our results show that radiation injury induces downregulation of SMPDL3b, and elevation of ceramide levels as well as early cytoskeletal remodeling. Overexpression of SMPDL3b and pretreatment with rituximab plays a radioprotective role in cultured podocytes. These findings suggest a potential role for SMPDL3b in radiation-induced podocytopathy.

Abstract # 2

Localization, expression and protein profiling reveal the ability of SLC35b4 to respond to glucose and inhibit glucose production through modulating molecular stress protein Hsp60 among others

Brigitte Wex[1]†, Rémi M. Safi[2]†, Gregory Antonios[1], Perla Z. Zgheib[3], Dania B. Awad[1], Firas H. Kobeissy[4], Rami A. Mahfouz[5], Marwan M. El-Sabban[2] and Soha N. Yazbek[3]**

1 Department of Natural Sciences, School of Arts and Sciences, Lebanese American University, Beirut, Lebanon

2 Department of Anatomy, Cell Biology and Physiological Sciences, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

3 Medical Laboratory Sciences Program, Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon

4 Department of Biochemistry and Molecular Genetics, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

5 Department of Pathology and Lab Medicine, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

Corresponding author: Soha Yazbek - Assistant Professor - E-mail: sy21@aub.edu.lb

Funding source: CNRS and URB

Keywords: Type II diabetes, SLC35b4, insulin resistance, subcellular localization, Hsp60.

Descriptive Statement: The human solute receptor SLC35b4 is associated with insulin resistance and gluconeogenesis in type II diabetes. This study aimed to investigate the subcellular localization and downstream protein targets of SLC35b4.

Introduction: SLC35b4, solute receptor for UDP-N-acetylglucosamine and UDP-xylose, is associated with diabetes and predisposing conditions. This study investigated regulation of protein expression, localization and differentially expressed proteins between a knockdown of SLC35b4 and controls in HepG2 cells.

Methods: Responsiveness to glucose, expression and localization were assayed using western blot and immunostaining. The localization was confirmed using PLA technique. 2D gel electrophoresis and MALDI-TOF were used to identify differentially expressed proteins; pathway analysis was performed to understand the downstream effect.

Results: SLC35b4 was increased by 60% upon glucose stimulation and localized in the Golgi apparatus and to a lesser extent endoplasmic reticulum. Presence of SLC35b4 in the Golgi apparatus confirms its involvement in the biosynthesis of glycoconjugate proteins. Four proteins were markedly under-expressed (Hsp60, HspA8, TUBA1A, and ENO1), and linked to the pathogenesis of diabetes or post-translationally modified by O-GlcNAc.

Conclusion: Our data suggest that glucose levels activate SLC35b4 expression and localization in the ER and Golgi apparatus, which in turn triggers a downstream effect via Hsp60 and other proteins; potentially via altering the glycosylation pattern; inside liver cells altering the ability to inhibit endogenous glucose production, and playing a triggering role in the association of the above listed genes with the pathogenesis of diabetes.

Abstract # 3

Sphingomyelin is Required for Efficient Influenza Virus Replication in Lung Epithelial Cells

Amani Audi[1,2,3], Nadia Soudani[2,3], jamilah borjac[1], Ghassan Dbaibo[3,4,5], Hassan Zaraket[2,3]

[1]Department of Biological and Environmental Sciences, Beirut Arab University, Faculty of Sciences, Lebanon. [2]Department of Experimental Pathology, Immunology and Microbiology, American University of Beirut, Faculty of Medicine, Lebanon. [3]Center for Infectious Diseases Research, American University of Beirut, Faculty of Medicine. [4]Department of Pediatrics and Adolescent Medicine, American University of Beirut Medical Center Faculty of Medicine, Beirut, Lebanon. [5]Department of Biochemistry and Molecular Genetics, American University of Beirut, Faculty of Medicine, Beirut, Lebanon

Corresponding author: Dr. Hassan Zaraket, email: hz34@aub.edu.lb

Funding source: This work was funded by MPP/, Faculty of Medicine, AUB.

Keywords: Influenza A virus (IAV), lipid rafts, sphingomyelin (SM), acid sphingomyelinase (ASMase).

Descriptive statement: influenza A virus (IAV) poses significant threat to human. The high evolution rate of influenza viruses results in the emergence of strains that are resistant to antiviral drugs or can no longer be encountered by annual vaccines. Therefore, it is important to better understand cellular factors involved in influenza virus life cycle, which can be then targeted to prevent infection.

Introduction: Sphingomyelinases (SMases) are enzymes that catalyze the hydrolysis of sphingomyelin (SM) into phosphocholine and ceramide. Attachment of some pathogens totheir receptors at the plasma membrane can activate acid sphingomyelinase (ASMase) and trigger the formation of ceramide platforms, which can modulate viral infections. IAV utilizes lipid rafts during its entry and budding from the cells, however, the details of entry mechanism and the role of SMases and their substrate SM in IAV infection have not yet been addressed. In this study, we aim to better understand the role of SM hydrolysis pathway in IAV pathogenesis.

Methods: The effect of desipramine, an ASMase inhibitor, on replication of IAV in human lung adenocarcinoma epithelial cell line (A549) was investigated. IAV replication in ASMase deficient fibroblasts (NPD cells) and normal human fibroblasts was assessed. ASMase activity was assayed in mock-infected and IAV-infected cells at different time points. Additionally, the effect of SM depletion using exogenous ASMase on IAV replication was examined. Viral titers were determined by either $TCID_{50}$ (50% Tissue Culture Infectious Dose assay) or plaque assay.

Results: Pharmacological inhibition of ASMase by desipramine had no effect on IAV replication in A549 cells. However, IAV replication in NPD cells was not compromised, but was rather enhanced compared to normal fibroblasts. In addition, ASMase activity levels were not changed in presence of IAV infection. Depletion of plasma membrane SM by exogenous ASMase reduced virus production, indicating that membrane SM might be required for IAV infection.

Conclusion: Our study reveals that ASMase negatively modulates IAV infection and that SM is an important modulator that is required for IAV replication. Studies to understand the exact mechanism underlying the modulation of IAV replication by SM are ongoing.

Abstract # 4

In vivo characterization of the underlying immunologic mechanisms of disease modulation in the context of _Toxoplasma gondii_ and influenza A virus co-infections

Najat Bdeir (student), Yolla German (student), Maguy Hamie (PhD student), Dr. Hassan Zaraket (Advisor) and Dr. Hiba El Hajj (Co-advisor)
Department of Experimental Pathology, Immunology, and Microbiology, Program and division of Microbiology and Immunology, American University of Beirut, Lebanon
Correspondence to: Dr. Hassan Zaraket, hz34@aub.edu.lb and Dr. Hiba El-Hajj, he21@aub.edu.lb
Funding source: MPP/URB
Key words: *Toxoplasma gondii*; influenza; co-infection; cytokines
Descriptive statement: This study investigates the immune mechanisms underlying disease modulation in the context of *Toxoplasma gondii* and influenza A virus (IAV) co-infection *in vivo*.

Introduction: *Toxoplasma gondii (T. gondii)*, an obligate eukaryotic intracellular protozoan parasite, is the causative agent of toxoplasmosis. In immunocompetent individuals, *T. gondii* infection in is asymptomatic; however, some patients may present with flu-like symptoms and sometimes lymphadenophathy. Contrarily, in immunocompromised patients, the infection may be life threatening. Another spectrum of the disease is congenial toxoplasmosis, which may lead to abortion, or severe fetal outcomes including mental retardation, hydrocephaly, microcephaly, chorioretinitis and impaired vision in newborn infants. Influenza A virus (IAV) is a major cause of acute respiratory tract infections in humans, which occasionally cause pandemics. Severe influenza infections are characterized by complications like pneumonia, encephalitis, and secondary bacterial pneumonia. Infection with *T. gondii* has been shown to modulate the outcomes of disease in the context of infection with other pathogens like *Helicobacter felis, Trichenalla spiralis, and Mycobacterium avium.* However, no studies investigated the disease outcome and underlying immunologic mechanisms of IAV infection in the context of acute toxoplasmosis. Therefore, the aim of this study is to characterize the effect of co-infections with these two pathogens in mice.

Methods: 6-8 weeks female Balb-c mice were intraperitoneally infected with 250 tachyzoites of type II *T. gondii* followed by the intranasal inoculation with IAV or vice versa. Mouse survival and weight change were monitored over the course of three weeks and acute toxoplasmosis was verified by western blot. Real time PCR was used to investigate the outcomes of the infections on the brain cysts formation using BAG-1 primers, which are specific for *T. gondii* bradyzoite stages responsible for the chronic phase of the infection.

Results: Survival experiments for IAV subsequent to *T. gondii* infection revealed increased levels of mortality relative to influenza control mice. On the other hand, mice with *T. gondii* subsequent to IAV infection showed decreased mortality. Quantitative real-time PCR for BAG-1 expression revealed decreased transcript levels in co-infected groups relative to mice mono-infected with *T. gondii,* implicating that the co-infection restricts the progression of *T. gondii* to the chronic phase. Experiments to address the outcome of either pathogen infection on the other during the acute phase of the infection are pending. These will address the viral and parasitic loads in mice tissues at 3 and 5 days post-infection. Moreover, pro- and anti-inflammatory cytokines including interferon-gamma, TNF alpha, IL-12, IL-10, and MCP in the context of co-infection, during both the acute and chronic phases of toxoplasmosis will be investigated

Conclusion: Results implicate an aggravating effect induced in the event of influenza subsequent to *T. gondii* infection. Transcript levels for pro and anti- inflammatory cytokines will provide insight into the mechanisms that govern disease outcome.

Abstract # 5

Deciphering the genome wide dynamics of regulatory regions during cancer progression using Next Generation Sequencing approaches

Salam Idriss[1], Abdallah Kurdi[1], Hassan Zalzali[2], Raya Saab[2], Pierre Khoueiry[1]
[1]Department of Biochemistry and Molecular Genetics, American University of Beirut. [2]Department of Pediatrics, American University of Beirut
Corresponding author: Pierre Khoueiry - Assistant Professor - E-mail: pk17@aub.edu.lb

Funding source: Medical Resource Package (Award # 100410), MPP (pending final approval)

Keywords: Next Generation Sequencing, bioinformatics, pineoblastoma, regulatory regions

Descriptive statement: Identifying novel genomic bio-signatures in pineoblastoma using high throughput methods.

Background and aims: Genes expression is controlled by DNA stretches lying outside the coding genome called regulatory regions. Substantial changes in the coding and/or regulatory genome have been implicated in disease establishment and progression (cancer, Alzheimer disease…). Yet, the activity dynamics and mechanisms linking regulatory elements to diseases are not fully explored. Identifying differential activity affecting regulatory regions and mediating diseases became possible through high throughput methods. Here, we aim at probing the genome-wide accessibility of regulatory regions in cancer, using a well-characterized mouse model of Cyclin D1-driven pineoblastoma. Regulatory elements accessibility and gene expression profiles in tumorigenic and control mice will be measured over a period of 3 months as the pineal gland enlarges and develops invasive lesions. Integrating Next Generation Sequencing (NGS) and bioinformatics approaches will bring new insights into regulatory regions activity and their contributions to cancer dynamics and evolution.

Methods: Multiple replicates of pineal tissue samples will be collected at different time points from tumorigenic and control mice. Chromatin accessible regions will be extracted and sequenced on Illumina platforms. Reads obtained will be subjected to bioinformatics analysis in order to identify genome-wide accessible regions. In parallel, RNA extraction from samples for the same time points will be performed followed by high throughput sequencing (RNA-seq) and computational analysis using in-house build scripts and pipelines based on state of the art open source software.

Results: We started collecting the required material and building the necessary computational pipelines for RNA-seq. Shell scripts for parallel processing of sequencing files were built allowing an automated processing of several files for quality check and downstream processing of the reads.

Conclusion: Advances in NGS will ameliorate our insights into the activity dynamics of regulatory regions implicated in pineoblastoma paving the way towards identifying novel genomic hallmarks for clinical uses.

Abstract # 6
Liver-Directed Differentiation of Stem Cells

Abdallah Shaito[1], Jessica Saliba[2], Joelle Sokhen[2], Larissa Ayoub[2], Mohammad Harakeh[3], Hussein Chhouri[3], Marwan El-Sabban[3]
[1]Department of Biological and Chemical Science, Faculty of Arts and Sciences, Lebanese International University, Beirut, Lebanon, [2]Department of Biology, Faculty of Science, Lebanese University, Beirut, Lebanon, [3]Department of Anatomy, Cell Biology and Physiological Sciences, Faculty of Medicine, American University of Beirut, Beirut, Lebanon
Corresponding author: Marwan El-Sabban, Professor, E-mail: me00@aub.edu.lb

Funding source: Lebanese National Council for Scientific Research (LNCSR)

Keywords: Mesenchymal stem cells, liver, extracellular matrix, differentiation

Descriptive Statement: Induction of hepatocyte differentiation in MSCs by Liver ECM.

Introduction: Liver transplantation is the best option for end-stage liver disease. However, shortage of donors and graft rejection remain a major worldwide challenge. The microenvironment of cells, by providing scaffold, soluble mediators and mechanical interaction, drives proper cellular differentiation and function. In this study, an acellular extracellular matrix (ECM) was obtained from porcine liver and applied onto mesenchymal stem cells (MSCs) to induce their differentiation into hepatocyte-like cells.

Methods: MSCs were treated with porcine liver ECM for a period of 3 weeks, during which morphological changes were evaluated regularly. At the end of the experimental period, liver-specific gene expression and protein levels were assessed.

Results: Differentiated cells occurred as islands of cells with modified cell morphology and significantly smaller nuclei. They stained positive for the carbohydrate-specific Periodic Acid Schiff's stain, suggestive of glycogen accumulation, a property of hepatocyte function. At the molecular level, differentiated cells showed an overall drop in the expression of gap junction protein (connexin 43) and tight junction protein (N-cadherin), mesenchymal markers highly expressed in MSCs but not in hepatocytes. Moreover, the expression of the liver-specific cytokeratin protein 18, an epithelial marker, was enhanced in the hepatocyte-like cells, further confirming their mesenchymal-to-epithelial shift. Further assessment of the functionality of these cells is underway.

Conclusion: These results demonstrate that human MSCs were reprogrammed into ''human liver-like" cells using liver ECM. This study highlights the potential use of *in vitro* generated liver cells for the treatment of end-stage liver disease.

Abstract # 7

Docetaxel neutropenia and *ABCB1* promoter methylation in peripheral blood: lessons learnt from a pilot toxicoepigenetic study

*Akika R[1$], Zgheib N K[1]**
(1) Department of Pharmacology and Toxicology, AUBFM
[$]Role: Research Assistant
***Corresponding author**: Nathalie K. Zgheib, MD – Associate Professor - E-mail: nk16@aub.edu.lb*

Funding source: American University of Beirut Faculty of Medicine Medical Practice Plan (AUBFM MPP)

Keywords: Docetaxel, Febrile neutropenia, *ABCB1*, Methylation, Toxicoepigenetics

Descriptive Statement: Docetaxel related febrile neutropenia in breast cancer patients is probably not associated with peripheral WBCs *ABCB1* promoter methylation alteration.

Background: To our knowledge, there is no report on the association of DNA methylation changes with cancer drug toxicity. In particular, there are no data on treatment related DNA methylation changes on peripheral white blood cells (WBCs) with febrile neutropenia.

Aim: This is a pilot and feasibility toxicoepigenetic study that aims to test the hypothesis that *ABCB1* promoter in WBCs of cases that developed febrile neutropenia after docetaxel therapy are hypermethylated (less *ABCB1* expression and hence less efflux of the drug from the WBCs) when compared to controls who did not develop febrile neutropenia.

Methods: This is a nested case-control study within a larger retrospective cohort that included 277 Lebanese breast cancer patients who were admitted for chemotherapy at our institution. Included in this evaluation are 13 patients who developed febrile neutropenia while on docetaxel alone or docetaxel with trastuzumab only. These cases were age-, BMI-, disease grade and stage, docetaxel and trastuzumab dose- and chemotherapy regimen- matched with 13 patients (controls) who did not develop febrile neutropenia. Peripheral blood samples were withdrawn (one per patient) at different time intervals from the first cycle of docetaxel-based therapy. Percent methylation of two CpG islands (CGI1 and CGI2) in *ABCB1* promoter area was analyzed using direct bisulfite sequencing.

Results: Concerning CGI2, subjects had 0% methylation at almost all CpG sites; therefore no comparative analysis was carried out. As for CGI1, the median (range) % *ABCB1* promoter methylation for cases compared to controls were 1.68(4.44) vs. 3.00(3.56) respectively, and these were not statistically significantly different. In addition, there were no differences in the patterns of % methylation distribution within time of blood withdrawal.

Conclusion: This study is a failed attempt to build on already recruited breast cancer patients with blood collected during therapy. Lessons learnt are that peripheral blood is probably not an adequate biological sample for toxicoepigenetic evaluation due to the very little potential of differentiation among samples that are almost all hypomethylated at the region of interest. In addition, this study is limited by a small sample size and the lack of serial sample collection. Finally, one could attempt to evaluate additional genes of interest such as more transporters and drug metabolizing enzymes.

Abstract # 8

The telomerase linked mechanisms behind the potential proliferation effect of Bisphenol A and its analogues (Bisphenol F and Bisphenol S) in breast cancer cell lines

*Awada Z[$], El-Mallah M[1], Nasr R[2], Akika R[1], Zgheib N K[1]**

(1) Department of Pharmacology and Toxicology, AUBFM

(2) Department of Anatomy, Cell Biology and Physiology, AUBFM

[$]Role: PhD candidate

***Corresponding author**: Nathalie K. Zgheib, MD – Associate Professor - E-mail: nk16@aub.edu.lb*

Funding source: American University of Beirut Faculty of Medicine Medical Practice Plan (AUBFM MPP)

Keywords: Bisphenol A (BPA), bisphenol S (BPS), bisphenol F (BPF), breast cancer cell lines

Descriptive Statement: BPA, BPF and BPS increase the cell proliferation of MCF-7 cells with BPA and BPF being 10 times more potent than BPS. This is potentially through an ER-dependent pathway.

Background: Bisphenol A (BPA) and the newer bisphenol F (BPF) and bisphenol S (BPS) are estrogen-like endocrine disruptors. Although few studies have already shown that these possess an estrogenic activity, rare studies examined the potential proliferative effect of these chemicals on breast cells or other cell types. Furthermore, very few studies examined their telomerase-linked mechanisms of action.

Aim: Herein, we aim to test the potential proliferation effect and telomerase-linked mechanisms of BPA and its analogues BPF and BPS in an in-vitro setting, using breast cancer cell lines (estrogen receptor positive (ER+): MCF-7 and ER negative (ER-): MDA-MB-231).

Methods: After treatment with BPA, BPF and BPS with or without ER antagonist (ICI182,780), the effect of BPA and its analogues BPF and BPS on cell proliferation and viability were assessed on MCF-7 cells using MTT and trypan blue cell exclusion assays. Similar assays will be performed on MDA-MB-231 cells. Relative telomere length and telomerase expression experiments are in progress.

Results: At day 1 of treatment, MCF-7 cells showed a marked increase in cell proliferation with high BPA doses only. Nevertheless, at days 2 and 3 of treatment, there was a time and dose dependent increase in cell proliferation at most BPA and BPF doses, and at very high BPS doses only. This was abolished in the presence of ER antagonist. Results from trypan blue cell exclusion assay confirmed the MTT results.

Conclusion: Our results indicate that BPA, BPF and BPS increase the cell proliferation of MCF-7 cells with BPA and BPF being 10 times more potent than BPS. This is potentially through an ER-dependent pathway. Further cell invasion, colony formation and molecular assays such as relative telomere length and telomerase expression are in progress. Our study will hopefully allow assessment and comparison of the role and mechanism of BPA and its analogues in breast cancer.

Abstract # 9

Innate immune pathway activation in Drosophila melanogaster by Epstein-Barr Virus DNA

Nour A. Sherri[1], Nathaline Haidar- Ahmad[1], Nour Salloum[1], Carine Mouawad[1], Margret Shirinian[1], Elias A. Rahal[1]

[1]Department of Experimental Pathology, Immunology and Microbiology, American University of Beirut, Beirut, Lebanon

Corresponding authors: *Elias Rahal Email:er00@mail.aub.edu*

Margret Shirinian Email:ms241@aub.edu.lb

Funding source: Asmar Research Fund

Keywords: *Drosophila melanogaster*, IMD, Toll, JAK-STAT

Descriptive Statement: Assess the role of Toll, JAK-STAT, IMD pathways in response to EBV DNA injection in *Drosophila melanogaster*.

Introduction: background and aims Epstein Bar Virus (EBV) belongs to the herpes family of viruses. Like other herpes viruses, EBV is capable of establishing latency. During latency only a small portion of EBV genes are expressed. Moreover, this virus is associated with several autoimmune diseases as well as malignancies. Innate immune responses are triggered against EBV infection particularly the activation of Toll-like receptor pathways (TLR) in humans. A previous study indicated that TLR9 may be involved in triggering IL-17 synthesis in response to EBV DNA injection in mice. In the same study upon inhibiting the TLR9 the IL-17 production decreased but it was still produced, suggesting that other immunological pathways may be activated as well. Hence, it is important to identify these immunological pathways that are activated in response to EBV DNA in a relatively *simple* but efficient model such as *Drosophila melanogaster*. The effect of EBV DNA in activation of *Toll*, IMD and JAK/STAT pathways in *Drosophila* was investigated.

Methods: *Under brief carbon dioxide anesthesia, three groups of* 1-day-old wild type adult flies were separately injected with 70, 140, and 280 EBV DNA copies. Transcriptional levels of target genes downstream of Toll, IMD and JAK-STAT were measured by quantitative real time PCR (qPCR) on days 1 and 3 post-injection.

Results: Upon injection of wild type flies with 70, 140, or 280 EBV DNA copies, Toll and JAK-STAT pathways were not activated compared to the positive control on days 1 and 3 post injection. On the other hand, upon injection of 70 EBV DNA copies, the IMD pathway was activated only on day 1 post injection, while no activation was observed at day 3 in response to any of the three copy numbers of EBV DNA.

Conclusion: Uncovering which innate immune pathway is activated or inhibited in response to EBV DNA injection may play a vital role in further understanding the immune responses that are triggered against EBV infection. After primary infection and establishment of latency, recurrences frequently occur resulting in viral DNA replication. The shed DNA may then result in immunomodulatory responses. Our data suggests that the IMD pathway is triggered by EBV DNA in Drosophila melanogaster. The significance of this activation and its effect on downstream responses will be further explored.

Abstract # 10

Regulation of Cellular Ceramide in Response to Influenza A Virus Infection

Nadia Soudani [1, 2], Mona Diab-Assaf [3], Rouba Hage' Sleiman [3], Ghassan Dbaibo [2, 4, 5, #], Hassan Zaraket [1, 2#]

[1]Department of Experimental Pathology, Immunology and Microbiology, Faculty of Medicine, American University of Beirut, Lebanon, [2] Center for Infectious Diseases Research, Faculty of Medicine, American University of Beirut, Lebanon,[3]Department of Biology, Faculty of Sciences, EDST, Lebanese University, Lebanon,[4]Department of Pediatrics and Adolescent Medicine, Faculty of Medicine, American University of Beirut Medical Center, Lebanon [5]Department of Biochemistry and Molecular Genetics, Faculty of Medicine, American University of Beirut, Lebanon.

 # Corresponding authors: Dr. Hassan Zaraket / Assistant professor - E-mail: hz43@aub.edu.lb and Dr. Ghassan Dbaibo / professor - E-mail: gdbaibo@aub.edu.lb

Funding source: MPP-URB

Keywords: influenza A, Ceramide, *de novo* pathway

Descriptive Statement: Elucidating cellular and molecular pathways that are mediated during viral infections provide a foundation for developing novel antiviral drugs against influenza A, which are crucial due to the emergence of antiviral drug resistance.

Introduction: Influenza A virus (IAV) is a negative-sense single strand RNA virus that belongs to *Orthomyxoviruses* family. Annual influenza outbreaks are associated with significant morbidity and mortality worldwide despite the availability of seasonal vaccines. This is attributed to the fast-genetic evolution and high genetic diversity of the virus. Studies have shown that entrance, replication and release of many RNA viruses into host cells are mediated through cellular lipids. Ceramide is a sphingosine-derived lipid that acts as a potent second messenger molecule in the regulation of diverse cellular mechanisms such as cell cycle arrest, apoptosis, and senescence. Studies highlighted the differential role of ceramide *de novo* synthesis pathway on virulence and life cycle of some viruses. For instance, the inhibition of ceramide biosynthesis pathway suppressed the replication and release of infectious West Nile virus particles, but it enhanced the replication and production of dengue virus. The interplay between influenza and ceramide pathways is not well-understood. Influenza virus modulates various cellular signaling pathways that overlap with the pathways regulated by ceramide. Thus, we hypothesize that ceramide produced through de *novo synthesis pathway* is involved in the influenza virus life cycle and the cellular events occurring during infection.

Methods: Wild-type influenza A/Peurto Rico/34/67 (PR8) strain (MOI:1) was used to infect adenocarcinomic human alveolar basal epithelial cells (A549). Lipid extraction was done using Bligh and Dyer method. Thin layer chromatography and confocal microscopy were used to measure ceramide accumulation. The variation in gene expression and vRNA synthesis was measured using qRT-PCR with respect to housekeeping genes. Drug cytotoxity was assessed using MTT and trypan blue. Virus titer was quantified using plaque assay.

Results: Significant Ceramide accumulation was observed starting 24hpi (hours post infection) followed by a peak at 48 hpi. The expression of serine palmitoyl transferase (SPT) and ceramide synthase (CerS); enzymes regulating *de novo* ceramide biosynthesis, increase in response to IAV infection. The treatment of A549 cells with 0.1 µM myriocin and /or 50 µM fumonisin B1; potent inhibitors SPT and CerS respectively, for 2h prior infection resulted in a significant decrease in ceramide accumulation compared to untreated infected cells. This elevation in ceramide levels was accompanied by a decrease in cell death and increase in vRNA synthesis.

Conclusion: This study proves that IAV infection mediates ceramide accumulation in lung epithelial cells mainly through the *de novo* biosynthesis. This increase in ceramide levels is involved in mediating cell death and has a minor effect viral progeny.

Abstract # 11

Assessing the Role of Neutral Sphingomyelinase during Influenza A Virus Infection

Wafaa Al Soussi[1, 2], Amani Audi[1, 2, 3], Nadia Soudani[1, 2] Ghassan Dbaibo[2, 4, 5], Hassan Zaraket[1, 2]

[1]Department of Experimental Pathology, Immunology and Microbiology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon. [2]Center for Infectious Disease Research, Faculty of Medicine. American University of Beirut. [3]Department of Biological and Environmental Sciences, Faculty of Science, Beirut Arab University, Debbieh, Lebanon. [4]Department of Pediatrics and Adolescent Medicine, Faculty of Medicine, American University of Beirut Medical Center, Beirut, Lebanon. [5] Department of Biochemistry Faculty of Medicine, American University of Beirut Medical Center, Beirut, Lebanon.

Funding Source: MPP/URB

Corresponding author: Dr. Hassan Zaraket, hz34@aub.edu.lb

Key Words: Influenza; neutral sphingomyelinase; ceramide

Descriptive Statement: This study investigates the role of neutral sphingomyelinase during influenza A virus infection by measuring its activity and assessing its effect on virus replication.

Introduction: Influenza A virus (IAV) is one of the most common causative agents of acute respiratory tract infections worldwide. It causes significant morbidity and mortality during its seasonal outbreaks and can occasionally cause pandemics. Since current influenza antiviral drugs target viral proteins, which can quickly evolve resistance to existing drugs, targeting host cell factors during infection is a promising antiviral approach as they are less prone for mutation, and thus the selection of resistance. Numerous studies have demonstrated the role of sphingolipids in various aspects of the life cycles of several viruses including attachment and fusion, intracellular transport, replication, and budding. Previous studies conducted in our laboratory have shown that IAV infection leads to increase in intracellular ceramide and apoptosis. Knowing that neutral sphingomyelinase (nSMase) is a key player in stress-induced production of ceramide by hydrolyzing the membrane lipid sphingomyelin, we hypothesize that it could play a role during IAV infection.

Aim: To investigate the role of nSMase during IAV infection in human lung adenocarcinoma epithelial cells

Methods: We assessed IAV replication upon inhibition of nSMase by GW4869 in A549 adenocarcinomic human alveolar epithelial cells. The cytotoxicity of GW4869 on A549 cells was measured using MTT assay. Viral titers were determined using plaque assay. Further, we assayed the activity of nSMase in IAV-infected lung epithelial cells at different time points using Amplex® Red Sphingomylinase assay kit.

Results: Pharmacological inhibition of nSMase using 20µM of GW4869 reduced virus titer in human lung epithelial cells by 2 $\log_{10}$ PFU/ml compared to mock-treated cells (*p-value xxx)*. On the other hand, nSMase activity was not altered in response to IAV infection.

Conclusion: This study for the first time reveals an important role of nSMase during IAV infection, which provides new avenues for antiviral drug development.

Abstract # 12

Effect of Clopidogrel and Aspirin on platelet aggregation in a rat model of Traumatic Brain Injury

Naify Ramadan[1], Mohammad Nasser[2, 3] Fatima Dakroub[1], Jamil Nehme[1], Kazem Zibara[4], Firas Kobeissy[3]¥, Aïda Habib[3]¥, Eva Hamade[2, 4]¥

[1]Department of Biochemistry and Molecular Genetics, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

[2] Cancer Immunology Laboratory, DSST, PRASE, Lebanese University, Beirut, Lebanon

[3] Department of Biochemistry and Molecular Genetics, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

[4]Department of Biology, Faculty of Sciences-I, Lebanese University, Beirut, Lebanon

Corresponding author: Aïda Habib - Professor - E-mail: ah31@aub.edu.lb

Firas Kobeissy – Associate Professor - E-mail: fk02@aub.edu.lb

Equal Contribution

Funding source: CNRS, Lebanese University grant and ER045, MPP and URB.

Keywords: TBI, ASA, CLOP

Descriptive Statement: Aspirin and clopidogrel increases TBI's severity in rats

Introduction:

Background: TBI is one of the leading causes of death worldwide. Antiplatelet agents inhibit platelet aggregation and are used as essential adjuncts to elderly patients with cardiovascular diseases.

Aims: Investigate whether the combination of aspirin and clopidogrel increases TBI's severity in rat. Systemic changes in platelets activation and TBI biomarkers of brain damage will be assessed.

Methods: Rats were treated in absence or presence of aspirin and/or clopidogrel for 48 hours prior to TBI and sacrificed 48h post-injury. Transferrin and fodrin expression in brain tissues and serum proteins associated to TBI and inflammation (UCH-L1, GFAP and Hexokinase) were analyzed by western blotting. The serum levels of thromboxane were measured by enzyme immunoassay.

Results: Platelets from treated rats showed complete inhibition of platelet aggregation, in comparison to control. Also platelet aggregation and TXB2 levels were totally inhibited or decreased when rats were treated with ASA, CLOP or ASACLOP prior to TBI, compared to control TBI. Treated rats decreased UCH-L1 and GFAP levels in serum post-TBI. Finally, Transferrin increased in ASA or CLOP, but not ASACLOP TBI treated rats which showed the highest fodrin cleavage.

Conclusion: Single or combination treatment of anticoagulation and anti-platelet therapy of ASA and/or CLOP is associated with an increased risk in an experimental TBI rat model.

Abstract # 13

Cigarette Smoking-Induced Cardiac Hypertrophy, Vascular Inflammation and Injury Are Attenuated by Antioxidant Supplementation in an Animal Model

*Lama Baki [1], Moustafa Al Hariri [1], Farah Najdi [1], Jessica Chedid[1], Richard Younes[1], Hassan Al Askari Hayek[1], Mohamad Kazma[1], Kazem Zibara[2], Asad Zeidan[4] and Firas Kobeissy[1]**

[1] Department of Biochemistry and Molecular Genetics, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

[2] ER045, PRASE, DSST, Lebanese University, Beirut, Lebanon

[3] Department of Physiology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

Corresponding author: Firas Kobeissy – Associate Professor - E-mail: fk02@aub.edu.lb

Funding source: - AUB-MPP grant - Grants from CNRS - Lebanese University grant and ER045, MPP and URB.

Keywords: cigarette smoking, pomegranate juice, cardiovascular diseases.

Descriptive Statement: Pomegranate juice can be considered as potential and therapeutic substance in attenuating the damaging effects of cigarette smoking.

Introduction:

Background: Cardiovascular diseases are the leading causes of mortality worldwide. Cigarette smoking remains a global health epidemic with negative effects on the cardiovascular system.

Aims: This study evaluate the effect of pomegranate supplementation on the cardiovascular system of an experimental rat model of smoke exposure.

Methods: Adult rats were divided into four different groups: Control, Cigarette smoking (CS), AO, and CS + AO. Cigarette smoke exposure was for 4 weeks and AO group received pomegranate juice while other groups received placebo. Assessment of cardiovascular injury was documented by assessing different parameters of cardiovascular injury mediators.

Results: Cigarette smoke exposure induced cardiac hypertrophy, which was reduced upon administration of pomegranate in CS + AO group. Cigarette smoke exposure was associated with elevation in oxidative stress. In addition, an increase in aortic calcification was observed after 1 month of cigarette smoke exposure. Furthermore, cigarette smoke induced a significant up regulation in Bdkrb1 expression level. Finally, pomegranate supplementation exhibited cardiovascular protection assessed by the above findings in cigarette smoke exposed animals.

Conclusion: Findings from this work showed that cigarette smoking exposure is associated with significant cardiovascular pathology in an animal model. Antioxidant supplementation attenuated indicators of atherosclerosis markers associated with cigarette smoke exposure.

ABSTRACT # 14

Hic-5 Deregulation in Lamin A/C and Emerin – Associated Myopathies

Ranim Daw[1], Dima Diab El Harakeh[1], Lara Kamand[1], Georges Nemer[2], Marwan Refaat[2,3,], and Diana E. Jaalouk[1,*]*

[1]Department of Biology, Faculty of Arts and Sciences; [2]Department of Biochemistry and Molecular Genetics; [3]Department of Internal Medicine, Division of Cardiology, American University of Beirut, Beirut, Lebanon

[*]**Corresponding authors**: Diana E. Jaalouk; email: dj11@aub.edu.lb, and Marwan Refaat; email: mr48@aub.edu.lb

Funding source: Farouk Jabre Interfaculty Grant, AUB (2015 – 2016); Faculty of Medicine Medical Practice Plan (MPP), AUB (2016-2017)

Keywords: Hic-5, Laminopathies, DCM, EDMD, Emerin

Descriptive Statement: Our study tests the deregulation of hic-5 in Emery-Dreifuss Muscular Dystrophy (EDMD) and Dilated Cardiomyopathy (DCM) MEF model cell lines under baseline and oxidative stress-induced conditions.

Background and Aims: The nuclear lamina underlies and associates with the inner nuclear membrane and with nuclear envelope (NE) proteins such as emerin. Laminopathies are a group of genetic diseases resulting from mutations or abnormal post-translational modifications of NE and/or lamina proteins. *LMNA* gene is ubiquitously expressed and is the most mutated gene in the human genome and in these diseases. Up till now, the molecular mechanisms harboring their phenotypic diversity are not deciphered. Hence, our aim is to better understand them, specifically in terms of the *LMNA* gene whose mutations contribute to EDMD and DCM. In this regard, Hydrogen peroxide inducible clone-5 (Hic-5) is oxidative stress and TGF-β sensitive with critical roles in myogenesis and muscle differentiation. We hereby hypothesize that there exists a deregulation in hic-5 expression and function in lamin A/C and emerin – associated myopathies. In this study, we evaluated the transcript and protein expression levels of hic-5 in mouse embryo fibroblast (MEF) lines taken from mice deficient in either lamin A (*Lmna*$^{-/-}$) or emerin (*Emd*$^{-/Y}$) with the EDMD phenotype and *Lmna*$^{N195K/N195K}$ MEFs which have the DCM phenotype versus wild-type controls under baseline and oxidative stress conditions.

Methods: Quantitative Real-Time PCR, Western Blots, and Immunofluorescence were performed on the previously mentioned MEF cell lines under baseline conditions and upon 0.1μM and 0.5μM treatments with H_2O_2 for 5, 15, 30, and 60min.

Results: Real Time PCR quantification demonstrated that under baseline conditions, *hic-5* normalized to *18S* increases significantly in *Lmna*$^{-/-}$ and insignificantly in *Emd*$^{-/Y}$ MEFs with respect to WT and *Lmna*$^{N195K/N195K}$ MEFs. While, transcript levels significantly decrease in WT MEFs after 30min of the 0.5μM H_2O_2 treatment with respect to the untreated controls. Whereas, in *Lmna*$^{-/-}$ and *Lmna*$^{N195K/N195K}$ MEFs, these levels significantly increase – unlike in *Emd*$^{-/Y}$ MEFs that establish minor insignificant fluctuations – upon 0.1μM and 0.5μM H_2O_2 treatments. On the other hand, Western Blot densitometry analyses revealed that under baseline conditions, hic-5α is significantly upregulated in lamin knockouts and insignificantly in the other two mutant cell lines with respect to the WT controls. Whereas, upon 30min exposure to 0.5μM of H_2O_2, the latter MEFs have decreased hic-5α levels with respect to untreated controls, while *Lmna*$^{-/-}$ MEFs show significant increases throughout the different time points upon this treatment. Yet, *Lmna*$^{N195K/N195K}$ and *Emd*$^{-/Y}$ MEFs demonstrate significant early increases upon both treatments. Immunofluorescence images illustrate that under baseline and oxidative stress-induced conditions, *Lmna*$^{+/+}$, *Lmna*$^{-/-}$, and *Emd*$^{-/Y}$ MEFs have relatively homogenous nuclear and cytoplasmic distribution of hic-5 whereas in *Lmna*$^{N195K/N195K}$ MEFs, Hic-5 is significantly more localized in the nucleus.

Conclusion: hic-5 transcript and protein levels are deregulated in EDMD and DCM MEF model cell lines at baseline and oxidative stress conditions. Localization of hic-5 is significantly restricted to the nucleus in the N195K DCM model under oxidative stress conditions.

Abstract # 15

p53 and Rb are indispensable for normal kidney development in mice

*JAAFAR Carine[1], Zalzali Hassan[2], AL LAFI Sawsan[1], SAAB Raya[2] and GHANEM Noël[1]**
[1] *Department of Biology,* [2]*Department of Pediatric and Adolescent Medicine, American University of Beirut, Beirut, Lebanon*
***Corresponding author**: ng13@aub.edu.lb

Position: PhD Student
Funding source: Kamal A. Shair (KAS) grant (CRSL, AUB)
Keywords: kidney, development, Rb, p53, renal failure

Descriptive Statement: In this project, we have investigated the combined roles of two tumor suppressor genes, Rb and p53, in kidney development and found that their dual loss leads to several developmental and functional defects during kidney development in mice.

Introduction: The kidneys have a vital homeostatic role in the excretion of nitrogenous waste products and regulation of blood composition in mammals. Renal development occurs between embryonic day (E) 8.5 and post-natal day (P) 2. The Rb and p53 pathways are master regulators of cell division and senescence in many organs. Previous studies have demonstrated that p53 is required for early renal development particularly during nephrogenesis, and metanephroi differentiation at later stages. Hence, p53 knockout mice exhibit abnormal metanephric and uterine development, however, this effect is strain-specific and not embryonic lethal. The role of Rb in kidney development has not been addressed to date. We recently generated an inducible deletion of Rb in p53-null mice during development that resulted in perinatal lethality with almost complete penetrance of the phenotype due to severe kidney failure.

Methods: We used an inducible Nestin-CreERT2-YFP/YFP system to conditionally delete Rb in p53-null (-/-) and Rb flox/flox mice, separately. Nestin is an intermediate filament protein specifically expressed in neural precursors in the brain, and, in mesodermal cells and theirs derivatives in the developing kidney. Only few animals survived the combined loss of Rb and p53 when carried at E18.5 but not at earlier stages, and their phenotype was analyzed at P40. To characterize the morphological and developmental defects observed in these animals, we performed: 1) histological analysis using Hematoxylin and Eosin (H&E) staining, and 2) immunostaining to examine the expression of key developmental genes in the kidney including the podocyte-specific marker, Nestin, and the differentiation marker, NeuN. To study the specific roles played by p53 and Rb in kidney development, we further generated double conditional knock-out mice (dcKO) Rb cKO-/-, p53 cKO-/- by crossing Rb/p53 double floxed/floxed mice and Nestin-CreERT2-YFP/YFP mice and induced recombination at different time-points between E13.5 and P60.

Results: We compared the kidney phenotypes in p53-/-; Rbflox/flox mice treated with tamoxifen and vehicle only, and detected the presence of severe renal developmental defects manifested by hypoplastic kidneys with dilated renal tubules and possible glomerular hypertrophy as well as severe kidney failure as indicated by a 5-6 fold increase in blood creatinine levels. We also studied the kidney phenotypes in p53+/+; RbcKO-/- mice compared with vehicle-treated controls. H&E staining revealed no difference in kidney morphology upon loss of Rb alone.

Conclusion: Rb and p53 are both required for normal kidney development and control critical developmental pathways that are indispensable for proper renal morphogenesis and function.

Abstract # 16

Comparative analysis of the role of Rb during embryonic and postnatal neurogenesis in the dentate gyrus and the olfactory system

Saad Omais[1], Carine Jaafar[1], Rayan Naser[1], Renaud Vandenbosch[2], Sawsan Al-Lafi[1], Ruth Slack[2], and Noël Ghanem[1]*

[1]Department of Biology, American University of Beirut, Beirut, Lebanon

[2] Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, ON, Canada

***Corresponding author**: Dr. Noël Ghanem, ng13@aub.edu.lb

Funding Source: AUB University Research Board (URB) grants and Kamal A. Shair Central Research Science Laboratory (KAS CRSL) fund to NG, and, Canadian Institute of Health Research (CIHR) and Heart and Stroke foundation of Canada to RS.

Keywords: Rb, neurogenesis, stem cells, progenitors, dentate gyrus, olfactory epithelium, olfactory bulb, conditional knock-out mice

Descriptive statement: We describe and compare here the distinct roles played by Rb in neurogenesis in the dentate gyrus (DG) in the hippocampus and the olfactory epithelium (OE) during development as well as in the DG and the olfactory bulb (OB) during adult neurogenesis.

Introduction: The Retinoblastoma protein, Rb, was found to be implicated in telencephalic-specific functions such as control of cell proliferation, differentiation and survival. However, it remains unclear whether these functions are conserved among different regions in the developing telencephalon on the one hand and during neurogenesis in the adult brain on the other hand. In this study, we investigate and compare the role played by Rb during neurogenesis in the embryonic DG and OE as well as the adult DG and OB.

Methods: We crossed Foxg1-Cre (Brain-Factor 1; telencephalon-specific marker) and Nestin-CreER^{T2}-YFP/YFP (neural stem cells and progenitors marker) mice with Rb$^{+/flox}$ (Control) and Rb$^{flox/flox}$ (Mutant) mice in order to generate Rb-conditional knock-out mice during embryogenesis and postnatal life, respectively. We analyzed the resulting phenotypes using immunohistochemistry.

Results: In the absence of Rb, we detected an increase in cell proliferation and apoptosis in immature neuronal progenitors (NeuroD+/Ki67+ and NeuroD+/AC-3+) in the DG but not in the OE. However, this phenotype was observed in late progenitors/immature neurons (Tuj1+ and DCX+) in both sites. Moreover, loss of Rb negatively affected neuronal migration in the olfactory system. This distinctive role for Rb is likely due to the early expression of Foxg1 (Cre-driver) in the dentate lineage compared to the OE lineage. During postnatal neurogenesis, Rb-null neural progenitor cells (but not stem cells) displayed increased proliferation (Ki67+;YFP+) without any obvious migration or differentiation defects (DCX+;YFP+ and NeuroD1+;YFP+) in both the DG and the adult subventricular zone (SVZ). However, loss of Rb severely compromised the survival of mature neurons (NeuN+;AC-3+) in both neurogenic sites with accelerated cell death in the DG compared with the OB.

Conclusion: Rb is an essential regulator of progenitor cell development as well as neuronal production and survival (both inhibitory and excitatory neurons) in the embryonic and the adult brain. However, this role is lineage-dependent and directly linked to the stage in neurogenesis at which loss of Rb is induced.

Abstract # 17

Assessment of placental cells permissivity to the apicomplexan parasite *Toxoplasma gondii* infection from an immunological facet

Wedyan Jomaa[1] (student), Hiba Mcheik[2] (Research Assistant), Rana El Hajj[1] (PhD student), Dr. Georges Daoud[2] (Co-advisor) and Dr. Hiba El Hajj[1] (Advisor)

[1]Department of Experimental Pathology, Immunology, and Microbiology

[2]Department of Anatomy, Cell Biology and Physiological Sciences

Funding source: MPP

Corresponding author:

Dr. Hiba El Hajj, he21@aub.edu.lb and Dr. Georges Daoud, gd12@aub.edu.lb

Keywords: *Toxoplasma gondii*, placenta, cytokines

Descriptive Statement: This study investigates the permissivity of human placental cell lines to *Toxoplasma gondii* infection and the elicited placental immune response triggered by the infection.

Introduction: *Toxoplasma gondii (T.gondii)* is an obligate intracellular parasite capable of infecting humans. *T. gondii* is the etiologic agent of toxoplasmosis, a disease that is usually asymptomatic to mild symptomatic in immunocompetent individuals, but severe to life threatening in immunocompromised patients. Another spectrum of the disease is the congenital toxoplasmosis where the outcome of the disease is highly dependent on the trimester of infection. In primo-infected pregnant women, the first trimester bears the greatest risk of abortion whereas the second and third trimesters bear severe and disabling disease in the developing fetus. *T. gondii* is known for its ability to hijack macrophages to travel out to various tissues. It also has a great capacity to stimulate and modulate the host immune response. In the current study, we aim at comparing permissivity to *T.gondii* among placental cell lines and investigating the immune response triggered by the parasite upon infection.

Methods: Placental cell lines HTR-8, BeWo, JAR and JEG-3, as well as the monocyte THP-1 derived human macrophages are used in this study. These cells were infected with the most virulent *T. gondii* strain (RH HX strain). The parasite replication was assessed by measuring the transcript levels of the surface marker SAG-1 (Surface Antigen-1). Different pro-inflammatory and anti-inflammatory cytokines transcript levels were also assessed using the Syber green Real time quantitative PCR.

Results: Our results show that the parasite capacity of replication in the used placental cells is different from its replication rate in the macrophages. This difference in the parasite capacity of replication is tightly modulated by a difference in the pro-inflammatory/anti-inflammatory cytokine response by the different tested cell systems.

Conclusion: This study will provide a better understanding of the congenital toxoplasmosis outcomes in relation with the host cell induced immunological response.

Abstract # 18

Behavioral and Molecular Alterations post repeated mild Traumatic Brain Injury r(TBI) on the Progression of Pre-existing Diabetic Neuropathy in Diabetic Mouse Model

Batoul Dia[1], Farah Najdi[2], Naify Ramadan[2], Stephanie Eid[2], Naify Ramadan[2], Lama Baki[2], Assaad Eid[1] & Firas Kobeissy[2]**

[1]Department of Anatomy, Cell Biology and Physiological Sciences, Faculty of Medicine, American University of Beirut, Beirut, Lebanon [2]Department of Biochemistry and Molecular Genetics, Faculty of Medicine, American University of Beirut, Beirut, Lebanon,*

Corresponding author: *Assaad Eid* & Firas Kobeissy**

Funding: Collaborative Grant Initiative, PI: Assaad Eid & Co-PI: Firas Kobeissy

Keywords: Brain Injury, Diabetes, cell injury Behavioral testing

Descriptive Statement: In this work, we wanted to study the impact of mild TBI (closed head injury) on the exacerbation of diabetic neuropathy.

Introduction: Diabetes is a major public health problem with major comorbidities. The World Health Organization (WHO) projects that diabetes will be the seventh leading cause of death in 2030. One of the most common and debilitating complications associated with diabetes is Diabetic Neuropathy (DN); it affects more than 50% of patients with longstanding diabetes. Several epidemiological studies have established that older adult patients with type 2 diabetes are at higher risk of falling sustaining concussive injuries that can exacerbate the overall diabetic complications in particular diabetic neuropathy. In this proposal, we hypothesize that exposure to repeated mild brain injury in diabetic animal model with preexisting diabetic neuropathy would contribute to exacerbate the diabetic neuropathy complications; on the behavioral level as well as cellular level. We aim to identify putative markers associated with TBI/diabetes that can be used as innovative diagnostics as therapeutic targets.

Methods: In this work: we will assess if repetitive mild TBI would exacerbate the preexisting diabetic neuropathic condition in C57BLKsJ-db/db transgenic mice affecting both the behavioral outcome scores as well neural injury levels utilizing the following approach.

Animals: Transgenic mice C57BLKsJ-db/db mice which are spontaneous type 2 diabetic animal model and developing diabetic neuropathy after 6 months of age will be used.

Brain Injury Setup: Controlled cortical impact machine will be used to induce closed TBI at three consecutive days

Cellular and Behavioral outcomes: Post r(TBI), behavioral assessment of MWM, forced swim test and RotaRod will be performed among the 4 different cohorts at 48 hrs, 1 week and 1 month post injury. Similarly, indices of neural injury will be evaluated for cell death, axonal injury and or demylenation will be assessed.

Results: Preliminary data from our study have indicated that Markers of neuronal injury (UCH-L1, S 100beta along with with alpha II-spectrin) showed to be altered with Diabetes along with TBI. Similarly, axonal guidance proteins (CRM-2) and oxidative stress markers (NOX) showed to be differentially expreseed in the diabetic bv the TBI cohorts On the behavioral testing, Preliminary results have shown the TBI-diabetes group exhibited elevated levels of anxiety related behavior with a marked change in the Rotarod motor function. Further studies including markers of demylenation and dendritic injury are being conducted to further elucidate the relationship between diabetes and TBI cross talk

Conclusion: Taken together, our work has indicated that exposure to repeated mild brain injury in diabetic animals would contribute to exacerbate the diabetic neuropathy complications; both on the behavioral level as well as cellular level.

Abstract # 19

Study of the combined roles of Rb and p53 in the control of adult neurogenesis *in vitro*

*SALIBA Afaf[1], AL LAFI Sawsan[1], JAAFAR Carine[1], OMAIS Saad[1], SAAB Raya[2] and GHANEM Noël[1]**

[1]Department of Biology, American University of Beirut, Beirut, Lebanon
[2]Department of Pediatric and Adolescent Medicine, AUBMC, Beirut, Lebanon
***Corresponding author**: GHANEM Noël, ng13@aub.edu.lb

Funding source: Kamal A. Shair (KS) fund and University Research Board (URB) grant

Keywords: Adult neurogenesis, Rb, p53, tumor suppressor, neural stem and progenitor cells, proliferation, differentiation, apoptosis

Descriptive Statement: In this study, we have investigated the combined roles of two tumor suppressor genes, p53 and Rb, in the control of adult neural stem cells (aNSCs) properties including their regenerative capacity and fate in culture. Identifying the mechanisms that regulate the development and expansion of aNSCs will help improve the regenerative capacity inside the brain in cases of injury and neurodegenerative diseases.

Introduction: Adult neurogenesis is a highly regulated process that is restricted to aNSCs found in the subgranular zone (SGZ) of the hippocampus and the subventricular zone (SVZ) lining the lateral ventricles in mammals. SVZ-aNSCs have unlimited self-renewal capacity and give rise to GABAergic interneurons in the olfactory bulb. This process requires a fine control and balance between cell proliferation, differentiation and death. Loss of p53 was previously shown to enhance the self-renewal capacity and the rate of differentiation of aNSCs both *in vivo* and *in vitro*. We have recently demonstrated that Rb specifically regulates adult progenitor proliferation and is needed for long-term survival of adult-born OB interneurons. Here, we have examined how both genes function together to regulate the developmental properties of aNSCs and progenitors *in vitro*.

Methods: We induced temporal deletion(s) of Rb and/or p53 (single and double conditional Knock-out; cKO and dcKO) in aNSCs/progenitors in young adult mice carrying Rb and/or p53 double floxed alleles and the Nestin-CreERT2-YFP/YFP cassette. We then performed primary cultures of dissected SVZ tissues followed by consecutive passages and conducted neurosphere assays and differentiation assays.

Results: Compared with wild type cultures, aNSCs/progenitors derived from p53-cKO and Rb;p53-dcKO showed a significant increase in their amplification rate over 4-8 passages with the highest rate detected in dcKO cultures. Moreover, our secondary neurosphere assays indicated that the self-renewal capacity of NSCs was strongly enhanced and this effect was mediated by p53 alone. Both single cKO-NSCs and dcKO cultures seem to have retained a differentiation potential similar to wt cultures; however, loss of both Rb and p53 led to massive cell death after neuronal differentiation.

Conclusion: The population of aNSCs/progenitors can be expanded *in vitro* by manipulation of the p53/Rb pathway(s) without affecting aNSCs differentiation potential. However, loss of both genes is not compatible with long-term neuronal survival both *in vivo* and *in vitro*.

Abstract # 20

Role of Sphingosine Kinase 1 in Bradykinin regulation of fibrotic markers in Vascular Smooth Muscle Cells

Moustafa Al Hariri[1], Zepur Kazezian[1], Rami A. Ballout[1], Miran A. Jaffa[2], Hesham M. El-Shewy[3], Fuad N. Ziyadeh[1], Ayad A. Jaffa[1].

[1]Department of Biochemistry and Molecular Genetics, Faculty of Medicine, [2]Epidemiology and Population Health Department, Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon, [3]Department of Medicine, Medical University of South Carolina, Charleston, SC, USA

Corresponding author: Moustafa Al Hariri, Biomedical Science PhD student, maa161@aub.edu.lb

Keywords: Bdkrb2, Sphingosine kinase, fibrosis, atherosclerosis, vascular smooth muscle cells.

Descriptive statement: Bradykinin promotes fibrotic protein deposition through sphingosine kinase 1 activation.

Funding source: MPP

Introduction: Background and Aim: Atherosclerosis is a worldwide health concern, which results from the deposition of fibrotic proteins in blood vessel walls leading to their stiffening and subsequent loss of elasticity. Bradykinin (BK) is a vasodilator nonapeptide that promotes proliferation and migration of vascular smooth muscle cells (VSMC). Sphingosine Kinase 1 (Sphk1) and its bioactive sphingolipid, Sphingosine 1 phosphate (S1P), have long been known to induce migration and vascular maturation via activation of S1P receptors (S1PRs). In this study, we tested whether Sphk1/S1P pathway plays a role in the induction of Connective Tissue Growth Factor (Ctgf) and Fibronectin (Fn1) by stimulation of Bradykinin Receptor B2 (Bdkrb2) in primary rat and murine VSMC.

Methods: Western blot and RT-qPCR were employed to study the effect of BK and S1P on the expression of Ctgf and Fn1 in the absence or presence of specific inhibitors of ERK, AKT, Sphk1 and S1pr1, as well as siRNA to downregulate CTGF and SphK1 in rat VSMC. In addition, GFP-S1PR1 plasmid construct was used to confirm the activation of the S1pr1, by confocal microscopy, in response to BK. We then used primary VSMC isolated from wild-type or Sphk1 knock out mice for validation.

Results: In our study, we found that BK induced the expression of Sphk1, Ctgf and Fn1 on the mRNA and protein levels compared to the basal levels. Moreover, BK induced the activation of Sphk1 and internalization of GFP-S1pr1. Down regulation or genetic ablation of Sphk1 abolished the BK-induced Ctgf and Fn1 expression. Inhibition of ERK and AKT reduced the BK-induced Sphk1 phosphorylation, and Ctgf and Fn1 protein expression, suggesting that ERK and AKT are upstream of Sphk1, Ctgf and Fn1. Furthermore, the BK-induced increase in Ctgf and Fn1 expression are S1pr1- and Sphk1 activation dependent. Finally, the BK-induced expression of Fn1 is Ctgf dependent.

Conclusion(s): Thus, our findings suggest that the BK-induced fibrosis, and consequently atherosclerosis, are partially attributable to the activation of the Sphk1, and subsequently S1pr1, in VSMC. This makes the BK-S1pr1 cross-talk pathway a possible target to ameliorate the initiation/progression of atherosclerosis.

Abstract # 21

A Middle Eastern family with Mal de Meleda, cutaneous skin malignancies and mutations in the putative squamous lineage tumor suppressor SLURP1

Christina Bergqvist[1], Remi Safi[1], Laetitia Daou[2], Georges Nemer[3], Dany Nassar[1], Humam Kadara[3] and Mazen Kurban[1,3]

Departments of [1]Dermatology and [2]Pathology and Laboratory Medicine, American University of Beirut Medical Center, Beirut, Lebanon. Department of [3]Biochemistry and Molecular Genetics, Faculty of Medicine, American University of Beirut, Beirut, Lebanon.

Corresponding author: Mazen Kurban, Associate Professor - Email: mk104@aub.edu.lb

Funding source: Medical Practice Plan (MPP) and University Research Board (URB) at AUB.

Keywords: Genodermatoses, Mal de Meleda, skin cancer, SLURP1, squamous lineage

Descriptive Statement: Mal de Meleda is a rare genetic skin disorder originally described in the island of Meleda in Croatia and characterized by severe abnormal skin. We encountered a Middle Eastern family with Mal de Meleda with affected members displaying different forms of skin cancers. We find that affected members display genetic alterations in a gene, termed *SLURP1*. We also show that this gene is abundant in normal skin and its levels decrease in progression of normal tissues to cancer. Our study sheds light on alterations that can be harnessed in the future to predict disease progression (i.e. cancer development) in patients with Mal de Meleda.

Introduction: Mal de Meleda (MDM) is a rare inherited autosomal recessive genodermatoses characterized by transgrediens palmoplantar keratoderma (PPK). MDM diagnosed is thought to be causally linked to mutations in the *SLURP1* gene. Uncommonly, cutaneous skin lesions have been found at PPK sites in MDM patients. We studied a Middle Eastern (Palestinian) family with high consanguinity that we encountered and who presented with clinical features of MDM and suspect skin lesions.

Methods: Histopathological analysis was performed on biopsies from skin lesions found in the affected individuals. Peripheral blood cells were isolated for genomic DNA extraction. Direct sequencing of all exons and exon-intron boundaries in *SLURP1* was performed. *In silico* analysis of *SLURP1* expression in normal and tumor specimens was performed using a publicly available expression dataset comprised of pan-normal specimens as well as sets constituting various squamous malignant tumors (of the skin, head/neck, cervix, esophagus), premalignant lesions and normal tissues. Statistical analysis was performed in the R environment.

Results: Affected members from the Middle Eastern family displayed severe forms of PPK consistent with MDM. Histopathological analysis of the skin lesions revealed that the affected members exhibited skin squamous cell carcinomas (SCCs) and melanoma. Sequence analysis revealed homozygous *SLURP1* mutations (c.82delT) in the affected members. Following analysis of various publicly available expression datasets, *SLURP1* mRNA levels were found to be markedly elevated in normal squamous tissue ($P<10^{-8}$), relative to other normal tissue types, and highly significantly correlated with various squamous markers (all $P<10^{-12}$). We also found that *SLURP1* was also significantly suppressed in malignant squamous tumors (e.g. of head/neck and cervix) relative to normal tissues (all $P<10^{-7}$), in primary melanomas relative to premalignant nevi ($P<10^{-5}$) and in metastatic melanomas relative to primary melanocytic tumors ($P<10^{-7}$).

Conclusion: Our study underscores cases of Middle Eastern MDM with *SLURP1* mutations and skin malignancies at PPK sites. Our findings also accentuate plausible squamous lineage-specific tumor suppressor profiles for the *SLURP1* gene that can be harnessed as markers for squamous skin cancer development in MDM patients.

Abstract # 22

Proteomic Analysis of Bradykinin Signaling in Podocytes

Richard Saoud[1], Pierre Khoueiry[1], Moustafa Al Hariri[1], Firas Kobeissy[1], Rui Zhu[2], Yehia Mechref[2], Miran Jaffa[3], Assaad Eid[4], Fuad Ziyadeh[1], Aida Habib[1], Ayad Jaffa[1]

[1]Department of Biochemistry and Molecular Genetics, [4]Department of Anatomy, Cell Biology and Physiological Sciences, Faculty of Medicine, [3]Epidemiology and Population Health Department, Faculty of Health Sciences, American University of Beirut, Lebanon,[2]Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79409, United States, ,

Corresponding author: Richard Saoud – Masters Student - E-mail: rss48@mail.aub.edu

Funding source: MPP, LNCSR

Keywords: Mass Spectrometry, Pathway Analysis, Prostaglandin H synthase-2, Bradykinin

Descriptive Statement: We wanted to study the change in Podocyte protein profile as a response to treatment with Bradykinin in a rat model.

Introduction:

Diabetic end-stage nephropathy is the main cause of long-term death for diabetic patients. Podocyte damage is one of the hallmarks of Diabetic Nephropathy (DN), where the loss of the podocyte filtration barrier leads to proteinuria and progressive renal damage. Bradykinin (BK) is a vasoactive peptide that has been implicated in the progression of renal damage. In this study, we aim to evaluate the changes in protein expression profiles of rat podocytes upon the treatment with BK by Mass Spectrometry in conjunction with pathway analysis. We aim to identify potential biomarkers associated with podocyte nephropathy that could potentially serve as focus points for targeted therapy that would ameliorate the progressive renal damage of DN.

Methods:

The Podocytes used were rat podocytes immortalized with the SV 40 T antigen. Mass Spectrometry (LC-ESI-MS/MS) Analysis was performed on immortalized rat podocytes with and without treatment of BK (10^{-7}) for 3 and 6 hours. Ingenuity Pathway Analysis (IPA) is used to analyze the Mass Spec data to suggest the possible changes in underlying cellular mechanisms and to point out interesting protein expression changes, such as the upregulation of Prostaglandin H synthase-2 (PTGS2), the major inducible enzyme responsible for the synthesis of prostaglandins (PG). The expression of PTGS2 was measured with western blots and qPCR. The product metabolite PGE_2 was measured by Enzyme Immuno-Assay (EIA).

Results:

Pathway analysis pointed out the upregulation of PTGS2 as the center of many cellular mechanisms involving cell death and cytoskeletal rearrangement. Preliminary results have shown the increased expression of PTGS2 protein expression in podocytes in response to stimulation with bradykinin by western blot, as well as the increase in levels of PGE_2, a downstream metabolic product which is usually representative of PTGS2 activity.

Conclusion:

Upregulation of PTGS2 in response to bradykinin hints at the importance of PTGS2 as a potential core regulator of diabetic nephropathy progression that could possibly be the target of therapy to ameliorate diabetic renal damage.

Abstract # 23

Molecular Mechanisms of the Protective Effects of Calcium Channel Blockers Against Cyclosporine Nephrotoxicity in Rats

Safaa H. Hammoud[1,2], Amal G. Omar[2], Mahmoud M. El-Mas[2], and Assaad A. Eid[2#]*
[1]Department of Pharmacology and Therapeutics, Faculty of Pharmacy, Beirut Arab University, [2]Department of Anatomy Cell Biology and Physiology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon and [3] the Department Pharmacology and Toxicology, Faculty of Pharmacy, Alexandria University, Egypt

***Presenter:** Safaa Hammoud
#Corresponding author: Assaad A. Eid (ae49@aub.edu.lb)

Keywords: Cyclosporine, nephrotoxicity, calcium channel blockers

Descriptive Statement: Despite its impressive effect in reducing acute rejection episodes, cyclosporine (CSA) nephrotoxic impact continues to present serious challenges in clinical practice. Understanding the mechanism leading to CSA induced-kidney injury will set a new paradigm in inducing adjunct therapy while on CSA treatment.

Introduction: Nephrotoxicity is a serious side effect for the immunosuppressant drug cyclosporine (CSA). In this study, we tested the hypothesis that the concurrent administration of calcium channel blockers such as verapamil or nifedipine guard against renal dysfunction induced by CSA in rats.

Methods: Studies were extended to investigate the roles of inflammatory, oxidative, and fibrotic pathways in the interaction. Six groups of male rats (n=6 each) were employed and allocated to receive one of the following treatments for 7 consecutive days: vehicle (cremophor), CSA (25 $mg.kg^{-1}.day^{-1}$), verapamil (2 $mg.kg^{-1}.day^{-1}$), nifedipine (3 $mg.kg^{-1}.day^{-1}$), CSA plus verapamil, or CSA plus nifedipine.

Results: Biochemical and histomorphometric analyses showed that compared with respective vehicle values, rats treated with CSA exhibited clear signs of nephrotoxicity that included: (i) proteinuria and elevations in serum creatinine and blood urea nitrogen, (ii) deposition of collagen IV in glomerular and tubular areas, and (iii) increases in the glomerulosclerosis index. While the single administration of nifedipine or verapamil caused no specific renal effects, the concurrent use of either calcium channel blocker significantly and equipotently ameliorated the biochemical and morphological derangements caused by CSA. We also report that the inflammatory (NF-κB expression), oxidative (NADPH-oxidase activity, reactive oxygen species production), and fibrotic (TGF-β1 expression) manifestations of renal toxicity induced by CSA were eliminated upon concurrent administration of nifedipine or verapamil.

Conclusion: Together, these results highlight the usefulness of calcium channel blocking agents in negating the CSA-induced nephrotoxicity and predisposing biochemical and molecular machinaries.

Funding source: Lebanese National Council for Scientific Research- Doctoral fellowship scholarship

Abstract # 24

Pomegranate (Punica granatum) Attenuates Cigarette Smoke–induced Nephropathy by Down Regulating Nox4 NADPH Oxidase.

Hijazi N[1]., Mikati N[1]*., Chahine A[1]*., Kreidieh F[1]*., Husary A.[1,2#] and Eid AA[#].*
[1]From the Department of Anatomy, Cell Biology and Physiological Sciences and [2]the Department of Internal Medicine, American University of Beirut, Faculty of Medicine and Medical Center, Beirut, Lebanon.

Presenter: *Hijazi Nour,*
Corresponding Authors: [#]Ahmad Husary (ah51@aub.edu.lb) and [#]Assaad A. Eid (ae49@aub.edu.lb)

Keywords: Cigarettes smoke, pomegranate, kidney injury, reactive oxygen species (ROS), TGF-β, NADPH oxidases

Descriptive Statement: Assessing the usefulness of pomegranate in alleviating the adverse effects of cigarette smoking (CS) on the kidney

Background and Aim of the study: Pomegranate, through its antioxidant properties, may be useful to treat or prevent human diseases. We have evidence suggesting that oxidative stress contributes to the pathogenesis of cigarettes smoking induced-acute kidney injury. We tested the hypothesis that pomegranate prevents cigarettes smoking-induced renal oxidative stress, attenuating renal injury.

Methods: Adult male C57BL/6J mice weighing between 22-25g were divided into four groups: Control (C) received placebo by oral gavage once daily, control mice that received pomegranate juice (80µmole/Kg) twice daily by oral gavage. Mice in group 3 (S) were exposed to cigarette smoke and group 4 (SP) mice were exposed to cigarette smoke and received pomegranate (80µmole/Kg) twice daily. At day 60 the animals were sacrificed and the kidney removed for biochemical and histological studies.

Results: The study shows that CS induces renal injury as assessed by PAS and trichrome staining. These changes are paralleled by an increase in ROS production through an NADPH oxidase dependent pathway, especially Nox4. Nox4-induced ROS production activates the TGF-β signaling pathway known to play a major role in renal injury. Interestingly, we show that pomegranate reverses the effect of smoke-induced collagen deposition and fibrosis in the kidney, reveling the reversal of renal damage, and reduces albuminuria. These beneficial effects are mediated by the fact that pomegranate reduces ROS production and reverse the alteration in TGF-β pathway.

Conclusion: Taken Together, our findings suggest that the consumption of pomegranate may ameliorate cigarettes smoke induced-kidney injury and may introduce a new paradigm in the treatment of the organ complication that are developed by smoking.

Abstract # 25

The Effect of Ciprofloxacin and Gentamicin on the Growth of Murine B16F10 Melanoma Cells

Dalal F. Jaber[1], Mary-Ann N. Jallad[1], Alexander M. Abdelnoor[1]
[1]Department of Experimental Pathology, Immunology and Microbiology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon
Corresponding author: Alexander M. Abdelnoor - Professor - E-mail: aanoor@aub.edu.lb

Authors: Dalal F. Jaber - Research Assistant – dj13@aub.edu.lb
Mary-Ann N. Jallad – PhD student – mnj07@mail.aub.edu

Funding source: the Lebanese National Council for Scientific Research (LNCSR)

Keywords: B16F10 melanoma cells, Cancer, Ciprofloxacin, Gentamicin, VEGF

Descriptive Statement: this study showed that the administration of certain antibacterial agents has promising results in the treatment of cancer-bearing mice.

Introduction: background and aims Immunosuppression caused by chemotherapy renders cancer patients more prone to infectious agents, including bacteria, and in need of antibacterial treatment. The aim of this study was to investigate the influence of ciprofloxacin and gentamicin treatment on the growth of murine B16F10 melanoma cells, in-vitro and in-vivo.

Methods: Groups of C57BL/6 female mice challenged with B16F10 melanoma cells were kept untreated or treated with sterile water, pyrogen-free saline, intraperitoneal ciprofloxacin, intraperitoneal gentamicin or ciprofloxacin through drinking water, for ten days. Serum levels of Vascular Endothelial Growth Factor (VEGF) were measured by ELISA, 1 and 3 hours after the last dose of ciprofloxacin or gentamicin. Mice were monitored for additional 10 days for survival assessment. Moreover, B16F10 melanoma cells were cultured in 24-well plates and exposed to different concentrations of ciprofloxacin (10-1000µg/ml) or gentamicin (100-2000 µM). Viability was determined, after 24 and 48 hours, using trypan blue.

Results: Serum levels of VEGF significantly decreased in ciprofloxacin-treated mice when compared to controls. None of the control mice survived beyond day 8, whereas 16.67% of those treated with ciprofloxacin survived up to 18 days. Serum levels of VEGF significantly increased in gentamicin-treated mice when compared to the control. In the saline control group, 66.66% of tumor-bearing mice survived, yet none of those treated with gentamicin survived (0% survival). Viability of B16F10 melanoma cells, in-vitro, significantly decreased with increasing concentrations of ciprofloxacin and with high concentrations of gentamicin.

Conclusion: Ciprofloxacin seems to exhibit anti-tumor activity, in-vivo and in-vitro, within therapeutic doses. Whereas gentamicin conveys its anti-tumor effect, in-vitro, at concentrations beyond its therapeutic window. These effects might be explained by several mechanisms such as, directly inducing cancer cell death by altering its DNA and/or RNA synthesis, affecting angiogenesis due to their effect on serum levels of VEGF or amending the immune response through modification of the normal microbiota.

Abstract # 26

Swine atrioventricular node ablation using radiation therapy: methods and an *in vivo* feasibility investigation for catheter-free ablation of cardiac arrhythmias

Atrioventricular node ablation by radiation therapy

Jad Ballout MD[1], Patrick Zakka MD[1*], Mostafa Hotait MD[2*], Karine Al Feghali MD[3], Ibrahim Abu Gheida MD[3], Phillip Taddei PhD[3], Charbel Saade PhD[4], Mukbil Hourani MD[4], Fady Geara MD PhD[3], Malek Tabbal PhD[5], Pierre Sfeir MD[6], Wassim Jalbout PhD[3], Wael Al-Jaroudi MD[7], Abdo Jurjus PhD[8], Bassem Youssef MD[3†], Marwan M. Refaat MD[1†]*

*[1]Department of Internal Medicine-Division of Cardiology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon ;[2]Department of Neurology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon; [3]Department of Radiation Oncology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon; [4]Department of Radiology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon; [5]Department of Physics, Faculty of Arts and Sciences, American University of Beirut, Beirut, Lebanon; [6]Department of Surgery- Division of Cardiothoracic Surgery, Faculty of Medicine, American University of Beirut, Beirut, Lebanon; [7]Division of Cardiology, Clemenceau Medical Center, Beirut, Lebanon; [8]Department of Anatomy, Cell Biology and Physiological Sciences, Faculty of Medicine, American University of Beirut, Beirut, Lebanon; *equal contribution*

Acknowledgement of financial support: Research funded by Farouk K. Jabre Biomedical Research Award (2014)

Background:
Stereotactic Radiosurgery (SRS) delivered to cardiac arrhythmogenic foci could be a promising catheter-free ablation modality. We tested the feasibility of in vivo atrioventricular (AV) node ablation in swines using SRS.

Objective:
The objective of this study is to use catheter-free ablation technique on the AV of swine.

Methods: 5 Large White breed swine (weight 50-75kg; 4 females) were studied. Single-chamber pacemakers were implanted in each pig. The pigs were placed under general anesthesia and CT scans were performed to localize the AV node. Orthogonal x-rays with matching of implanted fiducials were used for positioning. Stereotactic radiosurgery (dose ranging from 35 Gy to 40 Gy) was targeted at the AV node, and the pigs were followed up with pacemaker interrogations weekly to observe for electrocardiographic changes. Once changes were observed, the pigs were sacrificed and pathology specimens of various tissues, including the AV node and tissues surrounding the AV node, were taken to study the effects of radiation.

Results: All 5 pigs had disturbances of AV conduction with transition into complete heart block. Macroscopic inspection did not reveal damage to myocardium. Immunostaining revealed fibrosis in the target region, whereas no fibrosis was detected in the non-intended regions.

Conclusion: Catheter-free ablation using SRS is feasible in intact animal studies as an energy source for arrhythmia elimination.

Keywords: Stereotactic radiosurgery, noninvasive ablation, atrioventricular node, arrhythmia, atrioventricular node ablation

Abstract # 27

Diabetes and Depression: Unveiling a Potential Shared Biological Link

Barakat Rasha[1], El Massry Mohamed[1], Eid Assaad[1]
[1]Department of Anatomy Cell biology and Physiological Sciences, American University Beirut, Lebanon.

Corresponding Author: Assaad A. Eid - e-mail: ae49@aub.edu.lb

Funding Source: CEDRE, American University of Beirut and Paris Descartes University –Sorbonne Paris Cité.

Keywords: diabetes, depression, reactive oxygen species, central nervous system, peripheral nervous system

Descriptive Statement: Depression is twice as common in people with diabetes as in the general population. In this study we attempt to identify the metabolic consequences of signaling alteration in diabetes leading to structural and functional central and peripheral changes in the brain and the sciatic nerve, thus increasing the susceptibility to stress and depression.

Introduction: Epidemiological data showed that diabetic patients are at a higher risk of developing depression. However, the shared molecular and functional mechanisms between the two diseases remain unknown. Reactive oxygen species (ROS) have been shown to increase in both disorders but the sources and mechanisms by which ROS lead to peripheral and central nervous system injury need to be elucidated. This study aims to determine the role of NADPH-induced ROS in the onset of depression and diabetes. This project will evaluate the effect of depression, on the alteration of the NADPH oxidases pathway and its effect on the onset and development of diabetic neuropathy using functional, behavioral, structural, and molecular testing.

Methods: A chronic stress procedure was used to induce depression in the control or non-obese type 2 diabetic mice. Behavioral tests were performed to assess depression and behavioral malfunction in diabetic and depressed animals. RT-PCR allowed the measurement of mRNA levels of Nox1, Nox4, PLP, and MBP. Western blots were used to assess the protein expression levels of Nox1 and myelin proteins. NADPH oxidase activity was used to measure the NADPH-dependent superoxide anion generation.

Results: Behavioral assessment shows a depressed like behavior in the diabetic animals resembling that of the depressed animals. Interestingly, the diabetic depressed mice showed an increase in the severity of depression, NADPH-dependent superoxide production, as well as a dysregulation in the myelin of the central and peripheral nervous system. Treatment with GKT, a specific Nox1 and Nox4 inhibitor, decreased ROS production, restored the expression of myelin protein in the nervous system, and reversed significantly, the depressive-like behavior as well as sensorimotor dysfunction.

Conclusion: NADPH oxidases-induced ROS production might be a major player in the central and peripheral myelin injury inducing a depressive-like behavior in diabetes and causing an alteration in the sensorimotor function.

Abstract # 28

High-calorie Diet Induces Vascular and Hemodynamic Abnormalities in Absence of Change in Blood Glucose or Insulin Levels: Modulation by Oral Anti-hyperglycemic Drugs

Fatima Sleiman[1], Mohamed El-Khatib[2], Assaad Eid[1], and Ahmed El-Yazbi[1]*
[1]Faculty of medicine, American University of Beirut; [2]Faculty of pharmacy, Alexandria University.
***Corresponding author**: Ahmed El-Yazbi – Assistant Professor –
Email:.ae88@aub.edu.lb

Funding source: Seeding grant-AUBFM

Keywords: hemodynamics, VSMC, anti-hyperglycemic drugs.

Descriptive Statement: Different changes at the vascular level occur during the development of diabetes, and they are modulated using anti-hyperglycemic drugs regardless of their function on glucose levels.

Introduction: Few studies examined the early onset vascular changes occurring within the context of diabetes development. Moreover, recent clinical evidence suggests a vasculoprotective effect for anti-hyperglycemic drugs that is not a direct consequence of their effect on blood glucose level. We aim to understand the underlying pathophysiological mechanism governing the vascular complications during diabetes development and the role of anti-hyperglycemic drugs in protecting against these complications.

Methods: Rats were fed a high fat diet for 4, 8 and 12 weeks, at which point there was no increase in fasting serum glucose, serum insulin, nor mean arterial pressure (MAP). Measurement of aortic smooth muscle function was done using an isolated tissue bath. Immunohistochemistry was done on aortic tissue sections to stain for TGF-β1 and Smad 3. Vascular smooth muscle cells were isolated from rat aorta and then tested for their proliferation and migration characteristics.

Results: Aortic rings from these rats showed an increased contractile response to phenylephrine (PE) compared to rings from age-matched control animals, with an increased sensitivity (reduced EC50). The PE-induced contractions were resistant to Ca-free physiological solution and appeared to be more sensitive to Rho kinase inhibition. In parallel, the hypercontractile phenotype was manifested as an increase in the pressor effect of PE upon administration *in vivo* with a poor reflex bradycardiac response, despite the absence of a change in basal MAP. Histopathology and immunohistochemistry showed an increased intimal thickness of aorta from these rats together with increased TGF-β1 and Smad 3 expression. VSMC were isolated from the aorta of control rats and from high calorie-fed rats, whereby they exhibited different phenotypes. Moreover, it was shown that the high fat diet promotes proliferation and migration of VSMC. A two-week treatment with either pioglitazone or metformin reversed the increased contractility to PE, increased intimal thickness, and increased TGF-β1 expression with no change in fasting serum glucose.

Conclusion: Our results suggest that early vascular dysfunction associated with high calorie intake involve inflammatory changes that are showed to be ameliorated using anti-hyperglycemic drugs.

Abstract # 29

Adiponectin Attenuates Hypertension-Induced Vascular Remodeling through NHE-1 Activity and LKB1/AMPK Signaling

Crystal M. Ghantous[1], Zeina Radwan[1], Rima Houri[1], Rana Ghali[2], Nancy Chaaya[1], Ramzi Sabra[2], Asad Zeidan[1]

[1]Department of Anatomy, Cell Biology and Physiology, [2]Department of Pharmacology and Toxicology, American University of Beirut, Beirut, Lebanon

Corresponding author: Crystal M. Ghantous – PhD Candidate - E-mail: cmg00@aub.edu.lb

Funding source: MPP Grant to Dr. Asad Zeidan

Keywords: Vascular, hypertension, adiponectin, leptin, remodeling

Descriptive Statement: This study investigates the involvement of adiponectin and sodium hydrogen exchanger isoform-1 in the molecular mechanisms of hypertension-induced vascular remodeling.

Introduction: Background and Aims: Hypertension leads to vascular remodeling, affects circulating levels of leptin and adiponectin (APN), and is associated with increased sodium hydrogen exchanger isoform-1 (NHE-1) activity. The aim of this study is to investigate whether hypertension-induced vascular smooth muscle cell (VSMC) remodeling is mediated by NHE-1 activity, LKB1/AMPK signaling and attenuated by high APN/leptin ratio.

Methods: In order to study the effect of hypertension on VSMC remodeling, the *in vivo* rat model of angiotensin II (Ang II) infusion for 14 days and the *in vitro* model of mechanically stretching the rat portal veins (PVs) were used. APN and the selective NHE-1 inhibitor cariporide were added to the blood vessels. Activation of ERK1/2, AMPK and LKB1 in VSMCs was evaluated by Western blot. Leptin and APN expression was studied by Western blot and immunofluorescence. ROS production was assessed by DHE staining and immunofluorescence.

Results: Stretching the PVs for 10 min significantly increased ERK1/2 phosphorylation in VSMCs (as compared to control PVs), while cariporide and APN significantly reduced mechanical stretch-induced ERK1/2 phosphorylation. Mechanical stretch for 10 min significantly decreased LKB1 and AMPK phosphorylation, while cariporide significantly attenuated this effect in stretched PVs by increasing p-AMPK. Moreover, APN significantly increased p-LKB1 and p-AMPK in stretched PVs. Ang II-infusion for 14 days increased leptin, decreased APN and increased ROS significantly in PVs. Similar results were observed in the aortas of Ang II-infused rats compared to sham-operated rats. Consistent data were obtained by immunofluorescence for leptin, APN and ROS.

Conclusion: APN attenuates mechanical stretch-induced VSMC remodeling by activating the LKB1-AMPK axis and inhibiting ERK1/2, which are mediated by NHE-1 activity. Moreover, hypertension-induced vascular remodeling is associated with higher leptin synthesis, lower APN synthesis and higher ROS production in VSMCs.

Abstract # 30

Diminished expression of T-box transcription factors in preneoplastic lung lesions: translational opportunities for early detection of lung cancer

Athar Khalil[1], Smruthy Sivakumar[2], Tina McDowell[2], Avrum Spira[3], Fadi Bitar[4], Mazen Kurban[1], Paul Scheet[2], Georges Nemer[1], Humam Kadara[1,2]

[1]Departments of Biochemistry and Molecular Genetics and [4]Pediatrics and Adolescent Medicine, American University of Beirut, Beirut, Lebanon; [2]Division of Cancer Prevention, University of Texas MD Anderson Cancer Center, Houston, TX, U.S.A.; [3]Section of Computational Biomedicine, Boston University, Boston, MA, U.S.A.

Corresponding authors: Georges Nemer, Ph.D. Professor - E-mail: gn08@aub.edu.lb and Humam Kadara, Ph.D., Assistant Professor - Email: hk94@aub.edu.lb

Funding source: Medical Practice Plan (MPP) and University Research Board (URB) at AUB, Cancer Prevention and Research Institute of Texas grant RP150079 and NCI grant 1R01CA205608-01A1.

Keywords: T-box transcription factors, Non-small cell lung cancer (NSCLC), airway field of cancerization, lung preneoplasia, early detection

Descriptive Statement: We demonstrate here that the expression of members of the T-box (*TBX*) gene family is markedly suppressed in "normal" (to the "eye") yet mutagenized airway cells and in premalignant lung tissues, phases occurring prior to onset of overt lung cancer. Leveraging this property, we also find that diminished *TBX* expression is a powerful molecular tool to detect lung cancer in smokers.

Introduction: T-box (TBX) transcription factors transactivate or repress various genes involved in normal lung physiology. Yet, the expression of *TBX* genes in development of non-small cell lung cancer (NSCLC) remains elusive. In this study, we sought to probe expression profiles of *TBX* genes in early phases of NSCLC pathogenesis.

Methods: Expression of *TBXs* 2 through 5 was analyzed in public and in-house expression datasets comprised of: 1) pan-normal specimens from the cancer genome atlas (TCGA) and genotype-tissue expression (GTEx) projects; 2) NSCLCs and normal lung tissues; 3) matched normal lung, premalignant hyperplasias and NSCLCs that we profiled by RNA-sequencing; 4) NSCLCs, normal-appearing airways surrounding NSCLCs and distant normal lungs that we compiled 5) normal bronchial samples from 884 smokers undergoing diagnostic bronchoscopy for suspicion of lung cancer. Statistical analysis was performed in the R environment. Gene-gene network analysis was performed using Ingenuity Pathways Analysis.

Results: Overall, *TBX* expression was statistically higher ($P<10^{-15}$) in normal heart and lung tissues relative to other normal tissues. Expression of the *TBX*s was significantly suppressed in all NSCLCs relative to normal lung tissues (all $P<10^{-9}$). Network analysis revealed elevated expression of cell cycle promoting genes downstream of *TBX*s in NSCLCs. Expression levels of *TBX*s were significantly progressively decreased across premalignant lesions and NSCLCs relative to normal lungs (all $P<10^{-2}$). *TBX*s were significantly suppressed in NSCLCs and in surrounding normal-appearing airway cells relative to distant normal lung ($P<10^{-15}$). Further, *TBX* expression was not only lower in normal bronchial cells from smokers with lung cancer relative to cells from cancer-free smokers but was also a significant predictor ($P<10^{-5}$) of lung cancer status in suspect smokers.

Conclusion: Our translational study demonstrates that *TBX* genes are notably suppressed in "normal" and premalignant phases in lung oncogenesis and underscores their potential utility as biomarkers for early lung cancer detection in high-risk smokers.

Abstract # 31

Individual and institutional financial conflicts of interest reported by authors of randomized controlled trials: a systematic survey

[1]Hussein Noureldine, [2]Maram Hakoum, [3]Eliane Abou-Jaoude, [4]Rasha Raslan, [4]Joseph Habib, [5]Nahla Jouni, [4]Divina Hasbani, [6]Luciane Lopes, [7]Gordon Guyatt, [8]Elie A. Akl

[1]Faculty of Arts and Sciences, Lebanese American University, [2]Clinical Research Institute, American University of Beirut Medical Center, [3]Department of Internal Medicine, SUNY University at Buffalo, United States of America, [4]Faculty of Medicine, American University of Beirut, [5]Faculty of Agriculture and Food Sciences, American University of Beirut, [6]Pharmaceutical Science Master Course, University of Sorocaba, Brazil, [7]Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada, [8]Department of Medicine, American University of Beirut Medical Center

Presenter: Hussein Noureldine, BS – Student – han22@mail.aub.edu

Corresponding author: Elie A. Akl, MD, MPH, PhD –Professor of Medicine – ea32@aub.edu.lb

Funding source: This project was funded by the American University of Beirut Faculty of Medicine's Medical Practice Plan (MPP) funds.

Keywords: financial conflicts of interest, randomized controlled trial, methodological research

Descriptive Statement: A systematic survey to assess the characteristics of individual and institutional financial conflicts of interest (FCOI) reported by trial authors and to aid in future guidance for better reporting of FCOIs.

Background and Aims According to the Institute of Medicine, a COI is "a financial or intellectual relationship that may impact an individual's ability to approach a scientific question with an open mind". The field of healthcare research has recognized, studied and considered financial relationships when setting COI disclosure and management policies. Disclosures usually lack important details that would allow the judgment of their significance. We surveyed reports of randomized controlled trials (RCT) for the characteristics of individual and institutional FCOI disclosures.

Methods: We used standard systematic review methodology to survey reports of clinical RCT papers published in any of the 119 Core Clinical Journals in 2015. We categorized the types of disclosed FCOI as grant, employment, personal fees, non-monetary support, drug or equipment supplies, patent, stocks and other types. We collected data on general characteristics of the RCTs, the reported funding and the characteristics of the COI disclosures including type, source, relation of the source to the trial subject and funder, the duration and monetary value. We also collected data on the characteristics of authors that report the COIs, including authorship rank, title, affiliation and gender. We conducted descriptive and regression analyses.

Results: We included 108 RCTs of which 96% had the first author affiliated with an institution from a high income country and 57% were on a pharmacological intervention. All RCTs reported being funded, of which 58% were funded by a private-for-profit source. We identified 816 authors disclosing a total of 3,066 FCOI disclosures. Of the 816 authors, 65% held medical degrees and 53% were affiliated with an academic organization. Individual FCOIs were more commonly reported than institutional FCOIs (97% and 3% respectively). The most commonly reported individual FCOI subtypes were personal fees (78%), research support (69%) and employment (41%). Across all FCOI disclosures, the source of FCOI was reported in 99% of disclosures and was a private-for-profit source in 84% of cases. We found poor reporting of the FCOI details related to source's relation to the trial, duration and monetary value. Reporting of FCOIs was positively associated with trial funding from a private-for-profit organization, author holding a medical degree and author affiliation being an academic organization.

Conclusion: Journals should require better and more detailed reporting of FCOI disclosures. There is a need for verification methods to assess the accuracy and completeness of FCOI disclosures.

Abstract # 32

Modeling Chronic Myeloid Leukemia in *Drosophila Melanogaster*

Amani Al Outa [1], Ali Bazarbachi[1, 2], Marwan El Sabban[1], Margret Shirinian[3], Rihab Nasr[1*]*
[1]Department of [Anatomy, Cell Biology and Physiology], [2]Department of [Internal Medicine], [3]Department of [Experimental Pathology, Microbiology and Immunology], American University of Beirut, Beirut, Lebanon

***Corresponding authors**:
[Dr. Margret Shirinian/Dr. Rihab Nasr] - ms241@aub.edu.lb/rn03@aub.edu.lb

Keywords: *BCR-ABL*, chronic myeloid leukemia (CML), tyrosine kinase inhibitors (TKI), drosophila

Descriptive Statement: The use of the fruit fly to study chronic myeloid leukemia and screen for effective treatment.

Introduction: CML is caused by a balanced chromosomal translocation resulting in the formation of *BCR-ABL* fusion gene that encodes a constitutively active BCR-ABL tyrosine kinase, which activates multiple signal transduction pathways leading to cancer. Several treatment modalities have been proposed using TKIs; however, some mutations have proven elusive. *Drosophila melanogaster* is an established *in vivo* system to model human diseases, specifically cancer and for drug screening. Targeted expression of chimeric human/fly *BCR-ABL* to Drosophila eye imaginal discs and central nervous system demonstrated the effectiveness of this model in studying CML. The aim of our study is to model human *BCR-ABL* and its mutants in Drosophila to serve as a credible platform for treatment screening.

Methods: Transgenic flies, harboring the human *BCR-ABL* p210 (wild type *BCR-ABL* and the highly-resistant T315I mutant), were generated using the Phi C31 integrase system and were inserted on the 3rd chromosome for GAL4-UAS expression. Myc tag was added at N-terminus to identify expression of the BCR-ABL protein. Using the glass multimer reporter (GMR-GAL4) we overexpressed *BCR-ABL* p210 (wild type and T315I) in the developing eyes. Wild type flies (W1118) served as control. The ommatidial structure of the eye phenotype was analyzed by scanning electron microscope. The transgene expression in Drosophila heads was confirmed by western blotting.

Results: Both *BCR-ABL* wild type and mutant flies develop a severe rough eye phenotype characterized by smaller eyes with total loss of photoreceptors. Mechanosensory bristles were irregularly distributed and lost in some instances. The rough eye phenotype was more severe in flies harboring the T315I mutation.

Conclusion: These results show that human *BCR-ABL* induces transformation of the ommatidial structures in Drosophila and hence this model provides an important tool for further *in vivo* testing of the sensitivity of patients-derived mutations to TKIs.

Abstract # 33

Spectrum of RB1 gene mutations in children with heritable retinoblastoma in Lebanon

Zeina Merabi[1], Christiane Al-Haddad[2], Lina Farah[1], Ziad Bashour[2], Riad Ma'luf[2], Samar Muwakkit[1], Miguel Abboud[1], Nidale Tarek[1], Hassan El-Solh[1], Raya Saab[1]*

[1]Department of Pediatrics and Adolescent Medicine, American University of Beirut, Beirut-Lebanon

[2] Department of Ophthalmology, American University of Beirut, Beirut-Lebanon

*[*] **Corresponding author**: Zeina Merabi- Research Assistant- Email: zm42@aub.edu.lb*

Funding source: None

Keywords: Retinoblastoma, RB1 gene, Mutation spectrum

Descriptive Statement: Mutations in the *RB1* gene on chromosome 13 is associated with the childhood tumor retinoblastoma. We evaluated the rate and pattern of *RB1* mutations in children with retinoblastoma treated in Lebanon.

Introduction: Retinoblastoma, an embryonic neoplasm of retinal origin, is the most common primary intraocular malignancy in children. Inactivation of both alleles of the *RB1* gene during normal retinal development initiates the formation of the tumor retinoblastoma (RB). A broad spectrum of germline *RB1* mutations have been reported worldwide, including more than 1000 different *RB1* mutations. Our aim is to describe the distribution of *RB1* mutations in patients treated at the Children's Cancer Center of Lebanon at the AUBMC.

Methods: All children with bilateral tumors, and children with unilateral retinoblastoma diagnosed before 2 years of age, had gene testing performed for *RB1* mutation. We compared the resulting sequencing data with the reference sequence gene NM-000321.2

Results: A total of 28 patients with retinoblastoma were included. Nationalities included 18 Syrian (64.3%), nine Lebanese (32.1%) and 1 Palestinian (3.6%). Genomic variations were negative in 6 cases and positive in 22. Of these 22 patients, 19 had bilateral and 3 unilateral RB. Of the total mutations identified (n=22), 3 (13.6%) had gross deletions. These involved multiple exons in 2 cases and a whole chromosome deletion in 1 case. Another 10 (45.5%) had nonsense mutations, 2 (9.1%) had splice mutations, 1 (4.5%) had a single base-pair substitution, and 6 (27.3%) had missense mutations. One of the identified mutations was previously unreported or characterized, representing a novel mutation.

Conclusion: These findings help to characterize the spectrum of mutations present in children with retinoblastoma treated in Lebanon.

Abstract # 34

Anti-Tumor Efficacy of Arsenic/Interferon in Preclinical Models of Chronic Myeloid Leukemia Resistant to Tyrosine Kinase Inhibitors

Rabab El Eit[1], Abdul Rahman Itani[1], Nagham Rasbieh[1], Ahmad Iskandarani[1], Mark Jabour[2], Ahmad Santina[1], Ghazi Zaatari[2], François-Xavier Mahon[3], Hugues De Thé[4], Ali Bazarbachi[1,5], Rihab Nasr[1]

[1]Department of Anatomy, Cell Biology, and Physiological Sciences, American University of Beirut, Beirut, Lebanon, [2]Department of Pathology and Laboratory Medicine, American University of Beirut, Beirut, Lebanon, [3]Laboratoire d'Hématologie et Service des Maladies du Sang, CHU de Bordeaux, Université Victor Segalen Bordeaux 2, INSERM U876, Bordeaux, France, [4]Service de Biochimie, Equipe labellisée, Ligue Nationale Contre le Cancer, CNRS, INSERM, Université Paris Diderot UMR 7212, Hopital Saint Louis, Paris, France, [5]Department of Internal Medicine, American University of Beirut, Beirut, Lebanon.

Corresponding author: Dr. Rihab Nasr-Associate Professor-E-mail: rn03@aub.edu.lb

Funding source: MPP grant.

Keywords: Chronic myeloid leukemia (CML), arsenic trioxide (ATO), interferon alpha (IFNα), resistance, T315I.

Descriptive Statement: T315I mutation in ABL confers resistance to almost all tyrosine kinase inhibitors (TKI) established for the treatment of CML. Combination of ATO and IFNα (ATO/IFNα) preclinical efficacy is evaluated using *in vivo* and *in vitro* models of TKI resistant CML.

Introduction: TKI have been established for the treatment of CML. However, patients can develop resistance against TKI mainly due to kinase domain mutations. T315I mutation confers resistance to almost all TKI. Although some evidence suggests the potential efficacy of ponatinib against T315I mutation, recent studies demonstrated the emergence of ponatinib-resistant compound mutants which confer resistance to all TKIs, including ponatinib. Our study aims to test the anti-tumor efficacy of ATO/IFNα in preclinical models of CML resistant to TKIs.

Methods: Imatinib-resistant K562-R and AR230-R CML cells were treated with different concentrations of ATO and IFNα. The effect of the treatment on cell proliferation and apoptosis induction was performed using MTT and TUNEL assays, respectively. The effect of ATO/IFNα on the survival of T315I leukemic mice was studied using a retroviral *BCR-ABL* T315I transduction murine CML model.

Results: ATO/IFNα inhibited the proliferation of K562-R and AR230-R. Moreover, ATO and IFNα synergized to induce apoptosis of these cells. Leukemic mice treated with ATO/IFNα showed a significant prolonged survival as compared to untreated controls and to mice treated with each drug separately. As expected, imatinib had no effect on the survival of leukemic mice harboring BCR-ABL with T315I mutation. Importantly, ATO/IFNα severely impaired engraftment into untreated secondary recipients, with some recipients never developing the disease, demonstrating a dramatic decrease in CML Leukemia Initiating Cells (LICs) activity.

Conclusion: Our findings provide clear evidence of the preclinical efficacy of ATO/IFNα in resistant CML models, specifically in CML mouse models with the T315I mutation, and accordingly open the perspective of investigating ATO/IFNα in the therapeutic strategy of CML.

Presented by Abdul Rahman Itani Research Assistant

Abstract # 35

Thymoquinone Combination with Arsenic and Interferon Enhances Cell Death in Adult T-cell Leukemia

Maamoun Fatfat[1], Zeina Habli[1], Regine Schneider-Stock[4], Hiba El-Hajj[3], Ali Bazarbachi[2], Hala-Gali Muhtasib[1]*

[1]Department of Biology, and Department of Anatomy, Cell Biology and Physiological Sciences, American University of Beirut, Lebanon, [2]Department of Internal Medicine, American University of Beirut, Lebanon, [3]Department of Internal Medicine and Experimental Pathology, American University of Beirut, Lebanon, [4]Experimental Tumor Pathology, Institute for Pathology, University Erlangen-Nuremberg, Germany

Funding source: URB.

Zeina Habli: Master student

Keywords: ATL, HTLV-1, apoptosis, cell cycle, TQ, As/IFN- α

Descriptive Statement: The combination of Arsenic and Interferon alpha with Thymoquinone, at low concentrations, sensitized the resistant HTLV-1 positive cell line and increased the efficacy of the clinically used drugs.

Background and aims: Adult T-cell Leukemia (ATL) is a mature T-cell neoplasm associated with human T-cell lymphotropic virus (HTLV-1) infection. Due to intrinsic chemo-resistance and immunosuppression, the prognosis of ATL is poor with a median survival rate of 6 months after disease onset. According to the disease manifestations, several studies have displayed that the combination of Arsenic (As) and Interferon alpha (IFN-α) shows promising therapeutic potential against ATL with minimal adverse effects. With an approach to enhance the *in vitro* efficacy of these two targeted therapies used against ATL, we aimed to investigate the anti-cancer effects of Thymoquinone (TQ), the active principle of *Nigella sativa*, with lower concentrations of As and IFN-α, either alone or in combination on Human HTLV-1 positive (C91) and HTLV-1 negative (CEM) CD4+ malignant T-cell lines following 24 or 48 hours of treatment.

Methods: The efficacy of single and combination treatments was investigated using several assays including cell viability, cell cycle analysis, apoptosis, mitochondrial membrane disruption and western blot analysis.

Results: TQ/As/IFN-α combination resulted in pronounced time-dependent inhibitory effects on cell viability when compared to single and double treatments. The triple combination, in comparison to TQ single- and As/IFN-α- double treatments, significantly induced apoptosis, enriched the pre-G_1 population, disrupted the mitochondrial membrane potential and induced caspase-dependent apoptosis. The latter was confirmed by the cleavage of caspase 3, caspase 9 and PARP as well as the downregulation of the expression of the anti-apoptotic protein Bcl-2 by western blots. Human HTLV-1 negative CEM cells were more sensitive to TQ/As/IFN-α compared to the resistant HTLV-1 positive C91 cells.

Conclusion: Collectively, our results suggest a strong possibility of synergistic efficacy of TQ in combination with As and IFN-α for the treatment of CD4+ malignant T-cells. Therefore, this triple combination holds promise as a potential therapeutic approach for ATL patients.

Abstract # 36

Control of Spermatogenesis by the tumor suppressor p53 and the Cyclin D-Dependent Kinase Inhibitor $p18^{Ink4c}$ in Mice

Hasan Zalzali, Wissam Rabeh, Omar El Najjar, Raya Saab
Department of Pediatric and Adolescent Medicine, American University of Beirut, Beirut, Lebanon.

Email: hz13@aub.edu.lb (Research Scientist)

Keywords: Infertility, spermatogenesis, tumor suppressors, p53, $p18^{Ink4c}$

Introduction: The controlled regulation of spermatogenesis is crucial for normal sperm production and for male fertility. Based on the observation that *p53-/- Ink4c-/-* male mice have reduced fertility, we investigated the role of these two tumor suppressor proteins in spermatogenesis.

Methods: To evaluate the role of p53 and Ink4c in male infertility, mice lacking *p53* (p53-null mice) were bred with *Ink4c-null* mice to derive animals lacking both genes. Blood, Testis and epididymides were isolated at different ages, and investigated for morphology, cell cycle, apoptosis, and differentiation.

Results: We found that, compared to normal wild-type mice, *Ink4c-/- p53-/-* mice have testicular hyperplasia with larger testis size and weight. Microscopic examination revealed hyperplasia of Leydig cells. Mice lacking both genes showed a delay in spermatozoa entry into meiosis, leading to lower sperm counts and increase in apoptosis. Interestingly, these mice also had a higher number of immotile and sluggish sperm, as well as a higher number of abnormal sperm.

Conclusion: Our findings reveal a previously unknown role for *p53* and *Ink4c* in spermatocyte development and maturation, and identify these tumor suppressors as candidate players in human forms of male-only infertility, especially those in which early meiotic arrest is a hallmark. Further work should focus on evaluating the status of these tumor suppressor proteins in human sperm maturation and disorders of male fertility.

Abstract # 37

miR-183 Potential Targets in Breast Cancer Cell Lines

Farah Nassar[1], Rabih Talhouk[1], Rihab Nasr[2]

[1]Biology Department, Faculty of Arts and Sciences, American University of Beirut, Beirut, Lebanon

[2]Department of Anatomy, Cell Biology and Physiological Sciences, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

Corresponding author: Dr. Rihab Nasr- Associate Professor - E-mail: rn03@aub.edu.lb

Funding source: MPP and CNRS

Keywords: Breast Cancer, microRNA, miR-183, microarray

Descriptive Statement: Highly upregulated miR-183 in Lebanese breast cancer patients inhibits PDCD4, TET1, AKAP12 and PP2CA mRNA expression in breast cancer cells.

Introduction: microRNA (miRNA), small non-coding RNA molecules, are aberrantly expressed in breast cancer (BC). These molecules are master gene regulators involved in BC initiation, progression, metastasis, and therapy chemoresistance through controlling multiple signaling pathways. Our study aims to investigate the role of one of the differentially expressed miRNA in Lebanese BC patients in BC development.

Methods: miRNA microarray profiling was performed using breast tissues taken from Lebanese patients with early BC of invasive ductal carcinoma histotype and of estrogen and progesterone receptor positive profile. miR-183 expression was tested in different BC cell lines using real time PCR. miR-183 targets were predicted using in silico tools and their expression was studied in BC cell lines using real time PCR after transfection with miR-183 mimics. MTT assay was performed to test the effect of miR-183 overexpression on the proliferation of BC cells.

Results: Among the 74 differentially expressed miRNA in BC tissues of all Lebanese patients, we found that miR-183 was among the most upregulated miRNA. Selected predicted targets of miR-183 were AKAP12 (A kinase anchor protein 12), PDCD4 (programmed cell death 4), TET1 (dioxygenase gene), SMAD4 (SMAD Family Member 4), PP2CA (serine/threonine-protein phosphatase 2A catalytic subunit alpha isoform), FOXP1 (Forkhead box protein P1) and LATS2 (Serine/threonine-protein kinase). We found that transfection with miR-183 mimics inhibits the expression of AKAP12, PDCD4, TET1 and PP2CA mRNA in BC cell lines (MCF-7 and MDA-MB 231) without any significant change in cell proliferation.

Conclusion: The tested miR-183 targets are known regulators of cell cycle, apoptosis, invasion and metastasis. This preliminary study is the first to report a possible inverse correlation between miR-183 and TET1 as well as PP2CA. Hence, further functional studies should be performed to identify the molecular mechanism of miR-183 on BC development.

Position: PhD student

Abstract # 38

Anti-Angiogenesis therapy induce an inflammatory state in MDA-MB-231 breast cancer cell line *in vitro* and *in vivo*

Layal El-Hajjar[1], Abdallah Shaito[2], Kazem Zibara[3], Jalal Kazan[4], Jamal El-Saghir[4], Mohamed E. Moustafa[1] and Marwan El-Sabban[4]

[1]Department of Biological and Environmental Sciences, Faculty of Science, Beirut Arab University, Lebanon, [2]Department of Biological and Chemical Science, Faculty of Arts and Sciences, Lebanese International University, Beirut, Lebanon, [3]Department of Biology, Faculty of Sciences and DSST, Lebanese University, Beirut, Lebanon, [4]Department of Anatomy, Cell Biology and Physiological Sciences, American University of Beirut, Beirut, Lebanon

Corresponding author: Marwan El-Sabban, Professor, E-mail: me00@aub.edu.lb

Funding source: Lebanese National Council for Scientific Research (LNCSR)

Keywords: VEGF, avastin, inflammation, gap junction

Descriptive Statement: Study the ineffectiveness mechanisms to bevacizumab and investigate whether this is achieved by pre-activation of RAGE signaling pathway in metastatic breast cancer.

Introduction: VEGF-A stimulates angiogenesis in a variety of diseases, especially in cancer. Bevacizumab (avastin), the recombinant antibody targeting VEGF, improves progression-free but not overall survival in metastatic breast cancer. Recent studies showed that avastin treatment in a diabetic model increased inflammation by pre-activation of RAGE signaling. Furthermore, inflammatory factors in the tumor microenvironment induce epithelial-to-mesenchymal transition of non-transformed breast epithelial cells. On the other hand, both VEGF and direct cancer cell-endothelial cell interaction are crucial in extravasation. In this study, we evaluated the effect of avastin on inflammatory mediators in metastatic breast cancer (MDA-MB-231) cells and evaluated the levels of IL-1β, RAGE, and NF-κB pathway in a metastatic model of breast cancer *in vitro* and in a xenograft murine model injected with MDA-MB-231 or MDA-MB-231 overexpressing Cx43 cancer cells treated with avastin at the secondary site (lung tissues).

Methods: Quantitative PCR and western blot were performed to assess the changes in expression levels of inflammatory mediators and other factors upon treatment with avastin. Confocal microscopy was performed to document the expression of Nuclear Factor-kappa B (NF-κB) phospho-p65. Gelatin zymography, to assess the proteolytic activity of metalloproteinases (MMP2 and MMP9) and Enzyme linked immunosorbent assay (ELISA) to assess IL-1β, TNF-α, and VEGF levels.

Results: Avastin treatment increases expression of inflammatory mediators including RAGE, IL-1β and TNF-α as well as other metastatic factors including MMP2 and MMP9 at transcriptional and protein levels after treatment *in vitro* and *in vivo.* Interestingly, upregulation of Cx43 in combination with avastin treatment alleviated the effect of avastin on inflammation.

Conclusion: Ineffectiveness of avastin treatment may be due to avastin-induced inflammatory microenvironment. Overexpression of Cx43 enhances sensitivity to avastin treatment. It is postulated that anti-angiogenesis therapy with avastin is more significant in tumors that express Cx43 and may become more effective if coupled with Cx43 upregulation in breast cancer.

Abstract # 39

Effect of Intercellular Communication on Epithelial to Mesenchymal Transition in Metastatic Breast Cancer

Nour Jalaleddine[1], Abdallah Shaito[2], Kazem Zibara[3], Jalal Kazan[4], Jamal El-Saghir[4], Mohamed E. Moustafa[1] and Marwan El-Sabban[4]

[1]Department of Biological and Environmental Sciences, Faculty of Science, Beirut Arab University, Lebanon, [2]Department of Biological and Chemical Science, Faculty of Arts and Sciences, Lebanese International University, Beirut, Lebanon, [3]Department of Biology, Faculty of Sciences and DSST, Lebanese University, Beirut, Lebanon, [4]Department of Anatomy, Cell Biology and Physiological Sciences, American University of Beirut, Beirut, Lebanon

Corresponding author: Marwan El-Sabban, Professor, E-mail: me00@aub.edu.lb

Funding source: Lebanese National Council for Scientific Research (LNCSR)

Keywords: Cell-cell communication, Pannexins, Connexins, EMT, Metastasis

Descriptive Statement: The role and mechanism of action of pannexins on Epithelial to Mesenchymal Transition (EMT) and its association with connexins in metastatic breast cancer.

Introduction: EMT effectors play a critical role in cancer metastasis. Gap junctions contribute to cancer metastasis through intercellular interaction between subpopulation of cells and their microenvironment *via* cell-to-cell communication. Pannexins are vertebrate integral membrane proteins that share structural and functional features with connexins. To date, three pannexins have been described in human: PANX1, PANX2 and PANX3. These pore forming hemi-channels are involved in major signaling pathways; including intracellular calcium, extracellular ATP release, and ROS production.

Methods: The transcriptional level of pannexins was assessed in MDA-MB231, overexpressing Cx43 and in knocked down Cx43 *in vitro* and *in vivo* using quantitative- polymerase chain reaction. Live imaging microscopy was performed to document the functional activity of pannexin hemi-channels. Blocking of pannexin hemi-channels was performed by treating the cells with probenecid, a potent pannexin inhibitor. Probenecid effect on the viability of MDA-MB231 cells was assessed by trypan blue exclusion assay. Dye transfer assays were conducted to study the functionality of gap junctions upon pannexin inhibition. The levels of EMT markers were assessed using quantitative PCR and western blot.

Results: PANX 1 and PANX 2; but not PANX3, are expressed in MDA-MB231. Pannexin expression is significantly influenced by Cx43 expression *in vitro* as well as *in vivo*. We demonstrated that blocking pannexin hemi-channel with probenecid, not only affected intercellular communication, but also enhanced the epithelial marker E-cadherin, leading to a change in cellular morphology. Additionally, it decreased N-cadherin expression and the hypoxic marker HIF-1α.

Conclusion: Pannexins serve as promising prognostic biomarkers and may constitute a potential therapeutic target in metastatic breast cancer. These findings demonstrate the enhancement of anti-hypoxic effect and attenuation of cancer invasion induced by inhibiting pannexin hemi-channels, suggesting a therapeutic advantage of combining this treatment with other anti-metastatic and chemotherapeutic drugs.

Abstract # 40

The rhabdomyosarcoma-specific Pax3-FOXO1 fusion oncoprotein modulates exosome miRNA content and specifically upregulates mir-486-5p to enhance oncogenic signaling

Farah Ghamloush[1], Sandra E. Ghayad[2], Abeer Ayoub[2], Raya Saab[1,3]
[1]Children's Cancer Institute, American University of Beirut, Beirut, Lebanon, [2]Department of Biology, Faculty of Science II, Lebanese University, Beirut, Lebanon, [3]Department of Anatomy, Cell Biology and Physiology, American University of Beirut, Beirut, Lebanon
Corresponding author: Farah Ghamloush (Research Assistant)
E-mail: fg07@aub.edu.lb

Funding source: MPP grant, AUBMC

Keywords: Rhabdomyosarcoma, Pax3-FOXO1, exosomes, myoblasts, miR-486-5p

Descriptive Statement: The fusion oncoprotein Pax3-FOXO1, thought to be the initiating oncogenic lesion in the soft tissue tumor rhabdomyosarcoma (RMS), modulates the content and function of exosomes (small secreted microvesicles), which contributes to inducing invasion and metastasis in this aggressive tumor.

Introduction: Tumor-derived exosomes are shown to promote cancer survival and outgrowth by paracrine signaling through the delivery of their miRNA content to recipient cells. Alveolar Rhabdomyosarcoma (ARMS) is an aggressive childhood soft tissue tumor. It is characterized by a genetic translocation leading to a fusion oncogenic protein PAX3-FOXO1 (P3F) that mediates its aggressive phenotype. We investigated the role of P3F on exosome content and its effects on recipient cells.

Methods: Myoblasts are thought to be the cell of origin of RMS. We transduced mouse myoblasts (C2C12 cells) with vector containing the P3F fusion oncoprotein and isolated the secreted exosomes to determine their differential effects on recipient cell proliferation, invasion, migration and anchorage independent growth. We investigated the exosome miRNA cargo induced by P3F transduction, using Affymetrix microarray analysis.

Results: P3F expression in mouse myoblasts enhanced cell proliferation and colony formation in soft agar. Exosomes secreted by P3F-expressing myoblasts significantly enhanced recipient cell proliferation, invasion and migration. Array analysis revealed unique miRNA enrichment signatures in exosomes derived from P3F-transduced cells compared to control. Knockdown of mir-486-5p significantly reverted the effects of exosomes implying a role in P3F-specific paracrine signaling in tumor progression.

Conclusion: We have identified specific effects of the P3F oncogenic fusion protein on paracrine signaling in myoblasts and P3F-derived exosomes on recipient cells. P3F expressing cells specifically upregulate miR-486-5p in exosomes to enhance its oncogenic abilities. Findings will help devise targeted therapeutic interventions in ARMS, which are urgently needed.

Abstract # 41

Characterization of the Molecular and Pathophysiological Role of TET Proteins in Glioblastoma

Carine Mouawad[1], Tenzin Gayden [2, 3], Fredrik Hugosson[4], Nada Jabado [2, 3], Marwan EL Sabban[5], Margret Shirinian[1]**

[1]*Department of Experimental Pathology, Immunology and Microbiology, American University of Beirut, Beirut, Lebanon*

[2]*Division of Experimental Medicine, McGill University and McGill University Health Centre, Montreal, Quebec, Canada*

[3]*Departments of Pediatrics and Human Genetics, McGill University and McGill University Health Centre, Montreal, Quebec, Canada.*

[4]*Department of Molecular Biology, Umea University, Umea, Sweden*

[5] *Department of Physiology, American University of Beirut, Beirut, Lebanon*

Corresponding authors: Margret Shirinian E-mail:ms241@aub.edu.lb

Marwan EL Sabban E-mail:me00@aub.edu.lb

Funding source: MPP

Keywords: GBM; *Drosophila melanogaster;* TET

Descriptive Statement: The role of TET proteins in glioblastoma using *Drosophila melanogaster as a model.*

Introduction: Ten-eleven translocation 1-3 (TET 1-3) proteins are members of a family of DNA hydroxylases, a well-characterized epigenetic modification that plays an important role in regulation of gene expression and maintaining cellular identity. Acquired point mutations and deletions in TET proteins have been frequently observed in human cancers implicating their role in cellular differentiation and transformation. We have identified novel missense TET mutations in glioblastoma multiforme (GBM) patients in a set of exome-sequenced samples. We aim to investigate TET function in glioblastoma, using *Drosophila* as a model, by generating Tet loss-of-function (LOF) mutants and identifying its potential role *in vivo*.

Methods: We have generated drosophila TET (dTET) LOF mutants. RT-PCR and quantitative PCR for dTET confirmed the absence of transcripts. We further mapped the location of the insertion using inverse PCR methodology. Climbing and crawling assays for dTET LOF were performed to analyze locomotor activity. Furthermore, we analyzed larval brains and body wall muscles and examined the overall anatomical morphology by immunostaining. We have generated mammalian expression vectors of 11 TET mutant variants and wild type TET1, TET2 and TET3 expressing GFP and transfected them in iPS-MSCs (mesenchymal stem cells) for *in vitro* identification of Tet induced tumorigenesis.

Results: Adult dTET LOF flies exhibit lethality at post-pupal stages, however; at larval stages these mutants are characterized by abnormal muscle morphology and manifest defective locomotor activity.

Conclusion: The *Drosophila in vivo* model of TET and its mutants will help to understand and identify a yet undiscovered role of TET in humans and its potential involvement in brain tumor development.

Abstract # 42

Rhabdomyosarcoma exosome proteomics yield functional role for extracellular vesicles

Ghina Rammal[1], Sandra E. Ghayad[1], Farah Ghamloush[2], Mona Diab-Assaf[3], Firas Kobeissy[4], Yehia Mechref[5], Raya Saab[3, 6]

[1]Department of Biology, Faculty of Science II, Lebanese University, Beirut. [2]Children's Cancer Institute, American University of Beirut, Beirut, Lebanon. [3]Department of Chemistry and Biochemistry, Faculty of Sciences II/EDST, Lebanese University, Lebanon. [4]Department of Biochemistry and Molecular Genetics, Faculty of Medicine, American University of Beirut, Beirut, Lebanon. [5]Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, United States of American. [6]Department of Anatomy, Cell Biology and Physiology, American University of Beirut, Beirut, Lebanon

Corresponding author: Ghina RAMMAL, PHD student, E-mail: Ghinarml@gmail.com

Funding source: MPP grant, AUBMC, Lebanese University grant

Keywords: Rhabdomyosarcoma; Exosomes; Proteins cargo; Pathways.

Descriptive Statement: Rhabdomyosarcoma-derived exosomes carry biologic cargo involved in cancer progression.

Introduction: Rhabdomyosarcoma (RMS) is an aggressive childhood soft tissue tumor, with two distinct subtypes, embryonal (ERMS) and alveolar (ARMS) histologies. Exosomes are important intercellular communication vehicles, secreted into body fluids by multiple cell types, including tumor cells. They have been implicated in contributing to metastatic progression through paracrine signaling. Tumor exosomes contain intact and functional protein, mRNA and miRNA that may alter the cellular environment to favor tumor growth.
Thus we evaluated the protein cargo of RMS-derived exosomes and the molecular pathways they are implicated in to decipher their role in the progression of this aggressive disease.

Methods: We isolated and characterized exosomes from a 3 ERMS and 2 ARMS cell lines. In order to determine the protein profiles of exosomes, we conducted a mass spectrometry analysis validated by western blot and MRM. Furthermore, we used results Panther classification system software to determine the pathways and biological processes in which the different exosomal protein cargos are involved.

Results: We were able to isolate detectable amounts of exosomes from all 5 RMS cell lines with a diameter ranging from 40-120nm visualized using electron microscopy. The detection of exosomal markers TSG101, Hsc70 and GAPDH by western blot confirmed their exosomal identity. Mass spectrometry revealed the expression of 161 common proteins in all three ERMS-derived exosomes and 122 proteins in ARMS-derived exosomes among which 81 proteins were common to both subtypes. These commonly expressed proteins include exosomal markers, but also proteins involved in cell signaling, cell movement and cancer. The pathways engaging the identified proteins were analyzed by panther classification system revealing 37 common pathways including "Integrin signaling pathway", "Inflammation mediated by chemokine and cytokine signaling pathway" and "angiogenesis". These pathways may contribute to the paracrine signaling in tumor progression.

Conclusion: Through identifying the protein cargos of RMS-derived exosomes and the pathways involving these proteins, we were able to highlight the important role played by exosomes in cancer progression.

Abstract # 43

Roles of p53 and ceramide in response to hypoxia in solid tumors

Marguerite Mrad[1], Rouba Hage Sleiman[1], Raya Saab[2], Georges Nemer[1], Ghassan Dbaibo[1,2]
[1]Department of Biochemistry and Molecular Genetics, [2]Department of Pediatrics and Adolescent Medicine - American University of Beirut, Beirut, Lebanon
Corresponding author: Ghassan Dbaibo-Professor
E-mail: gdbaibo@aub.edu.lb

Funding source: CRS grant proposal submitted
Keywords: Ceramide, p53, hypoxia, solid tumor
Descriptive Statement: Tumor hypoxia is a common feature to almost all solid tumors. The p53 gene, which is associated with apoptotic response to hypoxia, is remarkably mutated in several solid tumors. Since p53 is involved in a diverse set of signaling pathways, more selective therapeutic strategies for p53 mutated tumors should be defined.

Introduction: background and aims Hypoxia occurs in solid tumors as a result of an inadequate supply of oxygen, due to exponential cellular proliferation. Under these circumstances, hypoxic cells may undergo a series of coordinated responses in order to maintain their viability and metabolic activity. It has been previously demonstrated that hypoxia modulates the expression of several genes and proteins including the tumor suppressor protein p53. Moreover, chronic hypoxia affected ceramide metabolism, essentially at the final step of its *de novo* synthesis. It has been proposed that ceramide can act either upstream or downstream of p53 protein through posttranscriptional regulation or through many potential mediators. The aim of this study is to elucidate the role of ceramide in p53-dependent response to hypoxia in order to establish a targeted therapeutic approach for p53 mutated tumors.

Methods: Colon cancer cells differentially expressing p53 (HCT 116 p53+/+ or p53-/-, and EB/EB1) will undergo sub-acute or chronic hypoxia (1% O_2). The biological response to hypoxia *vs* normoxia will be tested using cell viability assays, and cell cycle distribution. mRNA and protein expression levels of p53, HIF1α, DEGS1, caspases, Bcl2 family members and cell cycle proteins will be evaluated. DEGS1 enzymatic activity will be measured, and sphingolipid profile will be analyzed *via* Liquid Chromatography/Mass Spectrometry. HCT116 (p53+/+ and p53-/-) cells will be subcutaneously injected into BALB/c nude mice. Once xenografts are established, tumor volume will be measured. Hypoxic and normoxic regions from mice xenografts and human tumors (afforded by AUBMC) will be identified by IHC, and sphingolipid profile will be analyzed *via* Liquid Chromatography/Mass Spectrometry.

Results: Our preliminary results showed that HCT 116 p53-/- cells were more resistant to hypoxia-induced cell growth arrest compared to HCT 116 p53+/+ cells. Moreover, we observed a decrease in Noxa expression and a lower ceramide accumulation in response to hypoxia in the absence of p53.

Conclusion: Herein we unveil a potential role of p53 and ceramide in hypoxia-induced cell growth arrest in vitro. This novel project will lead us to establish more efficient and targeted therapeutic approaches for p53 mutated tumors.

Abstract # 44

Loss of Connexin 43 Induces Proliferation and Invasion Pathways in Non-neoplastic Breast Epithelium

Fostok, S.F.[1], Bazzoun, D.B.[1,2], Yassine, F.A.[1], Naser Al Deen, N.M.[1], Lelièvre, S.A.[2,3], El-Sibai, M.[4] and Talhouk, R.S.[1]

(1) Department of Biology, Faculty of Arts and Sciences, American University of Beirut, Beirut, Lebanon (2) Department of Basic Medical Sciences, Purdue University, West Lafayette, IN, USA (3) Purdue University Center for Cancer Research, Purdue University, West Lafayette, IN, USA and (4) Department of Natural Sciences, School of Arts and Sciences, Lebanese American University

Corresponding author: Talhouk, R.S. - Professor - E-mail: rtalhouk@aub.edu.lb

Position: PhD candidate in Cell and Molecular Biology Program at the American University of Beirut (AUB)

Funding source: University Research Board (URB; AUB, Lebanon) and Lebanese National Council for Scientific Research (LNCSR; Lebanon)

Keywords: Breast cancer, Connexin 43, Gap junction, Proliferation, Invasion

Descriptive statement: The loss of connexin 43 (Cx43), a gap junction protein, has been reported in breast cancer. We have previously shown disruption of apical polarity and mitotic spindle orientation in Cx43-silenced breast epithelial cells. In this study, we show that Cx43 loss induces proliferation and invasion pathways.

Introduction: background and aims Reduced expression of connexin 43 (Cx43) has been reported in breast cancer, suggesting a tumor suppressive role. Our earlier data have shown that silencing Cx43 in 3-dimensional (3-D) cultures of HMT-3522 S1 non-neoplastic human mammary epithelial cells (S1 cells), disrupted cell polarity and mitotic spindle orientation, and prevented cells from assembling around a lumen. The present study aims to delineate the role of Cx43 silencing in triggering proliferation and invasive events in non-neoplastic mammary epithelium.

Methods: Cx43 shRNA-transfected and control S1 cells were cultured under 2-D and 3-D conditions. Proliferation and cell cycle progression were monitored by cell count (2-D) or measurement of acinus size (3-D) and flow cytometry. Western blotting, co-immunoprecipitation, immunofluorescence and invasion/motility assays were used to decipher the mechanism of Cx43 signaling. Cells in 2-D cultures were assayed on days 4, 6, 9, and/or 11, while those in 3-D cultures on day 11.

Results: Silencing Cx43 enhanced proliferation of S1 cells in 2-D cultures, as shown by the increased cell counts throughout the culture period. Likewise, Cx43-silenced S1 cells in 3-D cultures exhibited increased acinar size by day 11, suggesting enhanced proliferation. Silencing Cx43 triggered cell cycle progression in 2-D (assayed on days 4, 6, 9 and 11) and 3-D (assayed on days 4 and 11) cultures, as shown by the reduced percentage of cells in G0/G1 phase (29%-44% decrease) and the increased percentages of cells in S phase (>230% increase) and G2/M phase (55%-110% increase). Cx43 associated with β-catenin in 2-D and 3-D cultures with apical colocalization in acini. Silencing Cx43 altered β-catenin distribution in 3-D cultures, but it did not alter total β-catenin levels, suggesting Cx43 involvement in the Wnt/β-catenin pathway. c-Myc and cyclin D1 were consistently upregulated in 2-D and 3-D (day 11) cultures of Cx43-silenced S1 cells. The 92 kDa gelatinase was also upregulated. Furthermore, silencing Cx43 enhanced, by two fold, the number of matrigel-invading cells, and induced migration of cells away from 3-D aggregates. Current studies investigating underlying canonical and non-canonical Wnt pathways are underway.

Conclusion: We propose a role for Cx43 loss in activation of proliferation and invasion pathways in non-neoplastic mammary epithelium.

Abstract # 45

CROSSTALK BETWEEN BRADYKININ AND RETINOIC ACID RECEPTORS SIGNALING PATHWAYS IN COLORECTAL CANCER CELLS

Fatima Ghamlouche[1], Patrick Aouad[1,2], Celine Khati[1], Oula Dagher[1], Moustafa Al Hariri[1], Rana Abdel-Samad[1], Miran Salame Jaffa[3], Nadine Darwiche[1*], Ayad Jaffa[1*]

[1]Department of Biochemistry and Molecular Genetics, Faculty of Medicine, [2]Department of Biology, Faculty of Arts and Sciences, [3]Epidemiology and Population Health Department, Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon

Corresponding authors:

Ayad Jaffa, PhD- E-mail: aj24@aub.edu.lb

Nadine Darwiche, PhD- E-mail: nd03@aub.edu.lb

Funding source: This work was funded by MPP

Keywords: Colorectal cancer, bradykinin, retinoic acid, cell growth and transformation, ERK1/2, receptor subcellular localization

Descriptive Statement: This study sheds light on the effect of bradykinin, a pro-inflammatory peptide, and retinoic acid, the active metabolite of vitamin A, on colon cancer cells. Specifically, it investigates the interplay between bradykinin and retinoic acid on colon cancer cell growth and signaling.

Introduction: Colorectal cancer is a main cause of morbidity and mortality worldwide and chronic inflammation is key in its development. Bradykinin (BK), an active peptide formed by the kallikrein-kinin system, is implicated in inflammation-induced tumor progression through its G-protein coupled receptors. On the other hand, all-*trans* retinoic acid (ATRA), the active metabolite of vitamin A, mediates essential cellular functions; and abnormalities in the retinoid receptor signaling are commonly observed in tumorigenesis. Here, we investigated the effects of BK on colorectal cancer cell growth and transformation and the crosstalk between BK and retinoid receptors signaling pathways.

Methods: We used human colorectal cancer cell lines with different *p53* status (HCT 116 and HCT 116 $p53^{-/-}$) and the normal-like counterpart (NCM460). Trypan blue exclusion assay was employed to measure the effect of BK on cell growth and soft agar colony formation assay was used to quantitatively assess the cell transformation potential upon treatment with BK, ATRA, and their combination. Kinin receptors (B_1R and B_2R) and retinoid receptors (RAR_α, RAR_β, RAR_γ, and RXR_α) expression profile was determined by western blot. The effect of BK on the activation of ERK1/2 was studied. We further investigated the subcellular localization of RAR_γ and B_2R by immunofluorescence.

Results: We observed that BK potently induced the colony growth of tested cancer cells while sparing the normal-like counterparts. Interestingly, ATRA abrogated BK-induced colony formation. We noted a differential protein expression of the kinin and retinoid receptors and an increase in the phosphorylation of ERK1/2 due to BK treatment. Finally, BK modulated the subcellular localization of RAR_γ and B_2R which was ERK1/2-dependent.

Conclusion: This research may lead to a better understanding of inflammation and its contribution to colorectal cancer development and novel therapeutic strategies.

Abstract # 46

Colorectal Cancer Risk in Diabetes: Double the Trouble in Metabolic Diseases

Fatima A. Mohsen[1], Suzan Boutary[1], Ali H. Eid[2], Assaad A. Eid[1#]*

[1]Department of Anatomy, Cell Biology and Physiology, and the [2]Department of Pharmacology and Toxicology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

***Presenter:** Fatima A. Mohsen

[#]Corresponding author: Assaad A. Eid - e-mail: ae49@aub.edu.lb

Funding source: National Priority Research Programs (NPRP) – Qatar National Research Foundation, Doha, Qatar.

Keywords: Diabetes, Colorectal Cancer, APC mice, NADPH oxidases

Descriptive Statement: This study aims to uncover the role of Diabetes-induced NOXs in the development and aggressiveness of colorectal cancer.

Introduction: NADPH oxidase (NOX) enzymes are a family of heme-containing transmembrane proteins whose basic function is reactive oxygen species (ROS) production [1]. In fact, Diabetes has been shown to increase the generation of ROS [2] and NOX-generated ROS have been linked to injury to various organs including the colon [3]. Our main aim is to explore the mechanism by which diabetes-induced ROS accelerate tumor development and tumor burden.

Methods: 2 month old male C57BL/6-APC mice that spontaneously develop colorectal polyps were divided into four groups; (A) a non-diabetic, (B) STZ-induced diabetes, (C) diabetic group treated with Metformin; AMPK activator, and a (D) diabetic group treated with Rapamycin (mTORC1 inhibitor). After 5 weeks, the number and size of the polyps were assessed in comparison with the APC control mice. Western Blots were performed to assess the protein expression of Nox1, Laminin, and p-mTOR. NADPH oxidase enzymatic activity was also assessed using the NADPH oxidase activity assay.

Results: APC mice exhibited an average of 4 polyps per mouse with an average diameter of 0.5 mm. However, APC diabetic mice developed almost double the number of polyps with approximately the same average diameter. Polyp numbers in animals treated with metformin and rapamycin were similar to those of the controls. Western Blots showed increased Laminin, p-mTOR, and Nox1 levels for APC diabetic mice compared to the control mice and for C57 diabetic mice compared to the C57 control mice. Treatments with metformin and rapamycin attenuated those levels. In addition NADPH oxidase activity was shown to increase in diabetic mice and decrease again in the treated mice.

Conclusion: These results reveal a novel mechanistic pathway involved in the progression of colorectal cancer during the onset and development of diabetes.

Abstract # 47

Assessment of Obstructive sleep apnea symptoms and excessive daytime sleepiness in hospitalized psychiatric patients.

Farid Talih[1], MD; Jean Ajaltouni[1], MD & Firas Kobeissy[2], PhD*

[1]Department of Psychiatry, American University of Beirut Medical Center, Beirut, Lebanon.

[2]Department of Biochemistry and Molecular Genetics, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

Corresponding author: Farid Talih, MD, Department of Psychiatry, American University of Beirut Medical Center, ft10@aub.edu.lb

Funding source: Faculty of Medicine- American University of Beirut

Keywords: Obstructive sleep apnea, excessive daytime sleepiness, depression and anxiety symptoms

Descriptive Statement: Assessment of obstructive sleep apnea symptoms and excessive daytime sleepiness among hospitalized psychiatric patients in Lebanon.

Introduction: This study evaluates the prevalence of obstructive sleep apnea (OSA) symptoms and excessive daytime sleepiness (EDS) in hospitalized psychiatric patients at the American University of Beirut Medical center (AUB-MC). Factors that correlate with the OSA and EDS, occurrence in this sample are also examined

Methods: The Berlin sleep apnea questionnaire and the Epworth sleepiness scale; which respectively evaluate OSA and EDS symptoms, were administered to individuals hospitalized at an acute psychiatric treatment unit at the AUM-MC between the dates of January 2014 and October 2016. Additional data collected included general demographics, psychiatric diagnoses, and questionnaires evaluating depression and anxiety symptoms. Statistical analyses utilizing SPSS were performed to determine the prevalence of OSA and EDS, as well as their respective correlates with patient profiles.

Results: Our results showed that 39.5% of participants were found to have a high likelihood of sleep apnea and 9.9% of the participants were found to have abnormal daytime sleepiness. OSA correlated with body mass index (BMI) ($r= 0.2977$, $p< 0.05$), age ($r=0.203$, $p=0.05$) and depression severity (PHQ-9 scores) ($r= 0.224$, $p<0.05$). Increasing severity of depressive symptoms was also associated with a higher likelihood of sleep apnea ($\chi^2= 8.10$, $p<0.05$). Of interest, the psychiatric diagnoses of the participants were not found to have a significant association with the likelihood of sleep apnea.

Conclusion: Sleep disorders in general and sleep disordered breathing in particular among psychiatric patients are frequently overlooked or underestimated. It is important to improve screening and offer appropriate therapeutic intervention to improve outcomes and quality of life in psychiatric patients.

Abstract # 48

Flupirtine analogues in the treatment of Batten Disease

Fadi Saadeh[1], Nihar Kinarivala[2], Karl Albert Mansour[1], Joelle Makoukji[1], Paul Trippier[2], Rose-Mary Boustany[1, 3]

[1]Department of Biochemistry and Molecular Genetics, American University of Beirut Medical Center, Beirut, Lebanon, [2]Department of Pharmaceutical Sciences School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, TX, [3]Neuro-genetics Program, AUBMC Special Kids Clinic and Division of Pediatric Neurology, Department of Pediatrics and Adolescent Medicine, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Dr. Rose-Mary Boustany - Professor - E-mail: rb50@aub.edu.lb

Funding source: NCL Research Award

Keywords: Batten disease, Neuronal Ceroid Lipofuscinoses, Flupirtine, Neurodegeneration

Descriptive Statement: Flupirtine analogues were tested and compared to Flupirtine regarding their neuroprotective ability in human cells mimicking Batten disease.

Position: Medical student

Introduction: Batten disease/the Neuronal Ceroid Lipofuscinoses or NCLs are fatal inherited neurodegenerative diseases with no cure. CLN3 disease is the juvenile and most common. Although rare, the disease often strikes multiple offspring in the same family that carry the defective NCL gene. Current treatment regimens are symptomatic and supportive but do not target the underlying disease. The need for disease-modifying drug candidates is urgent. This work aims to address this requirement by providing lead therapeutic compounds. Previous work from the lab shows that Flupirtine aborts etoposide-induced apoptosis in NCL and normal lymphoblasts and prevents death of neurons. The end goal of this application is to generate a full structure-activity relationship map of Flupirtine analogues as applied to NCL and deliver several derivative compounds with enhanced neuroprotective activity.

Methods: Optimum drug concentrations of 9 Flupirtine derivatives were tested by establishing growth curves under pro-apoptotic conditions (etoposide). Flupirtine derivatives with desirable activity were evaluated by Trypan blue staining after siRNA knockdown of *CLN3* gene in PC12 cells, and in CLN1, CLN2, CLN3, CLN6 and CLN8 patients' lymphoblasts. Also, BCL-2 and ceramide synthesis enzyme expression were determined in PC12 cells after siRNA knockdown.

Results: Three of the Flupirtine analogues proved to be neuroprotective after the application of etoposide to PC12 cells. After CLN3 knockdown, the same three drugs prevented neuronal death. Bcl-2 levels were increased in CLN3 knockdown PC12 cells treated with two of the analogues, separately. Also, these drugs were neuroprotective in CLN5 patient fibroblasts. CLN3 knockdown increases ceramide enzyme expression, and the addition of Flupirtine and two other analogues downregulates the expression of these enzymes (CerS2; CerS6; SMPD1 and DEGS2). In patients' lymphoblasts, drug 3 was significantly protective in CLN3 lymphoblasts, drug 5 in CLN6 lymphoblasts and drug 6 in CLN1, CLN2, CLN3, CLN6 and CLN8 lymphoblasts. All effects were better than those seen with Flupirtine.

Conclusion: These findings uncover analogous compounds to Flupirtine with enhanced activity for the treatment of Batten disease. These analogues even prove to possess greater neuroprotective activity than Flupirtine. BCL-2 and ceramide synthesis enzyme alterations support the possible implication of Flupirtine analogues in the ceramide synthesis pathway. Future experiments in *CLN3*$^{Dex7/8}$ knock-in mice will further shed light on the role of Flupirtine analogues in the treatment of some forms of NCL disease.

Abstract # 49

National prevalence and correlates of Autism: a Lebanese cross-sectional study

Dahlia Saab[1], Monique Chaaya[2], Rose-Mary Boustany[1,3]

[1]Department of Biochemistry and Molecular Genetics, [2]Department of Epidemiology and Population Health, [3]Department of Pediatrics and Adolescent Medicine American University of Beirut, Beirut, Lebanon

Corresponding author: Rose-Mary Boustany - Professor - E-mail: rb50@aub.edu.lb

Presenting author: Dahlia Saab, MPH, Senior Research Assistant (email: ds39@aub.edu.lb)

Funding source: OpenMinds

Keywords: autism spectrum disorder, prevalence, epidemiology, Lebanon, risk/protective factors

Descriptive Statement: In Lebanon, the percentage of autistic children is unknown. A previous study done by the same research team explored the prevalence of autism in Beirut and Mount Lebanon governorates. This study estimates the national percentage of autistic toddlers in nurseries. All the questionnaires were filled by parents of toddlers. Results of this study show that 1 in 68 children aged 16 to 48 months are potentially autistic. It is the first study of its kind to be conducted in Lebanon. The study also explored some factors associated with autism and found that delivery complications were a risk factor for autism and children with working mothers were more protected.

Introduction: There is a lack of data regarding autism prevalence and factors associated with it in Arab Countries, especially in Lebanon. A study conducted in Beirut and Mount Lebanon governorates estimated the prevalence of Autism Spectrum Disorder (ASD) at 1.53% toddlers attending nurseries. This study aims at obtaining a national ASD estimate and find factors associated with the disorder.

Methods: The same methodology as the previous study was used to collect data at a national level using the Modified Checklist for Autism in Toddlers for screening, and a self-administered questionnaire (associated factors). The final sample included 1,373 children aged 16-48 months. Prevalence estimates and crude and adjusted Odds Ratios (ORs) with 95% confidence intervals (95%CI) were generated.

Results: ASD national prevalence is 1.48% with 95%CI [0.84, 2.12], with a 1.13 male/female ratio. In the multivariable analysis, having an employed mother in the last year was protective against ASD (OR [95%CI]: 0.36[0.14, 0.93]). Presence of delivery complications was a risk factor (3.58[1.26, 10.15]). First/second born and moral support during pregnancy were protective, whereas mother not having a university education and family history of mental illness were risk factors. These variables were not significant in the multivariable analysis probably due to small numbers.

Conclusion: This is the first study estimating ASD prevalence in the Lebanese population, a much needed step to know the magnitude of the disorder. More robust studies are needed to better understand this disorder and factors associated to it in Lebanon and the region that have distinct cultural/environmental characteristics.

Abstract # 50

The Bayesian Risk Estimate at disease onset predicting early cognitive and physical disability in early MS patients

Marianne Said[1], Nabil El Ayoubi[1], Bassem I Yamout[1], Ribal N Haddad[1], Leslie Saba[2], Youmna Jalkh[1], Samia J Khoury[1]

[1] Nehme and Therese Tohme Multiple Sclerosis Center, American University of Beirut Medical Center, Beirut, Lebanon

[2] UCD School of Medicine, University College Dublin, Belfield, Dublin 4

Corresponding author: Samia J Khoury, MD - Professor of Neurology - email: sk88@aub.edu.lb

Funding source: Nehme and Therese Tohme Multiple Sclerosis Center

Keywords: BREMSO, SDMT, Multiple Sclerosis

ABSTRACT:

Descriptive Statement: A prospective study at the AUBMC Nehme and Therese Tohme Multiple Sclerosis Center

Background and purpose: Prevention of long-term disability is the goal of therapeutic intervention in relapsing remitting multiple sclerosis (RRMS). The Bayesian Risk Estimate for MS at Onset (BREMSO) was designed to give an individual risk score predicting disease evolution. A tool that anticipates early physical and cognitive deterioration is still lacking. The aim of this study is to investigate whether BREMSO correlates with physical as well as cognitive dysfunction during the early disease course.

Method: We investigated 100 patients with RRMS or clinically isolated syndrome enrolled in the AMIR study at our center since January 2012, with at least three years of follow-up and disease duration of less than six years. BREMSO score was calculated for all participants at disease onset. At each visit, cognitive function was assessed using the Symbol Digit Modalities Test (SDMT), and physical disability using the Multiple Sclerosis Severity Score (MSSS), Timed 25-Foot Walk Test (T25-FW) and 9-Hole Peg Test (9-HPT).

Results: The mean (SD) age was 28.1 (11.19) years, Expanded Disability Status Scale was 1.28 (1.03), and disease duration was 2.4 (1.78) years. In multivariate linear regression analyses, controlling for age and education, the BREMSO score correlated negatively with SDMT at visit 1 (β=-0.33 p=0.019), visit 2 (β=-0.34 p=0.017), and visit 3 (β=-0.34 p=0.014). BREMSO correlated positively with MSSS at visit 1 (r=0.38, p=0.006), visit 2 (r=0.47, p<0.0001), and visit 3 (r=0.42, p=0.002), but did not correlate with T25-FW and 9-HPT.

Conclusions: The BREMSO score predicted physical and cognitive disability in early multiple sclerosis.

Abstract # 51

Intravitreal Adalimumab for the Control of Breakthrough Intraocular Inflammation

*Wajiha J. Kheir[1], Carl-Joe Mehanna[1], Maamoun Abdul Fattah[1], Sara Al Ghadban[2], Marwan El Sabban[2], Ahmad M. Mansour[1] and Rola N. Hamam[1]**

[1] Department of Ophthalmology, American University of Beirut, Beirut, Lebanon

[2] Department of Anatomy, Cell Biology and Physiological Sciences, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

Descriptive Statement: This research project addresses the use of systemic therapy (adalimumab) locally in the eye for control of intraocular inflammation.

Presenter: Wajiha Jurdi Kheir, Chief Resident - Ophthalmology

Corresponding author: Rola N. Hamam, MD, Email: rh46@aub.edu.lb

Keywords: Uveitis, adalimumab, Behcet disease

Funding: none

ABSTRACT

Background and aims: Breakthrough inflammation occurs in patients treated with systemic adalimumab after months of control. Our aim was to investigate the efficacy of intravitreal adalimumab in breakthrough panuveitis in patients on systemic adalimumab for more than 3 months.

Methods: Retrospective study of patients on systemic adalimumab with breakthrough panuveitis, requiring intravitreal adalimumab therapy.

Results: Seven eyes of four patients with Adamantiades-Behcet disease panuveitis were included and all were maintained on systemic adalimumab for 7.25 months (range 3-11) with inflammation controlled for 4.1 months (range 2-10) before breakthrough uveitis. The total number of attacks was 13 over 24.5 months (range 12-30). Resolution of attack was defined as return to baseline visual acuity with resolution of inflammatory markers. 3 attacks resolved after only one injection and 10 attacks required an average of 2.4 injections (range 2-3). No systemic or ocular complications were noted.

Conclusions: Intravitreal adalimumab warrants further investigation as a potentially effective, practical and safe adjunctive therapy for control of breakthrough inflammation in patients maintained on systemic adalimumab.

Abstract # 52

Characteristics of funding of clinical trials: a methodological survey and a proposed guidance

[1]Maram B. Hakoum, [2]Nahla Jouni, [3]Eliane A. Abou-Jaoude, [4]Divina Justina Hasbani, [5]Elias Abou-Jaoude, [6]Luciane Lopes, [7]Mira Z. Hammoud, [4]Mounir Al-Gibbawi, [8]Sirine Anouti, [9]Gordon Guyatt, [1,9,10]Elie A. Akl

[1]Clinical Research Institute, American University of Beirut Medical Center, [2]Faculty of Agriculture and Food Sciences, American University of Beirut, [3]Department of Internal Medicine, SUNY University at Buffalo, United States of America, [4]Faculty of Medicine, American University of Beirut, [6]Pharmaceutical Science Master Course, University of Sorocaba, São Paulo, Brazil, [8]Department of Epidemiology and Population Health, American University of Beirut, [9]Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada, [10]Department of Medicine, American University of Beirut Medical Center

Primary author: Maram Hakoum, MD – Research Fellow – mh233@aub.edu.lb

Corresponding author: Elie A. Akl, MD, MPH, PhD – Professor of Medicine – ea32@aub.edu.lb

Funding source: This project was funded by the American University of Beirut Faculty of Medicine's Medical Practice Plan (MPP) funds.

Keywords: funding, role of funder, randomised controlled trial

Descriptive Statement: This is a methodological survey to describe the characteristics of the reported funding information of clinical trials and to develop guidance and an instrument for standardised reporting of funding information.

Introduction: Funding sources often influence the reporting of research findings and the interpretation of results. The current literature lacks a detailed, current characterisation of funding of a representative sample of trials. The objectives of this study were to provide such a characterisation and to develop guidance for standardised reporting of funding information and a form that would aid such reporting.

Methods: We addressed the extent to which clinical trial reports published in 2015 in any of the 119 Core Clinical Journals included a statement on the funding source (e.g., whether a not-for-profit organisation was supported by a private-for-profit), type of funding, amount and role of funder. A stepwise approach provided the structure for the development of guidance and an instrument for standardised reporting of funding information.

Results: Of 200 included trials, 178 (89%) included a funding statement, of which 171 (96%) reported being funded. The funding statements in the 171 funded trials indicated the source in 100%, amount in 1% and roles of funders in 50%. The most frequent sources of funding were governmental (58%) and private-for-profit (40%). Of 54 funding contribution statements in which the funding source was a not-for-profit organisation, we found evidence of undisclosed support of those organisations from private-for-profit organisation(s) in 26 (48%). The most frequently reported roles of funders in the 171 funded trials related to the design of the study (42%) and data analysis, interpretation, or management (41%). Of 139 RCTs addressing pharmacological or surgical interventions, 29 (21%) reported information on the supplier of the medication or device. The proposed guidance addresses both the funding information that RCTs should report and the reporting process. Attached to the guidance is a fillable PDF document for use as an instrument for standardised reporting of funding information.

Conclusion: Although the majority of RCTs report trial funding, there is considerable variability in the reporting of the funding source, funding amount and roles of funders. A standardised approach to reporting of funding information would address these limitations. Future research should explore the implications of funding by not-for profit organisations that are supported by for-profit organisations.

Abstract # 53

New Technique for Enhancing the Astigmatic Correction Effect of Intacs SK Corneal Ring Segments in Keratoconus eyes with a Central Cone

Rafic Antonios, MD, Maamoun Abdul Fattah, MD, Shady T. Awwad, MD.*

**Department of Ophthalmology, American University of Beirut, Beirut, Lebanon*

Corresponding Author: Shady T. Awwad, MD, Associate Professor of Ophthalmology, Director, Refractive Surgery Division Cornea & Refractive surgery, Ophthalmic Pathology, Department of Ophthalmology, at the American University of Beirut Medical Center, Cairo St, PO Box 110236 Beirut, Lebanon, Tel: +961-1-759637, Fax: +961-1-370837, Email: shady.awwad@aub.edu.lb

Funding source: The study didn't receive external funding.

Keywords: Keratoconus, Intracorneal Ring Segments, Intacs

Descriptive Statement: In keratoconus eyes with central cones, placement of two regular Intacs SK segments in a larger 7 mm tunnel, resulted in greater astigmatism correction albeit having less effect on overall corneal flattening.

Introduction: background and aims

To evaluate the refractive effect of 150° arc length intrastromal corneal ring segments (Intacs SK) placed in a larger tunnel to correct astigmatism in keratoconus eyes with a central cone. 150° arc length segments, implanted in a 7 mm tunnel instead of 6 mm, would yield an effective arc-length of 129°.

Methods: Six keratoconus eyes with central bow-tie astigmatism, underwent implantation of two 450 µm Intacs SK segments at 7.0 mm (SK-7 group) instead of the usual 6.0 mm tunnel. The refractive effects of the SK-7 group were compared to a control arm of 6 consecutive keratoconus eyes with central bow-tie which underwent two symmetric 450 µm intacs SK implantation at the usual 6mm position, obtained by a retrospective chart review (SK-6 group).

Results: There were no statistical significance between the baseline parameters of both groups, although mean SE was larger in SK-6 group and both refractive cylinder and corneal astigmatism were larger in SK-7 group. The average change in MRSE at 6 months was +2.21 ± 0.86 for the SK-7 group and +8.87 ± 3.22 for the SK-6 group (P=0.004). However, SK-7 group showed greater reduction in topographic surgical induced astigmatism (SIA) as compared to the SK-6 group (+5.55 ± 0.50 vs +2.47 ± 0.50, P=0.004). On corneal topography, the bow-tie shape was maintained in all eyes that underwent intacs SK implantation at 6mm (SK-6 group) while it became round in eyes that had the intacs SK implanted at 7mm.

Conclusion: Placement of two Intacs SK segments in a larger tunnel in eyes with central keratoconus leads to a greater astigmatism correction while having less effect on overall corneal flattening and spherical equivalent refraction.

Abstract # 54

Basal Ganglia and Thalamic Volume Measurements Associated with Fatigue in Multiple Sclerosis

Marianne Said,[*1] *Salem Hannoun*[*1,2], *Nabil El Ayoubi,*[1] *Samia J Khoury*[1,2]
[1] *Nehme and Therese Tohme Multiple Sclerosis Center, American University of Beirut Medical Center, Beirut, Lebanon;* [2] *Abou-Haidar Neuroscience Institute, Faculty of Medicine, American University of Beirut Medical Center, Beirut, Lebanon*

Corresponding author: Samia J Khoury MD - Professor of Neurology - email: sk88@aub.edu.lb

Funding source: Nehme and Therese Tohme Multiple Sclerosis Center

Keywords: Multiple Sclerosis, Fatigue, MFIS, MRI, Volumetry

Descriptive Statement: A cross-sectional study assessing the relationship between basal ganglia and thalamic volume measurements with cognitive, physical and psychosocial fatigue components in multiple sclerosis patients.

Background and Aim of the study: Multiple Sclerosis (MS) is an inflammatory and disabling disease characterized by widespread lesions affecting both white and gray matter. Fatigue is a very common symptom of MS that is usually underestimated. Assessing fatigue severity during routine clinical visits may be difficult unless standardized questionnaires are used. MRI is currently used to measure subclinical disease activity in MS. We hypothesized that gray matter atrophy may underlie MS fatigue.

Methods: Relapsing remitting and progressive MS patients were enrolled in this study and were asked to complete the "Modified Fatigue Impact Scale" (MFIS) which provides an assessment of fatigue in terms of physical, cognitive, and psychosocial functioning. Based on the MFIS sub-scores, patients were classified into four groups: those with physical, cognitive, or psychosocial fatigue and non-fatigued. MRI examinations (3DT1 post-gadolinium and 3DFLAIR) at the time of the clinical assessment (±6 months) were also reviewed. MRI images were then segmented and analyzed using volBrain. Statistical analyses were applied to assess significant differences between regions of interest volumes in the four patients' groups using One Way ANOVA with a Bonferroni correction.

Results: Sixty-three patients (41 relapsing and 22 progressive MS) were included in this study. Based on the MFIS sub-scores, these patients were classified in three subgroups and matched to non-fatigued patients: physical (33vs.30 non-fatigued patients), cognitive (28vs.35 non-fatigued patients), and psychosocial (7vs.56 non-fatigued patients). Significant differences were observed between physical and psychosocial fatigue and non-fatigued patients in several regions of the basal ganglia and the ventricles. There were also significant differences between cognitive fatigue and non-fatigued patients in the ICV and putamen.

Conclusion: Our main finding is that basal ganglia components and thalamic volume measurements significantly differed between patients with and without fatigue. This has implications for understanding the pathogenesis of this symptom and opens the door for therapeutic interventions.

Abstract # 55

Neuromuscular diseases: primary and secondary mitochondrial deficiencies

Sahar Traboulsi[1], Tarek Hamad[1], Farah Hakim[1], Mamdouha Ahdab Barmada[1] and Riyad El-Khoury[1]**

[1]Department of Pathology and Laboratory medicine, Neuromuscular diagnostic laboratory, American University of Beirut, Beirut, Lebanon.

***Corresponding authors** - E-mail: re70@aub.edu.lb/ma131@aub.edu.lb

Funding source: PLM department, Neuromuscular Diagnostics Laboratory

Keywords: Mitochondria, Neuromuscular diseases, Bioenergetics.

Descriptive Statement: Mitochondria are essential multifunctional organelles found in nearly all our cells. Deficiencies were reported as causal in various systemic diseases mainly neurological and metabolic. This study aims at illustrating the frequency of mitochondrial deficiencies in patients with well-defined neuromuscular diseases.

Introduction: Mitochondria are the major energy source required by all active and fundamental cellular processes. Today, genetic studies show that primary mitochondrial deficiencies are causing a substantial number of neuromuscular diseases. Likewise, mitochondrial dysfunctions have been diagnosed in other well-defined neuromuscular disorders as a consequence of secondary functional impairment. In the present study, we aimed at identifying primary & secondary mitochondrial defects in patients with diverse neuromuscular diseases.

Methods: Residual tissue from 88 muscle biopsies, which had been obtained for diagnostic studies of various neuromuscular conditions, were collected from the Neuromuscular diagnostic laboratory Biobank. Muscle tissue underwent extensive biochemical and histochemical analyses aiming at evaluating mitochondrial respiratory chain (RC) enzymes activities and function.

Results: Our findings show clearly a substantial contribution of mitochondrial dysfunction (42%) to the development of neuromuscular diseases, with 13 (20%) identified isolated RC deficiency cases involving mainly complex IV, 3 (5%) mitochondrial DNA depletion cases, 4 (7%) RC depletion cases and 7 (10%) mitochondrial depletion cases.

Conclusion: We believe that this global approach will undoubtedly shed light on the additional role of mitochondrial dysfunction in the loss of skeletal muscle volume and function, which will eventually pave the way for more accurate patient handling and therapy.

Abstract # 56

Histopathology, protein and molecular diagnosis of Limb girdle muscular dystrophy type 2A: Yield and pitfalls.

Tarek Hamad[1], Sahar Traboulsi[1], Farah Hakim[1], Riyad El-Khoury[1] and Mamdouha Ahdab Barmada[1]**

[1]Department of Pathology and Laboratory medicine, Neuromuscular diagnostic laboratory, American University of Beirut, Beirut, Lebanon.

***Corresponding authors** - E-mail: re70@aub.edu.lb/ma131@aub.edu.lb

Funding source: PLM department, Neuromuscular Diagnostics Laboratory

Keywords: Calpainopathy, neuromuscular disorders, Calpain-3.

Descriptive Statement: Limb girdle muscular dystrophy type 2A (LGMD2A) is the most common form of LGMD worldwide. It is caused by mutations in the Calpain-3 gene which encodes the CALP3 protease. Here we report and discuss advantages, limitations, and pitfalls related to protein testing in LGMD2A.

Introduction: LGMD2A is an autosomal recessive disorder that results in slow and gradual wasting of the proximal muscles of the hip and shoulder areas. It is caused by loss-of-function mutations in the calpain-3 gene that encodes a Ca^{2+}-dependent cysteine protease predominantly expressed in the skeletal muscle. In this work we aimed at characterizing muscle histopathology and CALP3 expression in a cohort of patients with potential muscular dystrophy.

Methods: Extensive histochemical and immunoblotting analyses were conducted on residual tissue from 34 muscle biopsies that were obtained for diagnostic studies from patients with potential muscular dystrophy. These were collected from the Neuromuscular diagnostic laboratory Biobank.

Results: We were able to show that LGMD2A occurs at a high frequency (35%) in our cohort of patients with potential muscular dystrophy. We also show that in 29 % of the cases, loss of calpain3 proteins is associated with other underlying dystrophies, mainly those associated with the loss of dystrophin.

Conclusion: In LGMD2A, the best diagnostic strategy should be determined on a case-by-case basis, with immunoblot analysis being the most useful tool to direct genetic testing, as detection of calpain-3 deficiency has high diagnostic value.

Abstract # 57

Characterization of Astrovirus-associated Gastroenteritis in Hospitalized Children Less than 5 Years of Age in Lebanon

Hadi Abou-El-Hassan[1, 2], Khalil Kreidieh[3], Nadia Soudani[1, 2], Zainab Ali[2, 4], Moza Hammadi[2, 4], Lina Reslan[2], Soha Ghanem[2, 4], Farah Hajar[2, 4], Adlette Inati[5], Mariam Rajab[6], Hassan Fakhouri[7], Bassam Ghanem[8], Ghassan Baasiri[9], Nada Melhem[2, 3], Ghassan Dbaibo[2, 4], Hassan Zaraket[1, 2]

[1]*Department of Experimental Pathology, Immunology, and Microbiology, American University of Beirut, Beirut, Lebanon*

[2]*Center for Infectious Diseases Research, American University of Beirut, Beirut, Lebanon*

[3]*Medical Laboratory Sciences Program, Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon*

[4]*Department of Pediatrics and Adolescent Medicine, American University of Beirut Medical Center, Beirut, Lebanon*

[5]*Department of Pediatrics, Nini Hospital, Tripoli, Lebanon*

[6]*Department of Pediatrics, Makassed General Hospital, Beirut, Lebanon*

[7]*Department of Pediatrics, Rafic Hariri University Hospital, Beirut, Lebanon*

[8]*Department of Pediatrics, Nabatieh Governmental Hospital, Nabatieh, Lebanon*

[9]*Department of Pediatrics, Hammoud Hospital, Saida, Lebanon*

Corresponding Authors: Hassan Zaraket, PhD - E-mail: hz34@aub.edu.lb; Nada Melhem, PhD - E-mail: melhemn@aub.edu.lb; Ghassan Dbaibo, MD - E-mail: gdbaibo@aub.edu.lb

Funding source: URB, MPP

Keywords: Astrovirus, pediatrics, children, gastroenteritis, Lebanon

Descriptive Statement: Astrovirus causes diarrhea in children and this study aims to assess the burden and identify the genotypes of astroviruses circulating in Lebanon.

Introduction, background and aims: Diarrhea is the second leading cause of childhood mortality in children less than 5 years of age. Astrovirus (AstV) has been recently identified as one of the major etiologic agents of gastroenteritis in children. Reported AstV infection rates among patients with GI range between 0.3 – 26 %. Nonetheless, the burden of AstV in the Middle East including Lebanon remains understudied. Our goal is to determine the prevalence of AstV in Lebanon and the circulating genotypes with the aim of guiding diagnosis and future vaccine development.

Methods: Stool samples were collected from children less than 5 years of age hospitalized for gastroenteritis at six medical centers across Lebanon between 2011 and 2013. Extracted viral RNA of eligible samples (n=739) was screened by two AstV-specific PCR assays followed by genotype-specific PCR. For genotypic characterization, Sanger sequencing and phylogenetic analysis were performed. Demographic and clinical data were collected and analyzed.

Results: AstV was detected in 41/739 (5.5%) of rotavirus-negative stool samples. AstV infections were detected throughout the year. AstV infections were most prevalent in Northern Lebanon. The 49-60 months age group was the most susceptible to AstV infections. The Vesikari Scoring System revealed severe gastroenteritis (score >11) in 85.4% (35/41) of the cases. Genotype-specific PCR identified 22 classical and 4 MLB-like AstV specimens. Further sequencing and phylogenetic analysis of *orf1b* and *orf2* genes revealed that AstV classical 1-3, 5, 6, and 8, MLB-1, VA-1 and -2 genotypes circulated in Lebanon.

Conclusion: AstVs are associated with 5.5% of non-rotavirus gastroenteritis-associated hospitalizations in children under five years in Lebanon. High genetic diversity was detected among AstVs circulating in Lebanon.

Abstract # 58

Automated Detection and Depth Measurement of Demarcation Line using Optical Coherence Tomography in Keratoconus Patients after Crosslinking

Manal Chokr, MSc[1]; Ahmad R. Dhaini, PhD[1]; Maamoun Abdul Fattah, MD[2]; Shady Awwad, MD[2]
[1]Department of Computer Science, American University of Beirut, Beirut, Lebanon
[2]Department of Ophthalmology, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Shady T. Awwad, MD
Associate Professor of Ophthalmology
Head, Cornea & refractive surgery division
E-mail: [sa11@aub.edu.lb]

Funding source: none

Keywords: demarcation line, cross-linking, depth measurement, novel software, keratoconus.

Descriptive Statement: A novel technology is devised to detect the presence and depth of corneal demarcation line after cross-linking.

Introduction: Corneal cross-linking aims at halting Keratoconus disease progression. A demarcation line is a hyper-reflective line that develops in the majority of treated eyes. It is detected on slit-lamp biomicroscopy and on optical coherence tomography (OCT) by human operators, and its presence and depth are considered an indirect sign of treatment success. We propose a novel technology to automatically detect and measure the demarcation line in OCT images.

Methods: Post-operative OCT images (128 cuts) of patients' eyes that underwent crosslinking were collected at 1 month and 3 months post-operatively. The images were inspected using the novel software. Additionally, two independent human operators examined the OCT images and evaluated the presence and depth of the demarcation line on two separate occasions. The operators were blinded to patients' names and results of other examiners. Repeatability and reproducibility of intra-observer measurements were calculated and compared.

Results: The mean corneal demarcation was 328.3 ±55.6 and 331.9 ±58.4 microns as computed by the automated technique and the human operators, respectively. The Intraclass correlation coefficient (ICC) between the software and the first and second operators were 0.855 and 0.826 respectively. The Pearson correlation coefficient between the software and the first and second operators were 0.811 and 0.769, respectively ($P<0.001$). The ICC for inter-operators' reproducibility was 0.882, and for intra-operator repeatability, 0.966. The ICC for inter-software repeatability was 1. The average time per OCT examination by the human operator was 31 seconds in addition to data population, whereas the software scored less than a second.

Conclusion: Demarcation line measurement by human operators is repeatable and reproducible, but can be standardized by an ultrafast and consistent automated software detection tool, providing a reliable indicator for treatment success.

Abstract # 59

Direct intra-arterial urokinase infusion in failed finger replantation

J. Bakhach, M.D., N. Habr, M.D., S. Badran, M.D., H. Janom, M.D.
Department of Surgery, Program and Division of Plastic and Reconstructive Surgery, American University of Beirut, Beirut, Lebanon
Corresponding author: Hamed Janom, MD, MRCS. E-mail: hj26@aub.edu.lb
Funding source: None

Keywords: microsurgery – replantation – no-reflow phenomenon – thrombolytics – urokinase – digital ischemia – hand

Descriptive Statement: Assessing the efficacy and safety of urokinase thrombolytic regimen in the management of failing microsurgical anastomosis after finger replantation

Introduction: background and aims Reconstructive microsurgery emerged in the seventies and allowed replantation of amputated digits and free tissue transfer. Despite the technical progress, failure rate remained relatively elevated. The causes are at times technical with failed anastomosis, iatrogenic vessel injuries or bad hemodynamics. However many times, digital ischemia occurs despite permeable and technically successful anastomosis. This condition is called "no-reflow phenomenon" where distal tissue perfusion cannot be restored by thromboembolectomy. Vascular thrombosis downstream the anastomotic site (at the capillary level) is thought to be the mechanism by which this condition occurs. The techniques used in the literature for salvage of failing anastomosis include: intravascular irrigation with heparin, papaverine and lidocaine, administration of continuous intravenous heparin, flap washing with streptokinase, and adventitia stripping.

Through our series of twenty two digital replantations having suffered "no-reflow phenomenon", we are going to show the efficacy of the fibrinolytic protocol we used and the outcomes obtained. These outcomes will be compared to literature findings using different protocols to derive a treatment protocol. In addition, baseline characteristics will be compared among patients to try to derive hypothesis evaluating possible risk factors for failed anastomosis.

Methods: Between 1992 and 2016, fourteen patients had "no reflow phenomenon" after microsurgical procedures. The fourteen patients underwent twenty two finger replantations in total and were complicated by no-reflow phenomenon. An intra-arterial catheter was inserted as soon as the diagnosis of « no reflow phenomenon » was confirmed. The antithrombotic protocol included a flash of 50,000 UI of urokinase, 36 ml of lidocaïne 1% and 40 mg of enoxaparine, followed by an electric seringue infusion the first six hours with 150,000 UI of urokinase, 36 ml of lidocaïne 1% and 40 mg of enoxaparine at 6 cc/h speed. The urokinase was then interrupted but the intra-arterial infusion maintained with 72 ml of lidocaïne 1% and 80 mg of enoxaparine for 24 hours, at a 3 cc/h speed, and this for ten days.

Results: In fourteen cases, the « no reflow phenomenon » was reversed and the digital vascularization restored. Success rate using this protocol was encouraging (64%). No significant bleeding or hematoma was observed in any of the cases.

Conclusion: Through our series, we proved a 64% success rate for catheter directed urokinase infusion in these cases. These rates are comparable to literature success rates using streptokinase and rt-PA thrombolytics. In contrast, in our case series no significant bleeding was noted compared to a 5-9% bleeding rate in published articles.

Abstract # 60

Neuropsychological Findings in Hamamy Syndrome: A clinical case study

Cynthia Roukoz[1, 2], Rama Kanj[1, 3], Fadi Maalouf[1], Pia Zeinoun [1, 4]

[1]American University of Beirut, Department of Psychiatry, [2]University of Angers, Department of Psychology, [3]American University of Beirut, Department of Education, [4]American University of Beirut, Department of Psychology

***Research Assistant**: Rama Kanj, MA Candidate, Email: rk153@aub.edu.lb*

***Corresponding author**: Pia Zeinoun, PhD, Assistant Professor - E-mail: pz05@aub.edu.lb*

Funding source: None

Keywords: Hamamy Syndrome, rare genetic disorder, neuropsychological profile, case study.

Descriptive Statement: First neuropsychological case study of a patient with Hamamy Syndrome.

Introduction: Background and aims: This case study is the first to describe the neuropsychological profile of a person with Hamamy Syndrome (HS). HS is a rare genetic disorder characterized by a unique set of physiological characteristics due to a single-gene mutation (1). Among published cases, there are no reports on the neuropsychological profile of children or adults with HS ([1,2,3,4]).

Methods: The patient is a 6-year old boy, seen for a neuropsychological evaluation at the Psychological Assessment Center at the American University of Beirut Medical Center in 2016 by the first author.

Results: Patient had relatively spared nonverbal intelligence, borderline-impaired language, and clinically impaired verbal reasoning, attention, and motor coordination. Additionally, parental reports and extensive behavioral observations showed clinically significant concerns with behavioral regulation, metacognition, attention- and hyperactivity/impulsivity. The patient was diagnosed with a DSM-V Language Disorder, Speech Sound Disorder, and Attention Deficit/Hyperactivity Disorder, combined presentation, in the context of low-average intelligence.

Conclusion: This is the first published report that describes the neuropsychological functions of a patient with HS. Based on the findings, we recommend patient diagnosed with HS undergo a neuropsychological evaluation to identify possible protective factors (e.g., nonverbal intelligence), and interventions of speech and language therapy, occupational therapy and behavioral therapy to address each of the neuropsychological deficits. Future research should assess the developmental trajectory of children with HS, and evaluate additional functions such as memory and social development.

Abstract # 61

Effect of Compliance with Follow-Up on Visual Outcome in Neovascular Age-Related Macular Degeneration: 5-Year Results

Carl-Joe Mehanna[1], Ziyad Mahfoud[2], Rafic Antonios[1], Joanna Saade[1], Ziad Bashshur[1]
[1]Department of Ophthalmology, American University of Beirut Medical Center, Beirut, Lebanon
[2]Department of Healthcare Policy and Research, Weill Cornell Medicine, Doha, Qatar
Corresponding Author: Ziad Bashshur, MD, Professor of Ophthalmology, Vitreoretinal service
E-mail: zb00@aub.edu.lb

Funding source: None

Keywords: wet macular degeneration; intravitreal injection; treatment outcome; visual acuity; follow-up; schedule; bevacizumab; vascular endothelial factor A/antagonist

Descriptive Statement: In neovascular age-related macular degeneration, patients with excellent compliance with their follow-up schedule maintain significantly better vision than patients who miss scheduled visits with an as-needed dosing regimen.

Introduction – Background and Aims: Neovascular age-related macular degeneration (AMD) is a chronic condition and a leading cause of visual impairment in the elderly worldwide. Several anti-vascular endothelial growth factor (anti-VEGF) agents are currently being used to treat it according to different dosing regimens, each with its risk of over- or under-treatment. Anti-VEGF therapy improves visual acuity (VA) of patients during the first two years of treatment, but all long-term studies show a progressive decline in these gains afterwards. We hypothesize that non-compliance with the follow-up schedule may contribute to this decline. Our aim is to study the effect of compliance on VA outcomes in patients with neovascular AMD who are on an as-needed treatment regimen.

Methods: Retrospective cohort study of patients with neovascular AMD treated with intravitreal anti-VEGF injections for at least 5 years, who were initially started on intravitreal bevacizumab (IVB). Compliance was defined as having a follow-up at least once every 12 weeks, and not missing a scheduled follow-up by more than 4 weeks and an intended treatment by more than two weeks.

Results: Eighty-one eyes of 60 patients with neovascular AMD met the inclusion criteria. Mean age was 73.1 years, and 57% were women. Fifty-three eyes (65.4%) met our definition of compliance, and the rest formed the non-compliant group. Mean baseline ETDRS VA was similar between the two groups (compliant: 65.3±16.6, non-compliant: 58.8±16.7, p=0.07). However, eyes of patients in the compliant group had significantly better vision at 5 years compared to non-compliant eyes (67.0±17.7 vs 52.4±27.7, respectively, p=0.03). More eyes in the non-compliant group had lost more than 15 ETDRS letters at 5 years (28.6% vs 9.4%) or had a VA of less than 35 on the ETDRS chart (25.0% vs 7.5%). Eyes in the compliant group received more anti-VEGF injections (25.5±13.1 vs 14.5±9.6, respectively, p=0.0004).

Conclusion: In neovascular AMD, strict adherence to follow-up and scheduled treatments promotes a better outcome in the long term, which may explain some of the poor results seen in other "real-life" studies. Therefore, patient education on compliance is paramount.

Abstract # 62

Teriflunomide treatment in clinical practice: The experience of an academic center in the Middle East

Bassem I.Yamout, Maya M.Zeineddine, Joelle Massouh, Nabil Ayyoubi and Samia J Khoury Nehme and Therese Tohme Multiple Sclerosis Center, Department of Neurology, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Maya M.Zeineddine, Clinical Pharmacist, Multiple Sclerosis Certified Specialist, E-mail: mz39@aub.edu.lb

Funding source: None

Keywords: Teriflunomide, multiple sclerosis, real-world

Descriptive Statement: To describe our experience with use of teriflunomide in patients with relapsing-remitting multiple sclerosis.

Background: Teriflunomide, a new oral disease-modifying therapy (DMT) with a favorable safety profile, significantly reduced annualized relapse rate (ARR), disease progression and magnetic resonance imaging (MRI) activity in relapsing-remitting multiple sclerosis (RRMS) patients in Phase III clinical trials. To our knowledge, there are no published studies addressing the real-world clinical efficacy and safety of teriflunomide in the Middle East.

Aim: To assess the efficacy and safety of teriflunomide in RRMS patients followed at a specialized academic MS center in Lebanon.

Methods: All patients treated with terfiflunomide and followed up for a minimum period of at least 6 months at our MS center were identified. Main efficacy endpoints were the proportion of patients free from relapses, disability progression and magnetic resonance imaging (MRI) activity. Safety and tolerability of teriflunomide were also recorded.

Results: A total of 32 patients were included: 56.2% were female; mean age 40.3 ± 10.1 years; mean disease duration 6.8 ± 5.3 years; mean duration of therapy 14.4 ± 4.8 months. 81.2% of the patients (n=26) were treated with interferon therapy before starting teriflunomide and were shifted because of flu-like symptoms and injection-site reactions. 15.6% (n=5) were treatment-naïve. The proportion of relapse-free patients improved from 71.9% before treatment to 96.9% on teriflunomide. The majority of patients (76.7%, n=23) on teriflunomide were free from disability progression as measured by Expanded Disability Status Scale (EDSS). The proportion of patients with no new T2 or enhancing lesions was 85.2%. Six patients discontinued teriflunomide (18.7%); of whom 2 patients failed therapy clinically and/or radiologically, 2 patients experienced adverse events (severe hair loss, gingival and vaginal bleeding), 1 patient converted to progressive MS and 1 patient had pregnancy plan and severe hair loss. Twenty-two patients (68.7%) experienced side effects with hair loss (n=9) being the most commonly reported side effect. None of our patients had lymphopenia or increase liver enzymes on teriflunomide.

Conclusion: In clinical practice, teriflunomide was effective in reducing disease activity and progression of disability over the treatment period. Discontinuation rates and adverse events were low.

Abstract # 63

Real-world use of dimethyl fumarate in patients with relapsing-remitting multiple sclerosis: The experience of an academic center in the Middle East

Bassem I. Yamout, Maya M. Zeineddine, Joelle Massouh, Nabil Ayyoubi and Samia J. Khoury
Nehme and Therese Tohme Multiple Sclerosis Center, Department of Neurology, American University of Beirut Medical Center, Beirut, Lebanon
Corresponding author: Maya M. Zeineddine, Clinical Pharmacist, Multiple Sclerosis Certified Specialist, E-mail: mz39@aub.edu.lb

Funding source: None

Keywords: Dimethyl fumarate, multiple sclerosis, real-world

Descriptive Statement: To describe our experience with use of dimethyl fumarate in patients with relapsing-remitting multiple sclerosis.

Background: Dimethyl Fumarate (DMF), approved by the FDA in 2013, is another oral disease-modifying drug (DMD) that demonstrated significant efficacy and a favorable benefit-risk profile in Phase III clinical trials. Safety and efficacy of DMF has been assessed in clinical trials, rather than in less-controlled, real-world population studies.

Aim: To assess the efficacy and safety of DMF in RRMS patients followed at a specialized academic MS center in Lebanon.

Methods: A total of 54 patients were treated with DMF at our MS center, of whom 36 had a follow-up of at least 6 months. We assessed the effect of DMF therapy on their annualized relapse rate, disability progression and magnetic resonance imaging (MRI). Safety and tolerability of DMF were evaluated by adverse events monitoring and laboratory tests.

Results: A total of 54 patients were included: 61.8% were female; mean age 34.7 ± 11.2 years; mean disease duration 6.2 ± 6.2 years; mean DMF use 8.4 ± 5.5 months; mean baseline Expanded Disability Status Scale (EDSS) 1.5 ± 0.7. Most of the patients were previously treated with other DMDs (66.7%; n=36), mainly interferons (53.5%; n=29). Patients treated with DMF for at least 6 months (n=36) showed a 65% reduction in their ARR. Neurological disability as measured EDSS was stable in 18 patients (58%) and improved in 7 patients (22.6%). The proportion of patients with no new T2 or enhancing lesions was 66.7%. Therapy was discontinued in 9 patients (16.7%). In 4 patients, it was stopped due to inefficacy; in 3 patients due to severe flushing and/or gastric adverse events, in 1 patient due to conversion to progressive MS and in 1 patient due to inefficacy and adverse events. Twenty-nine patients (53.7%) developed side effects with gastric and flushing side effects being the most common. None of our patients experienced lymphopenia or increase liver enzymes on DMF.

Conclusion: In clinical practice, DMF was well tolerated and effective in reducing disease activity.

Abstract # 64

Podocyturia is a predictor of cardiovascular outcome

*Shatila D[1§†], Dia B[2§†], Zgheib N K[1,3], Eid A A[2], Badr K[1,3]**

(1) Vascular Medicine program, AUBMC; (2) Department of Anatomy, Cell Biology and Physiology, AUBFM; (3) Department of Pharmacology and Toxicology, AUBFM; Division of Nephrology, Department of Internal Medicine, AUBFM

[§]Role: Research Assistants [†]Both authors had equal contribution

***Corresponding author**: Kamal Badr - Professor - E-mail: kbadr@aub.edu.lb

Funding source: American University of Beirut Faculty of Medicine Medical Practice Plan (AUBFM MPP)

Keywords: Cardiovascular disease, Podocyturia, Podocin

Descriptive Statement: Podocyturia measured by the relative expression of urinary *Podocin* mRNA is higher in patients with established obstructive coronary artery disease.

Background: A large body of high-quality evidence has established a direct and continuous relationship between albumin excretion rates (AER) and adverse renal and cardiovascular outcomes, ascertaining AER as an independent predictor of cardiovascular events (CVD), worse outcomes, and increased mortality in a wide range of clinical settings. A recent study by our team was performed on urine samples from control and diabetic patients provided powerful support to the hypothesis that podocyturia is a potentially clinically useful predictor of CVD and may significantly outperform albuminuria.

Aim: To test the hypothesis that podocyturia correlates with the presence of obstructive coronary artery disease (CAD).

Methods: Subjects who were admitted to the Coronary Catheterization Lab at AUBMC for cardiac catheterization were consented and included in the study for clinical data and urine collection. Urine was immediately processed and stored at -80°C until analysis. RNA was isolated using a standard kit from Qiagen and transformed into cDNA using a TaqMan Fast Universal PCR Master Mix. *Podocin/Nephrin* mRNA relative expression was then evaluated on real-time PCR using Taqman probes. Obstructive CAD was defined as the presence of at least 50% stenosis in any of the coronaries. This study was approved by the AUB IRB.

Results: Fifty one subjects were included in the analysis of whom 30 had obstructive CAD. Urinary Podocin mRNA relative expression was significantly higher in subjects who had obstructive CAD (Mean±SD: 4.27±3.26) when compared to those who did not have or had minimal CAD by cardiac catheterization (Mean±SD:2.58±1.80) (*P*=0.035).

Conclusion: This is a first validation study in which patients are definitively identified as having, or not having, significant coronary vascular injury. Our results may provide additional and more convincing evidence of the correlation between the degree of podocyturia and hard point vascular outcomes. Further recruitment and experiments are ongoing, and medical records are being reviewed for a more detailed analysis. Factors such as gender, age, smoking, and history of diabetes and hypertension will be included in the final analysis.

Abstract # 65

Vitamin D supplementation for obese adults undergoing bariatric surgery – Protocol

Chakhtoura M[1,2], Nakhoul N[2], Akl EA[2,3,4], Safadi BY[5], Mantzoros CS[6], Rahme M[1], El-Hajj Fuleihan G[1,2]

[1]Department of Internal Medicine, Calcium Metabolism and Osteoporosis Program, WHO Collaborating Center for Metabolic Bone Disorders, Division of Endocrinology, American University of Beirut Medical Center, Beirut, Lebanon. [2]Scholars in HeAlth Research Program (SHARP), American University of Beirut Medical Center, Beirut, Lebanon. [3]Department of Internal Medicine, American University of Beirut Medical center, Beirut, Lebanon. [4]Department of Health Research Methods, Evidence, and Impact (HE&I), McMaster University, Hamilton, Canada. [5]Department of Surgery, American University of Beirut Medical Center, Beirut, Lebanon. [6]Department of Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston MA, Massachusetts, USA

Corresponding author: Marlene Chakhtoura- Instructor of Clinical Medicine –
E-mail: mc39@aub.edu.lb

Funding source: This work was supported by a grant from the Medical Resource Plan at the American University of Beirut - Lebanon and made possible thanks to the Scholars in HeAlth Research Program (SHARP).

Keywords: vitamin D, bariatric surgery, malabsorption.

Descriptive Statement: The malabsorption of nutrients, specifically vitamin D, is a well-recognized complication following bariatric surgery. This systematic review of vitamin D trials compares the effect of various vitamin D doses on vitamin D status, and other outcomes, in patients undergoing bariatric surgery.

Introduction: Vitamin D deficiency is a common complication following bariatric surgery and results in an increased risk of hypocalcaemia, secondary hyperparathyroidism and bone loss. Vitamin D replacement guidelines in bariatric surgery patients are mostly based on expert opinion. Our objective is to compare the effects of different doses of vitamin D supplementation on vitamin D status, and skeletal and metabolic outcomes, in patients undergoing bariatric surgery.

Methods: This is a systematic review of vitamin D randomized and controlled clinical trials conducted in obese adults undergoing bariatric surgery. We will conduct a comprehensive search of 6 databases, in addition to registries of ongoing trials. We will calculate the mean difference and risk ratios, for continuous and dichotomous outcomes, respectively, and their 95%CI, when at least 2 studies are eligible in each comparison (low dose ≤ 600IU/d, moderate dose 600-3,500IU/d, high dose ≥3,500IU/d, compared to each other or to placebo). We will pool data using RevMan version 5.3. We will perform sub-group analysis by baseline BMI and surgery type. We will assess the risk of bias using the Cochrane's risk of bias assessment tool. We will present the overall quality of the evidence for each outcome according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results: This systematic review is currently ongoing. The review protocol is registered in the Cochrane Library CD011800.

Conclusion: This review will help define the optimal dose of vitamin D supplementation in obese subjects following bariatric surgery. It will inform and update vitamin D replacement guidelines in this specific population.

Abstract # 66

MRI measures, Cognitive function, and 25-Hydroxyvitamin D (25(OHD) in Multiple Sclerosis (MS): A pilot Study

Ribal Haddad[1], Hala Darwish[1,2], Salem Hannoun[1], Samia J Khoury[1,3]

[1] Nehme and Therese Tohme Multiple Sclerosis Center, American University of Beirut Medical Center, Beirut, Lebanon

[2] Hariri School of Nursing, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

[3] Neurology Department, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

Corresponding author: Hala Darwish PhD - Associate Professor of Nursing - email: hd30@aub.edu.lb

Funding source: MPP and CNRS

Keywords: multiple sclerosis, cognition, vitamin D, magnetic resonance imaging.

Descriptive Statement: This is a cross-sectional study assessing the differences in MRI metrics associated with cognition between MS patients with deficient or sufficient 25(OH)D levels.

Background and Aim of the study: Multiple Sclerosis (MS) is a chronic inflammatory disease of the central nervous system where low serum 25(OH)D level is a risk factor for the disease. Moreover, low 25(OH)D is associated with cognitive dysfunction in adults. Therefore, the aim of this study is to evaluate whether 25(OH)D serum levels correlate with cognitive performance and specific MRI metrics in patients with MS.

Methods: Patients with relapsing remitting MS or clinically isolated syndrome aged 18 years and older treated with interferon-beta and without signs of active inflammation or cognitive impairment were recruited. Subjects were screened for depression and anxiety using the Arabic-Hopkins Symptoms Checklist (HSCL-25), cognitive performance was measured using the Arabic-Montreal Cognitive Assessment (MoCA) and Stroop Test, Symbol digit Modalities Test (SDMT) and the Brief Visual Memory Test (BVMT). Blood was collected for 25(OH)D levels. MRIs were performed at AUBMC for clinical purposes within 3 months of their inclusion. Third ventricular width, corpus callosum index and bicaudal ratio were measured; as well, as volume and segmentation of areas such as corpus callosum, thalamus, basal ganglia, cerebellum and the hippocampus.

Results: 31 patients had MRIs done within 3 months of inclusion. 11 had a deficient 25(OH)D, less than 25 ng/ml, and 20 had a sufficient 25(OH)D, greater than 35 ng/ml. Descriptive data analysis of these 31 patients will be performed. MRI images will be analyzed. Spearman's rho correlation analysis will be conducted to examine the association between cognitive performance, 25(OH)D, and MRI measures. Further analysis, using independent *t*-test will compare the MRI metrics between the two different 25(OH)D groups to check for differences that are independent of cognitive testing results.

Conclusion: We expect this preliminary analysis to show a significant association between cognitive impairment, 25(OH)D level, and global atrophy measures, as well as specific disturbances in areas previously known to be associated with different aspects of cognition.

Abstract # 67

Development of the Verbal Memory Arabic Test (VMAT)

Pia Zeinoun[1,2], Natali Farran[3], Samia Khoury[4,5], Hala Darwish[3,5]

[1]Department of Psychology, Faculty of Arts and Sciences, American University of Beirut, [2]Psychological Assessment Center, American University of Beirut Medical Center, Beirut, Lebanon [3]Rafic Hariri School of Nursing, Faculty of Medicine, American University of Beirut, Beirut, Lebanon [4]Department of Neurology, Faculty of Medicine, American University of Beirut [5]Nehme and Therese Tohme Multiple Sclerosis Center, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Hala Darwish – Associate Professor –
E-mail: hd30@aub.edu.lb

Presenter: Natali Farran - Research Assistant - E-mail: nf35@aub.edu.lb

Funding source: Novartis and MENACTRIMS.

Keywords: Verbal Memory Arabic Test, Memory, Neuropsychological Testing.

Descriptive Statement: This is the first study in a multi-phase project aimed to construct the first Arabic memory test (Verbal Memory Arabic Test; VMAT) from the ground up, so that it is culturally and linguistically appropriate to Lebanon and the Arab region.

Introduction: Background and aims Verbal memory assessment requires the memorization of words across several trials, and recalling these words with and without aid across time. This testing type is integral to neuropsychological assessment and is widely used in clinical and research settings. However, verbal memory tests are often translated from existing Western tools – a process that poses serious cultural and psychometric problems when interpreting the findings. Our study aimed to develop a test that is culturally and psychometrically robust to memory impairment among Arabic-speaking people.

Methods: To identify 15 Arabic words that are culturally and linguistically appropriate, we recruited seventy-seven normal adults from across Lebanon and asked them to generate words for 7 semantic categories (e.g., animals, clothes, etc).

Results: We collected approximately 133 Arabic words per category, selected those with low to medium frequency, and further selected words based on 11 conceptual criteria. The most appropriate words constructed the primary memory list of 15 words (List A), and two lists that served as interference (List B) and recognition items. The final version of the VMAT is comprised of 5 trials of List A, followed by an interference list, then an immediate recall of List A with and without semantic cues, then a delayed recall after 15 minutes, and finally a recognition trial.

Conclusion: The VMAT is the first neuropsychological tool developed intentionally as a culturally and linguistically valid verbal memory test in Arabic. The next step is to provide normative data, and further evidence of its validity and reliability on 185 normal adults (older than 16 years), 50 Multiple sclerosis patients, and other special populations (e.g., adults with ADHD).

Abstract # 68

Effect of vitamin D replacement on maternal and neonatal outcomes Preg-D trial protocol

Chlela M[1], Chakhtoura M[2,3], Asaad M[2], Ajjour S[2], Attieh J[2], Rahme M[2], Nassar A[1], El-Hajj Fuleihan G[2,3]

[1]Department of Obstetrics and Gynecology. [2]Department of Internal Medicine, Calcium Metabolism and Osteoporosis Program, WHO Collaborating Center for Metabolic Bone Disorders, Division of Endocrinology, American University of Beirut Medical Center, Beirut, Lebanon.
[2]Scholars in HeAlth Research Program (SHARP), American University of Beirut Medical Center, Beirut, Lebanon.

Corresponding author: Marlene Chakhtoura – Instructor of Clinical Medicine –
E-mail: mc39@aub.edu.lb

Funding source: Resource Plan at the American University of Beirut, Lebanon.
WHO/EMRO under the EMRPPH grant scheme, project number EMIER1409518.
This project was made possible thanks to the Scholars in HeAlth Research Program (SHARP), NIH Grant D43TW009118.

Keywords: vitamin D replacement, pregnancy, Middle East, neonatal outcomes.

Descriptive Statement: Hypovitaminosis D affects one to two-thirds of pregnant women from the Middle East. This trial aims at comparing the effect of 2 vitamin D doses on vitamin D status in the mothers and their neonates, and on other neonatal skeletal and anthropometric outcomes.

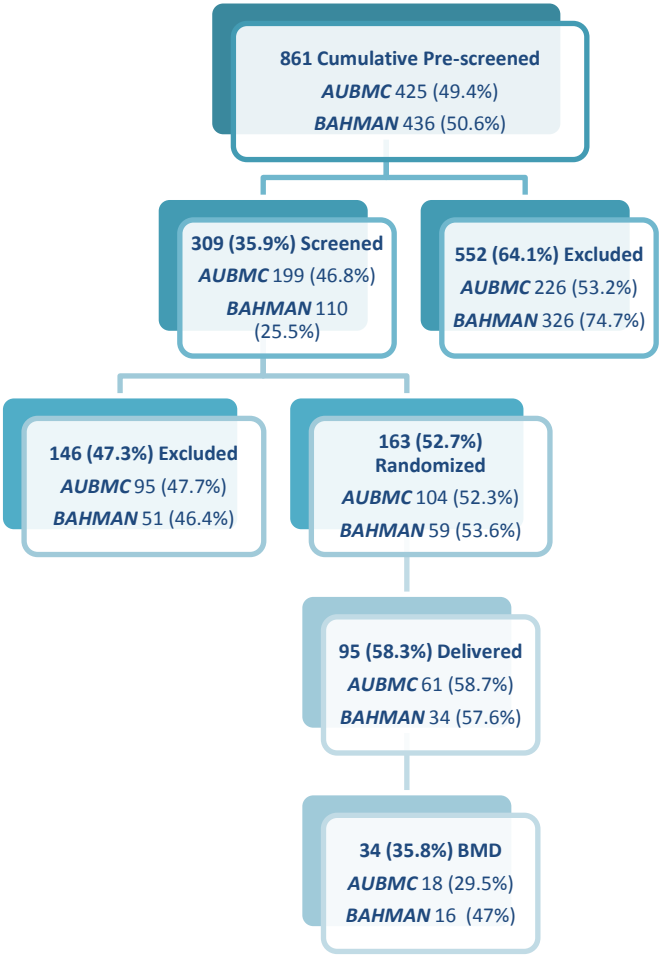
Introduction: The vitamin D recommended doses during pregnancy differ by organization, and are not evidence based. Our hypothesis is that in Middle Eastern pregnant women, at high risk of vitamin D deficiency, a vitamin D dose of 3,000IU/day is required to reach a desirable maternal 25-hydroxyvitamin D [25(OH)D] level, and to positively impact infant bone mineral content (BMC).

Methods: This is a blinded randomized controlled trial. Pregnant women presenting to the OB-GYN clinics at AUB-MC and Bahman hospital are being approached. Eligible women are randomized to equivalent doses of cholecalciferol, 600IU/d or 3,000IU/d, from 15-18 weeks gestation until delivery. Maternal 25(OH)D and chemistries are assessed at baseline, and at delivery. Neonatal anthropometric variables are measured at birth, and bone mass assessed by DEXA at 1 month of age. 280 pregnant women are needed to demonstrate a significant difference in the proportion of women reaching a 25(OH)D level ≥50 nmol/L at delivery, and a difference in infant BMC of 6(10)g (90% power; α=2.5%). The primary analysis is an intention-to-treat analysis of unadjusted results.

Results: The trial was launched in July 2015 and is ongoing. To-date, 861 pregnant women were pre-screened, 309 pregnant women were screened and 163 (53% of total approached women) were eligible and enrolled (Appendix). The mean (±SD) age is 29.8(±4.8) years, and the mean BMI is 24.6(±4.1) kg/m^2. The 25(OH)D level at randomization differs by center, 15.2(5.1) ng/ml at Bahman Hospital (N=59) and 18.9(6.8) ng/ml, at AUB-MC(N=101)(P<0.001). 95 women have delivered; 9 serious adverse events have been registered, none was related to vitamin D. Protocol registered on clinicaltrial.gov (NCT02434380)

Conclusion: This trial is the first to directly address the applicability of the Institute of Medicine vitamin D guidelines worldwide. Findings from our study will inform guidelines on vitamin D replacement in pregnant women in our region.

Consort Flow Diagram Detailing Recruitment Status from Pre-Screening to Study Completion.



Abstract # 69

Recurrence of Intermittent Exotropia after Bilateral Lateral Rectus Recession

Christiane Al-Haddad, MD[1]; Karine Ismail, MSc[1]; Samia Al Sayyid, MD[2]
Department of Ophthalmology, American University of Beirut, Beirut, Lebanon,
School of Medicine, American University of Beirut, Beirut, Lebanon
Corresponding author: Christiane Al-Haddad, MD, Associate Professor, American University of Beirut Medical Center, PO Box 110236, Beirut, Lebanon, Tel: +961-1-350000 ext 5550, Fax: +961-1-370837, Email: ca12@aub.edu.lb

Funding source: none

Keywords: Recurrence, Intermittent Exotropia, Bilateral Lateral Rectus, Recession

Descriptive Statement: Intermittent exotropia is the most common form of exotropia (XT). It is defined as an outward ocular misalignment and estimated to be present in 1% to 2% of the pediatric population. Treatment usually is surgical consisting of eye muscle surgery, most commonly lateral rectus recessions. Success rate is high; however, this entity is known to recur after eye muscle surgery with variable rates ranging from 41 to 83%.

Introduction: background and aims: To evaluate predictive factors for intermittent exotropia recurrence after bilateral lateral rectus (BLR) recession.

Methods This is a retrospective chart review of 33 patients who underwent bilateral lateral rectus (BLR) recession surgery between January 2007 and September 2016 with at least one post-surgical follow-up. Information collected included: age, gender, systemic diseases, history of prematurity, family history of eye diseases, visual acuity, refraction, ocular alignment in all position, slit lamp examination, fundoscopy and amount of BLR recession. Successful alignment was defined as <8 prism diopters of esotropia or exotropia postoperatively.

Results: Mean age of patients at the time of surgery and follow-up time were 9.0±11.8 years(y) and 20.9±29.6 months (m), respectively. Mean amount of bilateral lateral rectus (BLR) recession was 6.4±0.9mm. Recurrence rate was 39% on last follow-up. Age at surgery and at the time of last follow-up were significantly higher in the recurring group (p=0.002 and 0.01, respectively). Postoperative angle of misalignment during the first 3 months was correlated with exotropia recurrence (p=0.004). No statistical significance was found among the remaining factors studied.

Conclusion: In conclusion, we found that recurrence of exotropia was increased in patients operated at older age and amid those with significant exotropia detected in the early postoperative period (within 3 months of surgery).

Abstract # 70

Crossed Unfused Ectopic Pelvic Kidneys

Jad A. Degheili[1], M.D.; Murad M. AbuSamra[2], M.D.; Fadi El-Merhi[2], M.D.; Albert El-Hajj[1], M.D.*
[1] Division of Urology and Renal Transplantation, Department of Surgery, American University of Beirut-Medical Center, Riad El-Solh 1107 2020, Beirut, Lebanon. [2] Department of Diagnostic Radiology, American University of Beirut-Medical Center, Riad El-Solh 1107 2020, Beirut, Lebanon
CORRESPONDING AUTHOR: Albert El-Hajj, M.D., American University of Beirut – Medical Center, Division of Urology and Renal Transplantation, Department of Surgery, Riad El- Solh 1107 2020, Beirut, Lebanon, Email: ae67@aub.edu.lb
PRESENTER: Jad A. Degheili, M.D., Post-Graduate Year IV, Division of Urology and Renal Transplantation, Department of Surgery

KEY WORDS: Ectopia; Kidney(s); Fused; Unfused; Crossed

FINANCIAL DISCLOSURE: The authors declare that they have no relevant financial interest

DESCRIPTIVE STATEMENT: Renal ectopia is the presence of kidneys outside their normal anatomical location. Several variations and types of ectopia are present. This leads to variations in vascular supply to those kidneys; in such scenarios, knowledge and detection, prior to any intervention, is crucial.

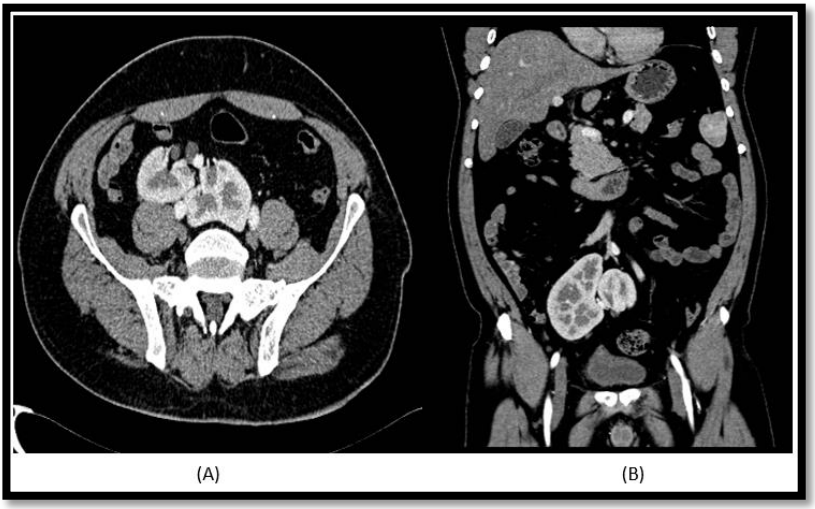
INTRODUCTION: Crossed renal ectopia is a rare entity detected incidentally in 20 to 30% of cases, and results from the aberrant migration and crossing of the midline by the metanephric blastema and the ureteral bud, usually occurring during the fourth to eighth week of gestation. Several types exists of crossed renal ectopia, of which the unfused form constitutes an incidence of 1:75000. We hereby present such a case detected on routine workup for gross hematuria.

METHODS: A 45-year-old gentleman, heavy smoker, presented with intermittent episodes of gross hematuria. An enhanced Computed Tomography with delayed phases was requested, revealing the presence of ectopically located kidneys. Both kidneys were located along the right para-median area within the pelvis, with no evidence of fusion. The ureters appeared unremarkable with normal anatomical implantation within the bladder.
On the vascular window, after reconstruction, the right kidney had two arteries, originating from the proximal right common iliac artery and the median sacral artery, respectively. The left kidney is supplied by two arteries, branching from the distal left common artery and the median sacral artery. Right and left renal veins joined to form one vein, which drained in the left common femoral vein.

RESULTS: Second in incidence after horse-shoe kidney, crossed renal ectopia witnesses a males-to-female's predominance of 1.4-2:1, and a two-to-three times more common left-to-right ectopy. Variations of vasculature in ectopically located kidneys have only been described in few case reports. On the contrary to the normal embryological degeneration of the caudal vessels upon migration of the kidneys to their usual anatomical location, renal vessels, in ectopic kidneys, do not degenerate; thus several variations in blood supply, may arise, resulting in more than one accessory and polar arteries.

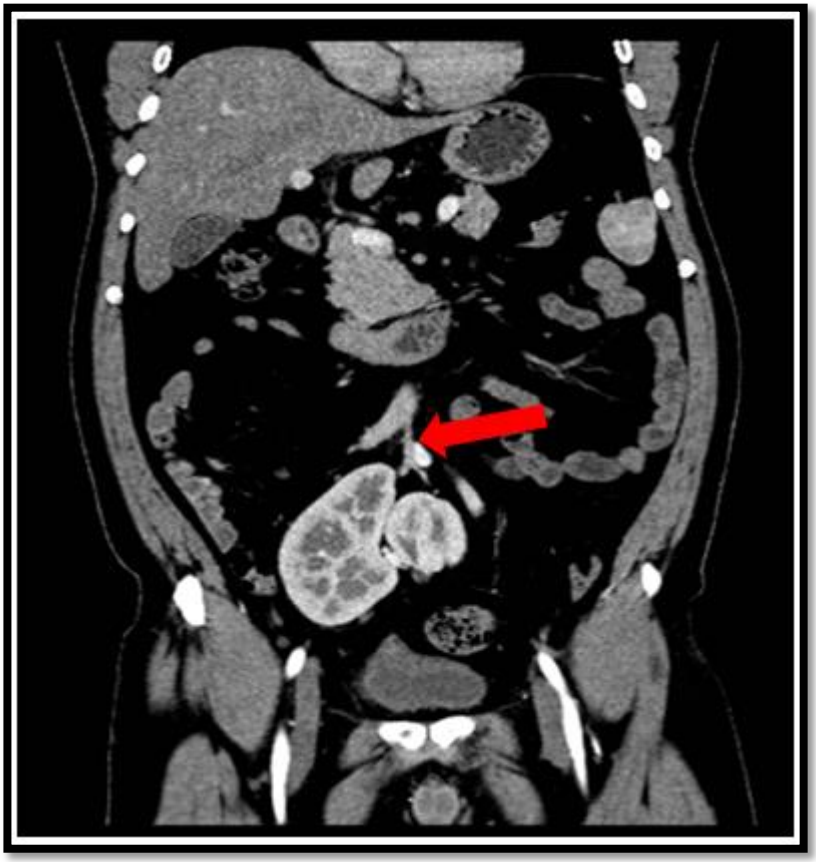
CONCLUSION: Ectopic kidneys are kidneys located in an unusual anatomical location, with diverse blood supply. Knowledge of such variations in vasculature, in ectopic kidneys, is crucial prior to performing any surgical or radiological intervention.

FIGURE 1



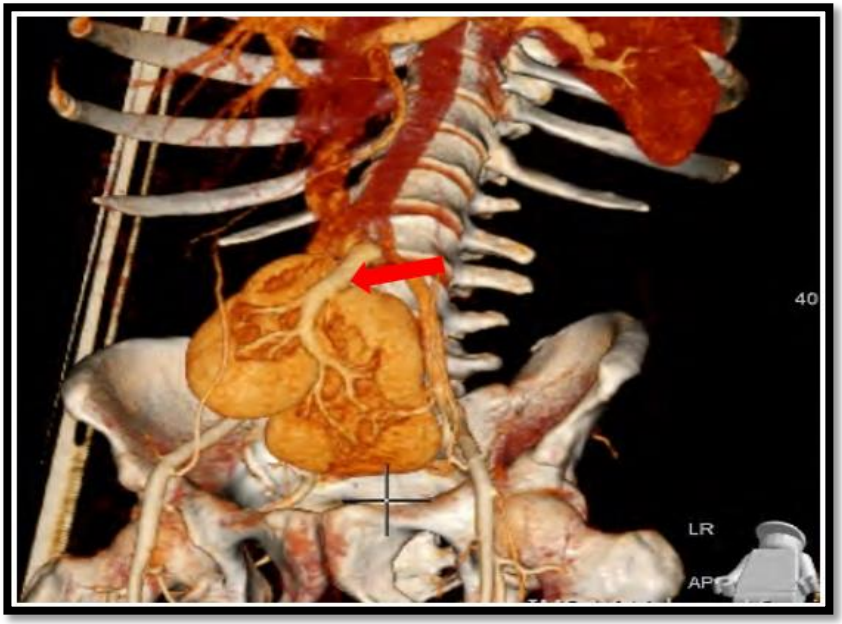
Axial (A) and coronal (B) CT scan, with intravenous contrast in the corticomedullary phase, showing clear plane of separation between the two kidneys

FIGURE 2



Coronal CT scan with IV contrast showing the median sacral artery (red arrow) giving right and left renal arteries

FIGURE 3



MDCT with VRT (volume rendering technique) showing the crossed unfused ectopic kidneys with the presence of joined draining vein (red arrow) of both kidneys

Abstract # 71

Effect of 25 Hydroxyvitamin D (25(OH)D) level on cognitive and radiologic findings in a 3 year cohort of Multiple Sclerosis patients

Rami Fakih[1], Hala Darwish[1,2], Nabil Ayoubi[1], Salem Hannoun[1], Ribal haddad[1], Samia J Khoury[1,3]
[1]Nehmeh and Therese Tohmeh Multiple Sclerosis Center, American University of Beirut Medical Center, Beirut, Lebanon
[2]Hariri School of Nursing, Faculty of Medicine, American University of Beirut, Beirut, Lebanon
[3]Neurology Department, Faculty of Medicine, American University of Beirut, Beirut, Lebanon
Corresponding author: Dr. Hala Darwish, E-mail: hd30@aub.edu.lb
Presenter: Rami Fakih, MD

Funding source: *[1]Nehmeh and Therese Tohmeh Multiple Sclerosis Center, American University of Beirut Medical Center*

Keywords: Multiple Sclerosis – Vitamin D – Cognition – Brain Atrophy - MRI

Descriptive Statement: This is a retrospective cohort study evaluating the relationship between deficient and sufficient levels of 25(OH)D level, cognitive and radiologic outcomes in MS patients.

Introduction: background and aims Multiple Sclerosis is a degenerative, inflammatory disease of the CNS that causes demyelination, and atrophy. Epidemiological observations revealed an association between inadequate 25(OH)D level and increased risk of MS. High 25(OH)D levels correlated with decreased axonal damage. Emerging evidence suggests that correcting 25(OH)D insufficiency in MS and CIS patients has a beneficial effect on clinical and MRI outcomes. We hypothesized that 25(OH)D levels have a protective effect on cognitive outcomes and MRI brain atrophy in MS patients.

Methods: A cohort of 50 MS patients enrolled in the Multiple Sclerosis Center AMIR database since January 2012, were followed up annually for 3 years. Patients without signs of active inflammation or cognitive impairment were included. 25(OH)D level was measured at baseline and annually. Brain MRI was performed annually within 3 months of the 25(OH)D test. Physical and cognitive disability was assessed using the Expanded Disability Status Scale (EDSS), and the Symbol Digit Modalities Test (SDMT), respectively. Brain volume of the gray matter, corpus callosum, thalamus, basal ganglia, cerebellum and the hippocampus were segmented and measured. In addition, manual measurements of the third ventricular width, corpus callosum index and bi-caudal ratio were analyzed.

Results: Descriptive data analysis will be performed. One-way-ANOVA, Pearson's correlation and multivariate repeated measure analysis will be conducted to study the longitudinal association between predictors of cognitive performance, 25(OH)D levels, and radiological outcomes.

Conclusion: It is expected that a sufficient 25(OH)D level will be significantly associated with better cognitive and radiological findings compared with lower levels.

Abstract # 72

Influence of time-in-NEDA on physical and cognitive disability as well as brain atrophy in a contemporary cohort of patients with multiple sclerosis

Rami Fakih[1], Nabil El Ayoubi[1], Ribal Haddad[1], Nancy Issa[2], Bassem Yamout[1], Hala Darwish[1,2], Samia J Khoury[1]

[1]Department of Neurology, Nehmeh and Therese Tohmeh Multiple Sclerosis Center, American University of Beirut, Beirut, Lebanon

[2]Medical Student, American University of Beirut, Faculty of Medicine, Beirut, Lebanon

[3]Hariri School of Nursing, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

Corresponding author: Samia J Khoury MD - Professor of Neurology - email: sk88@aub.edu.lb

Funding source: Nehme and Therese Tohme Multiple Sclerosis Center

Keywords: Multiple Sclerosis, NEDA, Brain MRI, physical disability, cognitive changes

Descriptive Statement: A prospective cohort study assessing the effect of time-in-NEDA on clinical outcomes and brain atrophy in a cohort of patients with RRMS treated at a specialized MS center.

Background and aim of the study: Relapsing-remitting multiple sclerosis (RRMS) is an autoimmune inflammatory disease of the brain and spinal cord. Escalation of treatment is warranted once a patient fails meeting the clinical and radiological criteria of NEDA (no evidence of disease activity). However, the relationship between NEDA and clinical or brain atrophy outcomes is still debated. Our aim was to explore the effect of time-in-NEDA on clinical outcomes and brain atrophy in RRMS patients.

Methods: We studied a cohort of RRMS patients enrolled in the Nehme and Therese Tohme MS Center AMIR study since January 2012, followed up annually for 3 years. At each visit, physical disability was assessed using the Expanded Disability Status Scale (EDSS), 25 Foot Walk Test (25FWT) and 9 Hole Peg Test (9HPT), and cognitive function via the Symbol Digit Modalities Test (SDMT). Follow up brain and spine MRI was performed regularly as clinically pertinent, and gray and white matter volumes were measured. NEDA status, cumulative time-in-NEDA, and percentage of total disease duration in NEDA were determined. The predictors of long vs short Time-in-NEDA were also explored.

Results: 95 patients with RRMS (60% women), with a mean (SD) age and disease duration of 32.8 (11.1) years and 50.2 (56.2) months, respectively, and at least 3 years of follow up were included. Their mean (SD) EDSS at baseline was 1.4 (1.1), 39 (41.1%) patients were not on any MS treatment at enrollment, while 41 (43.2%) were on interferons, 11 (11.6%) on Fingolimod, and 4 (4.2 %) on other medications. After 3 years, 40 (42.1%) patients maintained NEDA, with 33 (34.7%), 8 (8.4%), 5 (5.3%), and 9 (9.5%) losing NEDA due to new lesions on MRI, relapses, worsening EDSS, or combination of reasons, respectively. Among all patients the mean (SD) cumulative Time-in-NEDA was 23.3 (16.9) months. The mean (SD) proportion of disease duration spent in NEDA was 37.1% (30.8%). Of note, 65 (68.4 %) patients had NEDA for less than half of their disease duration (short Time-in-NEDA). There were no differences between patients with short vs long Time-in-NEDA in terms of physical and cognitive disability cross-sectionally at any of the visits, or longitudinally during follow up.

Conclusion: In a contemporary cohort of MS patients followed up for 3 years, there were no statistically significant correlations between Time-in-NEDA and physical or cognitive disability. As a continuation of this project, we will study the differences between atrophy on brain MRI and Time-in-NEDA.

Abstract # 73

Utility of periodic evoked potentials to monitor disease activity in patients with multiple sclerosis

Nabil El Ayoubi[1], Ribal Haddad[1], Nour Hijazi[1], Anastasia Chahine[1], Rami Fakih[1], Samia J Khoury[1]

[1] Nehme and Therese Tohme Multiple Sclerosis Center, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Samia J Khoury MD - Professor of Neurology - email: sk88@aub.edu.lb

Funding source: Nehme and Therese Tohme Multiple Sclerosis Center

Keywords: evoked potentials, multiple sclerosis, disease modifying therapy, disability progression.

Descriptive Statement: a prospective cohort study assessing the usefulness of periodic evoked potentials in monitoring disease activity in patients with multiple sclerosis.

Background and Aim of the study: Relapsing remitting multiple sclerosis (RRMS) is an autoimmune inflammatory disease that affects the central nervous system. Therapeutic escalation is indicated if new lesions on MRI or clinical deficits are found. The clinical utility of evoked potentials (EPS) during periodic follow up in MS is not clear. The aim of this study was to explore associations between conducting periodic EPs, changes in disease modifying therapy (DMT), and physical or cognitive disability, in a cohort of patients with RRMS followed up at a specialized MS center.

Methods: RRMS patients enrolled in the Nehme and Therese Tohme MS Center AMIR study since January 2012, followed-up over a 3-year time period were included in this study. At each of the bi-annual visits, cognitive function was assessed using the Symbol Digit Modalities Test (SDMT), and physical disability using the Expanded Disability Status Scale (EDSS), 25 Foot Walk Test (25FWT) and 9 Hole Peg Test (9HPT). MRI of the brain and spine as well as routine EPs were performed annually or biannually as indicated by the treating physician.

Results: The study sample consisted of 151 patients with RRMS. The mean (SD) age at visit 1 was 28.1 (11.19) years, EDSS was 1.28 (1.03), and disease duration was 2.4 (1.78) years. The number of patients that completed visits 1, 2, 3, and 4 were: 151 (100%), 139 (92%), 124 (82.1%), and 43 (28.5%), respectively. Up to 26% (15-26%) of patients underwent periodical EPs at each visit, in addition to the regular clinical and radiological follow-up, to amount to a total of 128 EPs performed. Between 7-23% of these patients underwent a change in DMT. This was similar to the 4-33% of patients that did not undergo periodic EPs but changed DMT. From those that underwent routine EPs, 52 (41%) had worsening results as compared to previous EPs, with 7 patients changing DMT (13.4%; disease activity = 4, side effects = 3). In contrast, of the 76 (59%) that did not have worsening EPs, 10 patients (13.1%; disease activity =7, side effects = 3) had a change in DMT. Nevertheless, worsening EPs correlated with worsening in physical and cognitive disability variables such as the dominant hand 9HPT at visit 2 (19.19s vs 21.97s, P= 0.008), and SDMT score at visit 3 (58 vs 46, P= 0.002) with a trend towards a worse EDSS at visit 2 (0.89 vs 1.61, P= 0.06).

Conclusion: The routine use of EPs over 3 years was not related to changes in management of this cohort. However, the correlation between worsening EPs and some physical and cognitive tests could point toward subclinical neuro-inflammation. This needs to be further explored, due to its implications on therapeutic escalation.

Abstract # 74

Cost-benefit analysis of a projected national Human Papilloma Virus vaccination program in Lebanon.

Ghinwa El Hayek[1], Rania Bzieh[1], Sarah Bahr[1], Salim Adib[1]*

[1]Department of Epidemiology and Population Health, Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon.

Corresponding author: Ghinwa El Hayek - Research Assistant- E-mail: gye01@mail.aub.edu

Funding source: None

Keywords: Cervical cancer, HPV, women's health, health economics, health policies, prevention, Middle-East, Arab

Descriptive Statement: This study is a Cost Benefit Analysis (CBA) that will compare the annual cost of vaccinating all 11 year old girls against Human Papilloma Virus (HPV) against the annual cost of Cervical Cancer (CC) treatment in Lebanon.

Introduction: background and aims: WHO recommends including Human Papilloma Virus (HPV) vaccination in national immunization programs, as a preventive measure against cervical cancer (CC). The opportunity of adopting a population-based HPV vaccination program is debated in Lebanon on epidemiological, socio-cultural, logistical and most importantly economic grounds. The debate has not been informed so far by any quantitative evidence regarding costs and outcomes. This cost-benefit analysis (CBA) contributes to generating evidence necessary for a decision through locally available data.

Methods: Various sources of data were mined to obtain variables needed for the two sides of the CBA equation:

1. Estimation of the cost of HPV vaccination campaigns targeting 11 year-old girls, using the vaccine with the lowest retail price in Lebanon in 2016.
2. Estimation of the management cost for treatment of a yearly average case-load of CC in Lebanon, assuming the incidence remains stable at the current levels.

Results: The implementation of a Cervarix®-only vaccination in a given year would cost about 5,407,790 USD to vaccinate 38,083 11-year old girls. In contrast, the estimated cost of managing a mean annual mixed case-load of 100 incident CC cases was about 1,649,320 USD. The ratio of expected cost of vaccinating all 11-year old girls to the expected cost of managing all incident CC cases in a given year was 3.3/1. The nearest break-even point may occur after 3 years of this current analysis, if the inflation in the cost of CC management increases from the current 15.6% to a potential 21%.

Conclusion: This CBA using limited available data indicates that massive HPV vaccination would not be cost-beneficial in Lebanon under the circumstances existing in 2016 and for several years to come, even under several alternative scenarios. Nevertheless, some indications point to the need for a re-assessment of this conclusion around 2020. This finding will serve to inform Public Health decision-makers in Lebanon and similar neighboring countries.

Abstract # 75

Robotic Assisted Radical Cystectomy with Intracorporeal Neobladder Construction: A first in the Middle East.

Mohammed Hout,MD; Ali Merhe,MD; Mazen Mansour,MD; Ramzi Alami,MD; Mohammed Bulbul MD; Faek Jamali,MD; Albert El Hajj, MD

[1]Department of Surgery, [2]Program and Division of Urology, American University of Beirut, Beirut, Lebanon

Corresponding author: Albert El Hajj, MD – Email : ae67@aub.edu.lb

(Drs Merhe and Hout contributed equally to this work)

Funding source: None

Keywords: Neobladder, Intracorporeal, Robotic cystectomy

Descriptive statement:

Robotic Assisted Radical Cystectomy (RARC) with Intracorporeal Neobladder construction (INC) is one of the most complex procedures to be done robotically. While very few centers in the US and Europe perform this technique we report our initial experience and technical description.

Background:

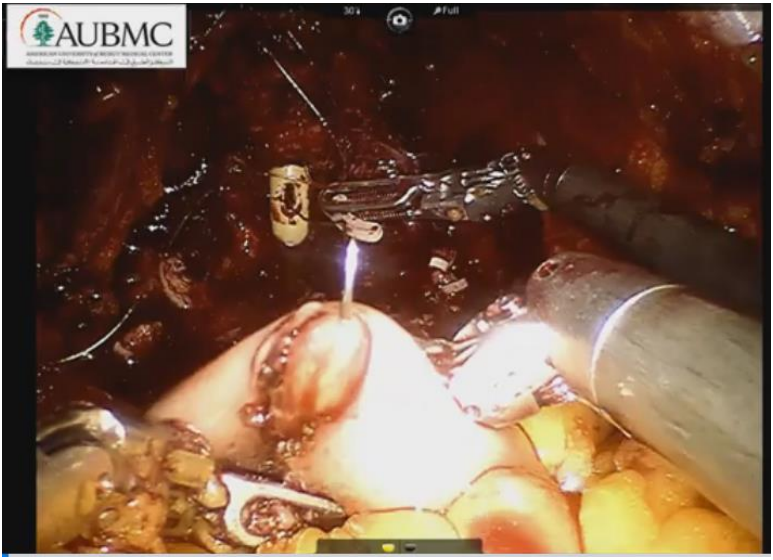
Muscle invasive bladder cancer (MIBC) is an advanced form of the disease that warrants a radical cystectomy as the standard of treatment. As technology is advancing, robotic surgery is taking over and in particular RARC due to shorter hospital stay, and quicker recovery. In most centers the bladder is removed robotically while the patient's neobladder is constructed extracorporeally similar to open surgery. We report the first series of RARC with INC in the Middle East with early outcomes.

Results

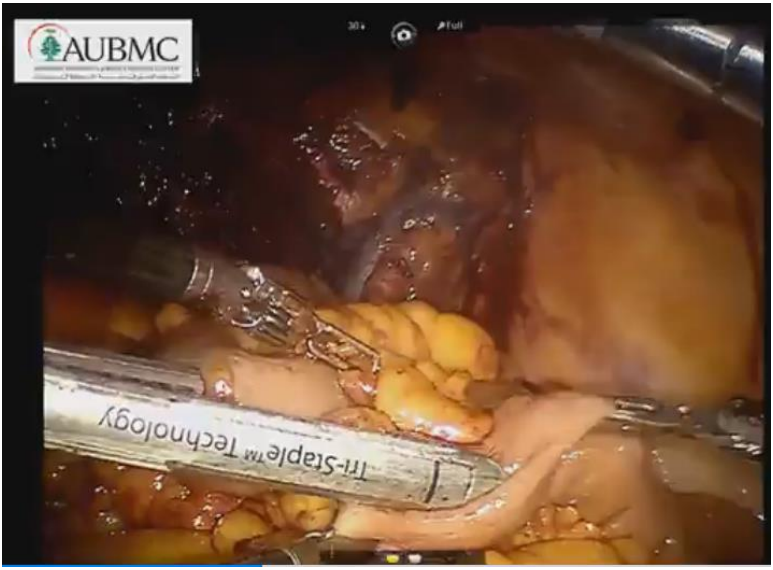
From January 2014 till October 2016, 5 RARC+INC cases (4 males, 1 female) were performed. Mean age was 62 years (51-70). Indications were MIBC in 2 patients and T1 High grade with aggressive features (micropapillary and nested cell variant) in 2 patients. One patient had high volume unresectable T1 high grade with hemorrhage requiring transfusions. There was no conversion to open surgery. Mean EBL was 600 mL with one patient requiring transfusion. Mean hospital stay was 9 days (6-12). All pathologies reported negative margins, negative lymph nodes with on average 21 lymph nodes dissected per case. There were no major complications, two patients had UTI requiring antibiotic treatment (Clavien I). Ureteral stents were removed 2 weeks postoperatively. Short-term follow up within a span of 6 weeks revealed 3/5 patients regaining early continence and 2/4 reporting erections. All patients are disease free with a mean follow up of 15.4 months.

Conclusion

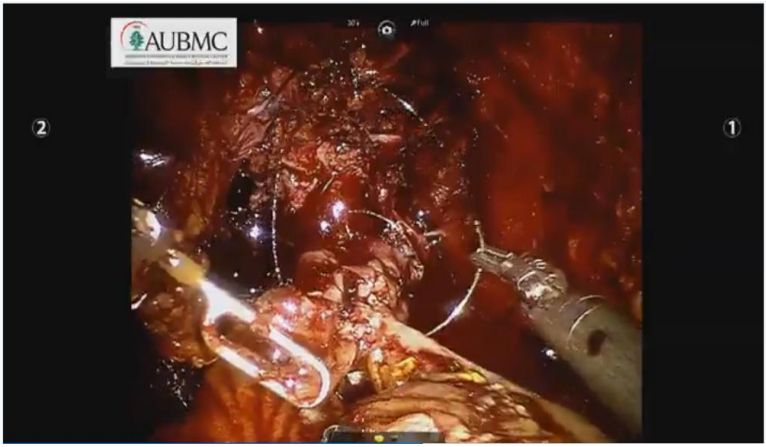
In the first reported case series in the Middle east of RARC with INC, this approach was found to be safe and feasible in selected cases of bladder cancer. This minimally invasive technique allows fast recovery with less complications than the traditional open approach and similar oncological outcomes.



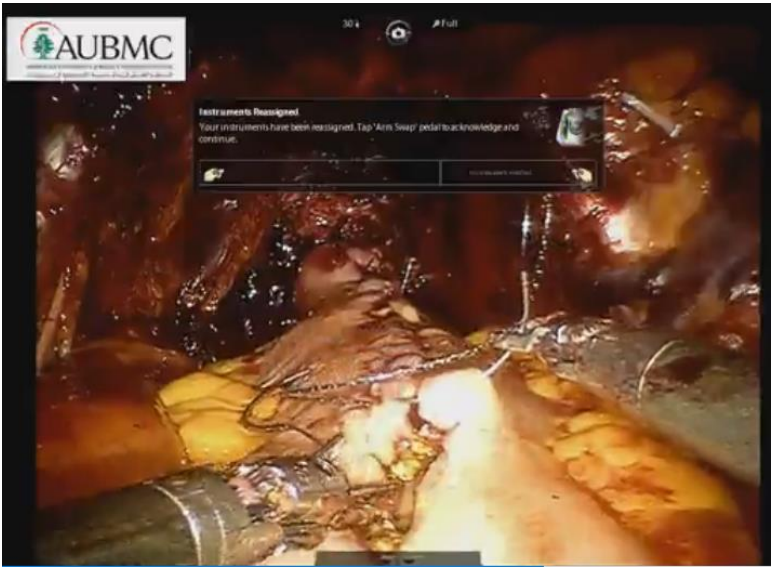
Anastomosis between urethra and ileal loop before reconstruction into a neobladder



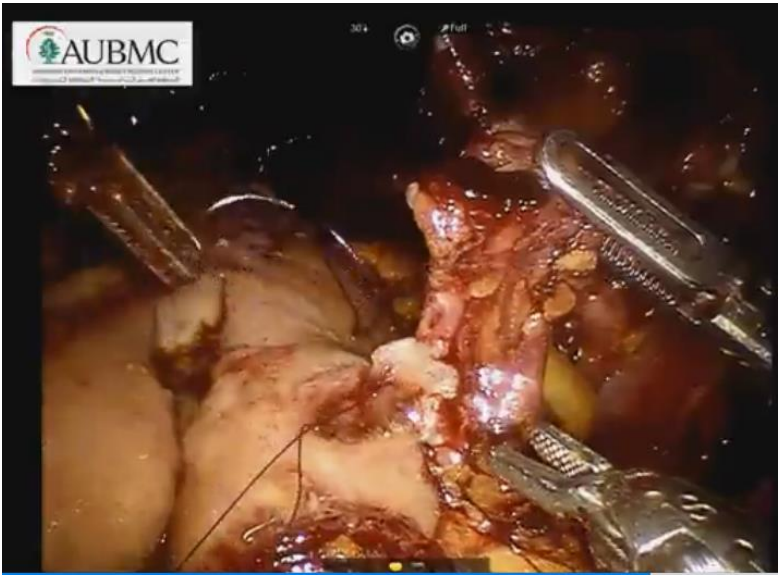
Reconstruction of ileum to become a neobladder



Suturing of the anterior wall of the reservoir



Suturing of the anterior wall of the reservoir



Anastomosing the ureter with the reservoir

Abstract # 76

New modifications of the nasal alveolar molding appliance (NAM) for cleft lip/palate patients

Ramzi V. Haddad, Pamela G. Genno
Division of Orthodontics and Dentofacial Orthopedics, Department of Otolaryngology-Head and Neck Surgery, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: rh52@aub.edu.lb; pg07@aub.edu.lb
Presenter: Pamela Genno pg07@aub.edu.lb (PGY3 resident)

Keywords: cleft lip/palate, NAM, alveolar, upper lip, nasal segment.

Descriptive Statement: NAM therapy is known to reduce the severity of the cleft lip/palate prior to surgery. We introduce modifications in this appliance critical to increase its efficiency while achieving more practical and controlled activation.

Background: To improve esthetic and long-term results, nasal alveolar molding (NAM) reduces the severity of the cleft lip/palate presurgically by reshaping the alveolar, lip and nasal segments.

Aims: 1-Modify the NAM appliance for easier manipulation and less irritation by the adhesive tape on the soft tissue. 2-Quantify changes after applying two different NAM modifications.

Methods: 9 patients (1.2mos±0.2) having a bilateral (n=6) or a unilateral cleft lip/palate (n=3) were included; 8 were treated with the 1st modification **(M1)** and 1 with the 2nd modification **(M2)**. The **M1** includes an acrylic-embedded wire that applies spring-like pressure against the philtrum and premaxilla. The 1st stage of the **M2** consists of a removable acrylic bar activated by two elastics from the main NAM appliance to bring down the premaxilla and elongate the philtrum; the 2nd stage includes two original nasal stents and two additional constrictive alar pads to compress the alae of the nose bilaterally and elongate the columella. Changes in soft tissue nasal segments were measured on pre-NAM, post-NAM and post-surgery photographs.

Results: Cleft size was reduced by 64% in 4 to 5 months. This accompanied significant improvement in nasal symmetry, including increase of nasal tip projection, columellar dome and nostril heights and decrease of nostril width and bialar width (by 15%). Both modified appliances achieved elongation of the philtrum of the upper lip by 25% and less skin irritation. After lip closure surgery, the width of the philtrum was approximated to the norm, more in males than females.

Conclusion: NAM therapy should be started as early as possible, ideally within the 1st month of life. The modified NAM provided easier activation of the appliance and placement by the parents and significantly reduced skin irritation. More promising results are anticipated with the 2nd modification.

Abstract # 77

Adherence in orthodontics: Design and application of an instrumented orthodontic appliance to measure compliance

Maria Doughan[1], Ahmad Sharaf Aldine[2], Iman Sonji[2], Mohamad Shaaban[2], Imad Elhajj[2], Joseph Ghafari[1]

[1]Division of Orthodontics and Dentofacial Orthopedics, Department of Otolaryngology-Head and Neck Surgery, [2]Department of Electrical and Computer Engineering, American University of Beirut, Beirut, Lebanon

Corresponding author: Maria Doughan – PGY3 resident/student – E-mail: md83@aub.edu.lb

Funding source: Not present

Keywords: Adherence, compliance, cooperation, instrumented headgear.

Descriptive Statement: An instrumented headgear with sensors linked to a mobile application is used by orthodontic patients to monitor their compliance with headgear wear and increase their compliance to treatment.

Introduction: Compliance is "the extent to which a person's behavior coincides with medical or health advice". One of the essential aspects of adherence during orthodontic treatment relates to wearing removable appliances as instructed. Unfortunately, lack of patients' cooperation presents a prevalent encounter that can lead to reduced effectiveness, increased length of treatment and at times more invasive alternatives like extractions, placing bony anchorage (mini-screws) and surgery.

Aim: To provide 1- the orthodontist with an objective tool for measuring patient compliance, 2- the patients with an interface allowing them to track their wear time and progress.

Methods: The design of the hardware consisted of three distinct sensing models. The first one was a temperature model able to sense body heat; the second was a force model activated upon pulling of the headgear spring; the third a capacitive sensing model sensitive to the dielectric difference specific to human tissue and activated upon touch. The output of the sensors links via Wi-Fi to a mobile application accessible by the patients who accordingly can track their progress.

Results: The designed hardware combines the strengths of all three sensing methods. When put together, the sensors can read values for the timer to activate it and start generating interval measurements. The use of these three methods greatly minimizes the possibility of cheating or tampering. The "quantified self" concept allowing the patients to monitor their progress of headgear wear is expected to increases their compliance to treatment in an upcoming clinical testing.

Conclusion: Besides being the first such instrument in orthodontics, the designed instrumented orthodontic device includes a novel sensing technology used to enhance the motivation and compliance of orthodontic patients without the possibility of tampering. We hypothesize that the use of this device is more effective and sustainable in enhancing motivation.

Abstract # 78

Limitation of Dentofacial Orthopedics in Class II Facial Convexity

Manoel Khoury[1], Joseph G. Ghafari[1,2,3]
American University of Beirut[1], Lebanese University[2], University of Pennsylvania[3]
Department of Otolaryngology-Head and Neck Surgery, Division of Orthodontics and Dentofacial Orthopedics
American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Manoel Khoury – E-mail: Mk197@aub.edu.lb

Keywords: Dentofacial Orthopedics, Class II malocclusion

Descriptive statement: Knowing the limitation of dentofacial growth modification through studying the relevant components can help in achieving more thorough diagnosis and prediction of treatment outcome, thus ending up with personalized and more realistic treatment plans.

Background: Dentofacial orthopedics or growth modification aim to correct or reduce the severity of dentoskeletal discrepancies in growing children. Limitations to this modality are inherent to the growth potential of each individual patient determined by his genome. Class II malocclusion is characterized by a retruded position of the mandible relative to the maxilla and its treatment outcome depends on the configuration and therapeutic response of constitutional components. Growth modification, usually by enhancement of mandibular growth relative to the maxilla (differential growth) may avoid future orthognathic surgery after growth ceases.

Aims: Determine major predictors of favorable treatment outcome of Class II division 1 malocclusions, thus determine the dentofacial components contributing to the limitation of growth modification.

Methods: A sample of growing Class II patients is contrasted with a group of adults treated at the AUBMC Division of Orthodontics and Dentofacial Orthopedics. Treatment outcome was defined as "good response" or "bad response" on the basis of pre and post-treatment: a- ANB angle (sagittal discrepancy between the jaws), b- the maxillary incisor to vertical, c- the mandibular chin projection (pogonion) to vertical and d. the anterior slope of the symphysis. Statistical analyses included analyses of variance for group differences and multiple regressions.

Results: The anterior symphyseal angle indicates (in nearly 70% of the younger patients) the presence and maintenance of skeletal Class II characteristics, particularly mandibular retrognathism. In all patients with an initial ANB angle greater than 6.5^{o} apparently, the Class II phenotype, characterized with facial convexity, did not transform toward the normal (Class I) phenotype.

Conclusion: The initial discrepancy between the jaws, measured through the ANB angle, and the form of the chin, delineated through the cant of the anterior symphysis, are predictors of the response to treatment of the Class II malocclusion.

Abstract # 79

Upper and lower lip characteristics in vertical malocclusion

Nancy Abdo[1], Anthony T. Macari[1], Joseph G. Ghafari[1,2,3]
American University of Beirut[1], Lebanese University[2], University of Pennsylvania[3]
Department of Otolaryngology-Head and Neck Surgery, Division of Orthodontics and Dentofacial Orthopedics
American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Nancy Abdo (PGY2 resident/MS student)-e-mail: na182@aub.edu.lb

Keywords: lip length; lip thickness; face; mandible; divergence

Descriptive statement: Facial appearance is a reflection of the bony understructures and the masking soft tissues (muscles and skin). We report differences in thickness and length of the upper and lower lips in patients with different vertical facial types, namely long, normal or short faces.

Introduction: Background: While soft tissue thickness and upper lip characteristics in different sagittal skeletal malocclusions have been extensively investigated, knowledge lacks regarding these features in different vertical growth patterns.

Aims: To evaluate 1- characteristics of upper and lower lip length and thickness in various vertical skeletal dysplasias, and 2- the relationships between lip features and skeletal divergence, hard tissue lower facial height (HT LFH) and soft tissue lower facial height (ST LFH).

Methods: Measurements on lateral cephalographs of eighty untreated non-growing males (n=40; average age=27.93±7.78 years) and females (n=40; 29.25±9.28 years) included skeletal (ANB, HT LFH, PP/MP; SN/MP) and soft tissue (upper and lower lip length and thickness, ST LFH) variables. Patients were classified according to the vertical pattern, into four categories: High, Medium-High, Medium-Low and Low groups. Statistics included analysis of variance and post-hoc test for group differences; and Pearson correlations for associations among variables.

Results: Both upper and lower lips were longest in the hyperdivergence group (UL: 22.50+3.96mm; LL: 19.54+4.10mm) and shortest in the low angle group (UL: 20.24+2.90mm; LL: 16.01+2.81mm), but differences were statistically significant between groups only for lower lip length (p=0.004). However, the upper lip was thickest in the Medium-Low group (14.25±2.89mm) and thinnest in the High group (13.88±2.77mm), but no statistical significant difference show among the groups at all levels of lips thickness. The highest correlation between lips features and skeletal divergence was found between lower lip length and MP/PP (r=0.46). Stronger correlations among variables were observed between lips length and lower facial height, the highest being upper lip length to ST LFH (r=0.82), followed by lower lip length HT LFH (r=0.67).

Conclusion: As dynamic structures developing along with, or independent of, their skeletal substructure, lips may compensate for skeletal dysplasia, or may shift treatment into the range of orthognathic and cosmetic surgery.

Abstract # 80

Novel findings on Class III malocclusion: genetic origin of mandibular prognathism and subphenotypes disclosed in treatment response

Robin El Khoury[1], Ramzi V. Haddad[1], Pamela Genno[1], Makram Ammoury[1], Ammar Kassab[1], Joseph G. Ghafari[1,2,3]

American University of Beirut[1], Lebanese University[2], University of Pennsylvania[3]

Division of Orthodontics and Dentofacial Orthopedics, Department of Otolaryngology-Head and Neck Surgery, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Robin El Khoury (PGY2 resident/MS student)-e-mail: re81@aub.edu.lb

Keywords: Class III malocclusion, mandibular macrognathism, genetic study, subphenotype.

Descriptive Statement: In this critical assessment of our research on Class III patients (characterized by mandibular prognathism and facial concavity), we determine novel findings on etiology and treatment outcome.

Introduction: Treatment of growing patients with Class III malocclusion (CLIII) is most challenging because of the difficulty to predict mandibular growth potential, thus possible relapse after treatment with uncontrolled additional growth. **Aim**: Establish guidelines for growing patients treated for CLIII based on the results of a series of studies conducted at AUBMC.

Material and methods: Four studies focused on etiology and early treatment. Etiological investigations included a cephalometric assessment of 147 patients that examined a new theory on developmental/environmental components, and a genetic evaluation of the inheritance pattern and genetic susceptibility to identify the gene responsible for mandibular prognathism. Treatment studies: one focused on the potential and limitations of orthopedic correction, the other on uncommon treatment responses after facemask therapy (FM).

Results: Results on etiology indicated that CLIII with mandibular prognathism was likely to be genetically determined, whereas maxillary retrognathism was more affected by environmental factors. In the genetic study a potential novel gene (C1orf167) could be implicated in mandibular prognathism. The treatment studies supported early intervention with FM in avoiding later surgeries particularly in girls, as boys were prone to greater amounts of growth because of longer periods of development. Atypical responses in specific patients in whom growth was normalized or altered toward an opposite pattern, indicated the existence of different phenotypes of the CLIII.

Conclusion: Our findings indicate that Class III malocclusion is multifaceted in etiology and treatment outcome, laying the basis for the study of its various components that contribute to these differences. Our hypothesis on the genetic prevalence of mandibular prognathism seems to be supported. Early treatment approaches, while generic in nature (usually facemask), find variation among gender and possibly phenotypes in practice, suggesting that future research should be focused on the individual characteristics that might predict the personalized response

Abstract # 81
Mandibular components in growth and treatment

Rhea Souaid[1], Roula Tarabay Anthony T. Macari[1], Joseph G. Ghafari[1,2,3]
American University of Beirut[1], Lebanese University[2], University of Pennsylvania[3]
Department of Otolaryngology-Head and Neck Surgery, Division of Orthodontics and Dentofacial Orthopedics, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Rhea Souaid – E-mail: rs173@aub.edu.lb

Keywords: Mandibular length, ramus height, corpus length, skeletal malocclusion.

Descriptive statement: Separate mandibular components have not been compared across the various malocclusions. We noted differences in ramus and corpus lengths between the extreme malocclusions.

Introduction: Background: Mandibular length has been evaluated in various malocclusions, but the separate mandibular components (ramus height and body) have not been studied.

Aim: Evaluate the associations among the different components of the mandible: ramus height (condylion-gonion, Co-Go), body (gonion-pogonion, Go-Pg) and total (condylion-gnathion Co-Gn) lengths in various malocclusions.

Methods: Cephalometric measurements of the mandible, including divergence, ramus height, corpus length and the mandibular length were taken of 154 non-growing patients (ages above 16 in females and 18 in males) presenting with class I (CLI), class II division 1 (CLII/1), class II division 2 (CLII/2) and class III (CLIII) malocclusions. Malocclusions were classified according to sagittal relationship between the jaws: ANB angle (0< CLI <3.5, CLII > 4.5, CLIII <0), the overjet (2-3mm for CLI and CLII/2, >5mm for CLII/1, <0 for CLIII) and the overbite (30% for CLI, >80% for CLII/2). Statistical analyses included analysis of variance for group differences and regression analyses for associations among variables.

Results: Statistically significant differences ($p<0.05$) were noted for Co-Go, Go-Pg and Co-Gn between CLII/1 and CLIII, Co-Gn between CLII/2 and CLIII. When malocclusions were combined, Co-Go and Co-Gn were greater in males than females. Multiple regression analysis indicated that mandibular length is predictive of sagittal jaw relations (ANB), and ramus height of vertical divergence (PP/MP). The corpus length and the ANB were inversely proportional. The corpus length and the vertical divergence were proportional, but the ramus height and the vertical divergence were inversely proportional.

Conclusion: Associations among mandibular components differ, exhibiting the most deviations between Class II/1 and Class III. Mandibular components can be used to predict skeletal discrepancies and divergence. The observed variations imply that a range of overlap among mandibular components forces the consideration of individual variation in treatment planning and outcome.

Abstract # 82

Three Dimensional Simulation of Facial Changes before Orthognathic Surgery: Correspondence of Prediction with Outcome

Christophe K. Zoughaib, Michelle R. El-Chekie, Sarah A. Khamis, Naji Abou Chebel, Anthony T. Macari
Division of Orthodontics and Dentofacial Orthopedics, Department of Otolaryngology- Head and Neck Surgery

Corresponding author: Christophe K. Zoughaib; cz14@aub.edu.lb

Position: PGY1 Resident, Division of Orthodontics and Dentofacial Orthopedics, Department of Otolaryngology-Head and Neck Surgery.

Keywords: Orthodontics; Orthognathic surgery; Computer simulation; Software, imaging; three-dimensional.

Descriptive statement: Three-dimensional (3D) pre-surgical simulation has been recently introduced in the Division of Orthodontics and Dentofacial Orthopedics, American University of Beirut-Medical Center. We observed greater precision in predicting treatment outcome in comparison with the two-dimensional (2D) simulation specifically in patients exhibiting facial asymmetries.

Introduction: Background: The number of adult individuals seeking orthodontic treatment has increased tremendously in the past few years inducing an increase in orthognathic surgery approach to restore functional and esthetical characteristics in adult patients exhibiting skeletal deficiencies. Nowadays, and with the technological advances in radiology, photography and software processing, 3D simulation is replacing the classic 2D pre-surgical virtual planning. **Aims:** Illustrate and evaluate correspondence between pre-surgical 3D facial simulation and actual surgical outcome in patients with jaws' discrepancy requiring combined orthodontic and orthognathic surgery treatments.

Methods: The following pre-surgical records including Cone beam computed tomography (CBCT) of the face and 3D facial photography were taken on two individuals seeking orthodontic treatment in the Division of Orthodontics and Dentofacial Orthopedics. All images were imported in the computer simulation software (Dolphin Imaging and Management Solutions, La Jolla, California). Teeth are first identified on the CBCT in the centric occlusion of the patient, then the facial photographs are superimposed over the CBCT. Virtual Osteotomies cut were then performed and bony movements (including maxillary and mandibular osteotomies) were simulated to induce the desirable facial changes. Correspondence between pre-surgical simulated faces and actual surgical outcome was performed through image superimposition. **Results**: Accurate prediction of the surgical outcome was viable and high correspondence between pre-surgical simulated faces and actual surgical outcome existed. Patients were highly satisfied with the predictive model.

Conclusion: Along with accurate diagnosis, 3D computerized simulation offers a valuable guide, contributes to treatment planning and helps in interacting with patients regarding potential outcome.

Abstract # 83
Stray bullet injuries in a tertiary care center

NICHOLAS BATLEY, RINAD BAKHTI, RANA BACHIR, AFIF MUFARRIJ
Email address of corresponding author: Dr. Afif Mufarrij - **am66@aub.edu.lb**

Presenter: Dr. Phillipe Doueihi (postdoctoral fellow)

Funding source: Research not funded

Descriptive statement: This study looked at all patients presenting to the Emergency Department of AUBMC with stray bullets injuries.

Background. A stray bullet injury is defined as an accidental firearm injury occurring outdoors by an anonymous attacker. Stray bullet injuries are rare, but not uncommon in certain parts of the world. In Pakistan, 165 patients with stray bullet injuries were recorded between 2006 and 2010.

Objectives. In Lebanon, gunshots may occur during politicians' speeches, funerals and after exam results are published. No studies to date have looked at the details and consequences of these gunshot injuries.

Methods. A retrospective chart review of patients presenting to an emergency department (ED) in Beirut, Lebanon, from 2010 to 2015, with clear stray bullet injuries was conducted. Variables included: demographics, injured body part, admission to hospital, number of days in hospital, length of stay in the ED, mortality, past medical history, emergency severity index, and consequences of injury including surgery.

Results. Out of 154 bullet injuries, 12 stray bullet injuries were recorded. Injuries of the lower extremity were most common, followed by the head, shoulder/thorax, abdomen/pelvis and upper extremity. Surgery was needed in 7 patients (58.3%). The median length of stay was 3.08 hours in the ED and 4.78 days in hospital. There were no recorded deaths. Consequences of each stray bullet injury are presented.

Conclusion. Stray bullet injuries are commonly reported on in news and media outlets. This is the first study in Lebanon and the region to document cases of stray bullet injuries presenting to the ED. Better laws and educational policies need to be implemented to help discourage this practice.

Key words: stray bullets, emergency department, injured body part, consequences of stray bullets, hospital admissions, severity of injury, surgical intervention, Lebanon

Abstract # 84

The effects of eccentricity and separation on interocular positional judgements in amblyopia

Zahra Hussain (1), Ben Webb (2) and Paul McGraw (2)
1: American University of Beirut, Department of Psychology
2: University of Nottingham, UK, School of Psychology
Corresponding author: Zahra Hussain, Assistant Professor; Email: zahra.hussain@aub.edu.lb
Funding Source: Leverhulme Trust

Keywords: interocular suppression, fusion, strabismus, visual cortex

Descriptive statement: This work examines the role of visual field position and distance between targets on accuracy of positional matches made between the eyes in individuals with amblyopia (lazy eye). The results suggest that suppression of the weaker eye by the functional eye depends on stimulus configuration in addition to visual field position.

Introduction: In amblyopia, relative positional judgements of spatially separated targets are most impaired near the fovea, and closer to normal in the periphery. We examined whether the pronounced central impairment is due to foveal presentation per se, or due to the smaller separation of targets at smaller eccentricities.

Methods: Observers performed a two-dimensional free-localization task along three axes (diagonal, horizontal and vertical). Each positional judgement comprised simultaneous bisection and alignment of a response stimulus relative to a target stimulus, using the central fixation cross as a reference. Target eccentricity (1 - 7 deg) and target-response separation (0.76 - 13 deg) were varied independently. The stimuli were dots of uniform luminance viewed dichoptically, and the fixation cross was viewed by both eyes. Normally sighted and amblyopic observers were tested. We calculated the precision (standard deviation) and bias (mean displacement) of responses in all conditions.

Results: For normally sighted observers, performance depended primarily on eccentricity, and showed a moderate dependence on stimulus separation. Conversely, amblyopic observers showed a larger dependence on stimulus separation than on eccentricity. Although performance of amblyopes was worse in the central visual field compared to the periphery (consistent with previous findings), performance was disproportionately worse at small stimulus separations than at large separations, at all eccentricities.

Conclusion: These results suggest the presence of interocular interference for spatially proximal stimuli throughout the visual field in amblyopia, rather than just at the center of gaze. The strength of interocular suppression in amblyopia may depend less on visual field position than on the distance between competing stimuli viewed by both eyes.

Abstract # 85

Are Cancer Patients with Sepsis and Bacteraemia at a Higher Risk of Mortality? A Retrospective Chart Review Study.

Gilbert Abou Dagher[1], Christopher El Khuri[1], Ahel Al-Hajj Chehadeh[1], Ali Chami[1], Rana Bachir[1], Dina Zebian[1]

[1]Department of Emergency Medicine, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Gilbert Abou Dagher – MD/Assistant Professor - E-mail: ga66@aub.edu.lb

Presenter: Dr. Christopher El Khoury (postdoctoral fellow)

Funding source: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Keywords: Cancer, Sepsis, Emergency Department

Descriptive Statement: This study looked at patients with sepsis (infection with associated systemic inflammation) that presented to the emergency department and split them into cancer and non-cancer cohorts in order determine if having a malignancy independently predicted hospital mortality in this setting.

Introduction: Most sepsis studies have looked at the general population. The aim of this study is to report on the characteristics, treatment and hospital mortality of cancer patients diagnosed with sepsis or septic shock.

Methods: Single center retrospective chart review study looking at cancer patients who presented to our hospital in sepsis, septic shock or bacteremia between 2010 and 2015. A total of 1017 patients were recruited of which 176 (17.3%) patients had cancer at the time. From the remaining 841 patients, 176 were chosen by computer random number generation as the non-cancer controls. Data points were collected from the EHR and analyzed using dedicated statistical software.

Results: A total of 352 patients were analyzed. The mean age at presentation for the cancer group was 65.4 39 ± 15.04 years, whereas the mean age for the control group was 74.68 ± 14.04 years ($p<0.001$). In the cancer cohort having the respiratory system was the most common site of infection (37.5%) followed by the urinary system (26.7%), while in the cancer-free arm, the urinary system was the most common site of infection (40.9%). IV fluid replacement for the first 24 hours, was higher in the cancer cohort. ED, ICU and GPU LOS were comparable in the 2 groups. 95 (54%) cancer patients died compared to 75 (42.6%) in the cancer-free group. The 28-day hospital mortality in the cancer cohort was 87 (49.4%) versus 46 (26.1%) in the cancer-free cohort ($p=0.009$). Cancer patients had a 2.320 (CI 95% 1.225-4.395 $p=0.010$) odds of dying compared to non-cancer patients in the setting of sepsis.

Conclusion: This is the first study looking at an in-depth analysis of sepsis in the ED oncology population. Despite aggressive care, cancer patients have higher hospital mortality than their cancer-free counterparts while adjusting for all other variables.

Abstract # 86

Impact of Ramadan on Emergency Department Visits and on Selected Medical Emergencies

Reem Al Assad, MD, Rana Bachir MPH, Mazen El Sayed, MD, MPH*
*** Corresponding Author**

Email address of corresponding author: Dr. Mazen El Sayed
melsayed@aub.edu.lb

Presenter: Dr. Reem El Assaad (postdoctoral fellow)

Funding source: Research not funded

Descriptive Statement: This study looks at the impact of Ramadan on ED visits.

Abstract:

Background: Fasting during the month of Ramadan is of vital significance to Muslims. Little is known about the impact of fasting on emergency department (ED) visits and frequencies of specific emergency medical conditions.

Objective: This study describes changes in ED visits and in frequencies of emergency medical conditions during Ramadan in a tertiary care center in Beirut, Lebanon.

Methods: Patients presenting to the ED during Ramadan, one month before and one month after Ramadan over a 3 year period with the specific conditions (acute coronary syndrome, stroke, seizure, diabetes (hypoglycemia, hyperglycemia), renal colic, headache or hypertension) were included. Patients characteristics, ED length of stay, mortality, bounce back, ED volume and diagnoses were examined during the two periods (Ramadan Vs. Non Ramadan). A logistic regression was performed to identify predictors of high risk re-admissions within 72 hours.

Results: A total of 3536 patients were included, of these 1190 (33.65%) presented during Ramadan, and the remaining 2346 (66.34%) during the pre- and post- Ramadan months. Daily average ED visits volume was higher during non-Ramadan months (145.65 ± 22.14) compared to Ramadan (128.85 ± 14.52). There was no statistical significant difference in frequencies of selected diseases in Ramadan compared to non-Ramadan months. Analysis of the subgroup of patients who were Muslims (1219 (34.47%)) showed similar findings; Admission rates were similar for the different periods and were comparable for all selected diseases. Patients who presented during Ramadan were 1.338 times (CI: 1.031, 1.737) more likely to return back to the ED within 72 hours as compared to those who presented during the pre- and post- Ramadan months.

Conclusion: Emergency departments might experience a drop in ED volumes during Ramadan however changes in the frequencies of ED visits related to common medical conditions are not expected. Large prospective studies documenting fasting status might provide more insight on changes in patterns of specific diseases.

Keywords: Emergency, Medical conditions, Ramadan, tertiary care center, Beirut-Lebanon

Abstract # 87

The Adult Disease Spectrum in Emergency Department across a Tertiary Care Center in Beirut, Lebanon

Hitti, E[1], Geha, M[1]
[1]Department of Emergency Medicine
American University of Beirut, Beirut, Lebanon
Corresponding author: Eveline Hitti, M.D
E-mail: mirabelle.geha@gmail.com

Presenter: Dr. Mirabelle Geha (postdoctoral fellow)

Funding source: None

Keywords: Emergency Department Visits, Emergency Department Utilization, ED presentations

Descriptive Statement: This study looks at the most common Emergency Department presentations in adults at AUBMC, a tertiary center in a middle income country.

Introduction: There is an increase in Emergency Department utilization globally [1]. Understanding what patient present to EDs with is important for resource allocation, training and staffing purposes. There is no available data on ED presentations in Lebanon. This study describes the spectrum of diseases among the adult population that presents to a tertiary care center in Lebanon, an upper middle income country, to better guide future resource allocation and training.

Methods: The Medical Records Department at AUBMC provided the data for this study and it contains demographics, payment method and diagnosis. The latter is coded according to the ICD-9-CM code, which was then mapped to CCS, classifying them into 17 categories, making statistical analysis easier.

Results: During the study period, there were 32787 adult visits to the ED, with only 18.7 % resulting in hospital admission. Though the most common age group visiting the ED was 19-44 years of age, this group only accounted for 23.9% of those requiring hospital admission. The most common diagnosis in ED patients were injuries and conditions due to external causes, abdominal pain and chest pain. In the patients older than 85 years, who comprised 2.3% of visits and had an admission rate of 56%, the top most common diagnosis that resulted in admission were pneumonia, heart diseases and urinary tract infections.

Conclusion: The top most common reasons for ED visits in our ED were injuries due to external causes followed by abdominal pain and chest pain, compared to North America where abdominal pain, chest pain and fever were the top three most common diagnosis[2]. Similar to North America, patients 85 years and older had the highest admission rate among all adult age groups [3] with most common reasons for admission mirroring closely those of North American and including pneumonia, heart disease and UTI. Admission rates to the hospital increased with increasing age among patients, a finding comparable to other studies [3].

Abstract # 88

Nurse-Led Competency Model for Emergency Physicians: A Qualitative Study

Lina Daouk-Oyry, PhD[1]; Afif Mufarrij,MD[2]; Maya Khalil, MHRM[3]; Tina Sahakian, MA[4]; Miriam Saliba, MPH[2]; Rima Jabbour, RN; Eveline Hitti, MD, MBA[2]

[1]Olayan School of Business; [2]Department of Emergency Medicine, AUBMC; [3]Campus Procurement & Contract Administration Department; [4]Office of the EVP for medical affairs/Dean's Office

Email address of corresponding author: Dr. Eveline Hitti - **eh16@aub.edu.lb**
Presenter: Tina Sahakian, MA
Funding source: Research not funded

Descriptive statement: This study developed a competency model for emergency physicians from the perspective of nurses.

Background: Interprofessional collaboration in the emergency medicine field has been the focus of considerable research, with strong evidence for the positive effect of effective emergency physician–nurse teamwork and communication on patient outcomes.

Study objective: We develop a competency model for emergency physicians from the perspective of nurses, juxtapose this model with the widely adopted Accreditation Council for Graduate Medical Education (ACGME) model, and identify competencies that might be unique to the nurses' perspective.

Methods: The study relied on secondary data originally collected as part of nurses' assessment of emergency physicians' nonclinical skills in the emergency department (ED) of an academic medical center in the Middle East. Participants were 36 registered nurses who had worked in the ED for at least 2 years and had worked for at least 2 shifts per month with the physician being evaluated.

Results: Through content analysis, a nurse-led competency model was identified, including 8 core competencies encompassing 33 subcompetencies. The 8 core competencies were emotional intelligence; problem-solving and decision making skills; operations management; patient focus; patient care, procedural skills, and medical knowledge; professionalism; communication skills; and team leadership and management. When the developed model was compared with the ACGME model, the 2 models diverged more than they converged. Patient focus, emotional intelligence and team leadership and management were unique to the nurse led competency model.

Conclusion: The nurses' perspective offered distinctive insight into the competencies needed for physicians in an emergency medicine environment, indicating the value of nurses' perspective and shedding light on the need for more systematic and more methodologically sound studies to examine the issue further. The differences between the models highlighted the competencies that were unique to the nurse perspective, and the similarities were indicative of the influence of different perspectives and organizational context on how competencies manifest.

Keywords: competency model, emergency physicians, nurses' perspective

Abstract # 89

The rise of prostate cancer surgery volume at AUBMC: Impact of the Robot

Mansour M[1], Bulbul M[1], Khauli R[1],Nasr R[1], Wazzan W[1], Bachir B[1], Hout Y[1], El Hajj A[1]
[1]Department of surgery, Program and Division of Urology
American University of Beirut, Beirut, Lebanon

Corresponding author: Albert El Hajj, MD
E-mail: ae67@aub.edu.lb

Funding source: No fund

Keywords: Robotic surgery, Robotic assisted radical prostatectomy(RARP), prostate cancer

Descriptive Statement: This descriptive study will look into the impact of introducing a state-of-the-art technology in minimally invasive surgeries on the load of prostate cancer surgeries at our center since its introduction in July 2013.

Introduction: background and aims
The introduction of the robotic technology has made a difference in the area of minimally invasive surgeries specially overcoming the limitations of pre-existing minimally invasive techniques. Its use has led to the elimination of physiological tremor and the ability to a 3D visualization. It also promises to improve perioperative morbidity and ease of recovery. This new technology is gaining its access to the referral centers worldwide. It is also acquiring a great value in the field of Urology and specially in prostate cancer (PC) surgeries. This technology gained its access to AUBMC in July 2013 and we evaluated its effect on the load of PC surgeries since then.

Methods: The number of prostate cancer surgeries performed at our center was collected from January 2010 till December 2016. Patients were distributed according to surgical approach performed (open radical prostatectomy vs Robotic) and date of surgery.

Results: We found that since the introduction of robotic surgery in July 2013, the volume of PC surgeries has been increasing steadily (Fig 1). This increase started to appear after July 2014. In the year 2016 the total number of prostate cancer surgeries performed was 63 cases compared to a mean of 24 cases/year from 2010 to 2012. Furthermore, the steady rise in the total number of PC surgeries saw a decrease in the open cases in favor of robotic surgery.

Conclusion: Introduction of robotic surgery lead to an increase in the volume of prostate cancer surgeries performed at AUBMC. This has been associated with a shift in practice in favor of the robotic approach probably related to better perioperative morbidity, faster recovery and shorter hospital stay.

Fig 1-Trend of radical prostatectomy cases at AUBMC

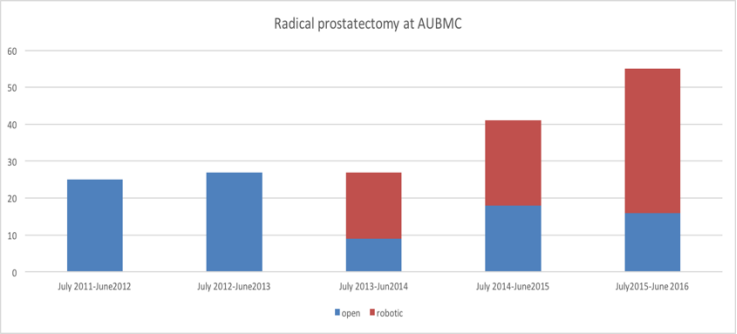
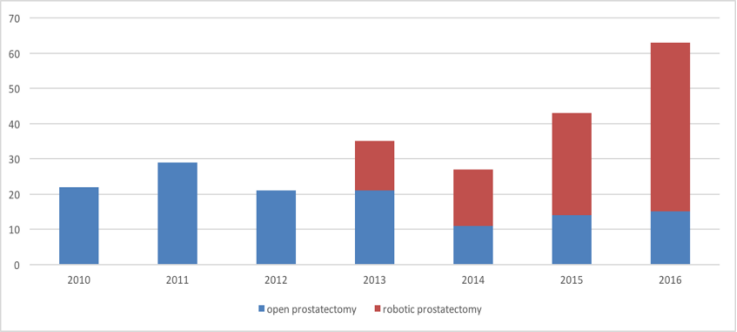


Fig 2- Total number of prostate cancer surgery by year.



Abstract # 90

Perioperative and pathological outcomes of the largest robotic assisted radical prostatectomy series in the Middle East

Robert Zakhia El Doueihi, MD; Mazen Mansour, MD; Wassim Wazzan, MD; Raja Khauli MD; Mohammed Bulbul MD; Albert El Hajj, MD

[1]Department of Surgery, [2]Program and Division of Urology, American University of Beirut, Beirut, Lebanon

Corresponding author: Albert El Hajj, MD – Email: ae67@aub.edu.lb

Funding source: None

Keywords: Robotic assisted radical prostatectomy, pathology, perioperative parameters

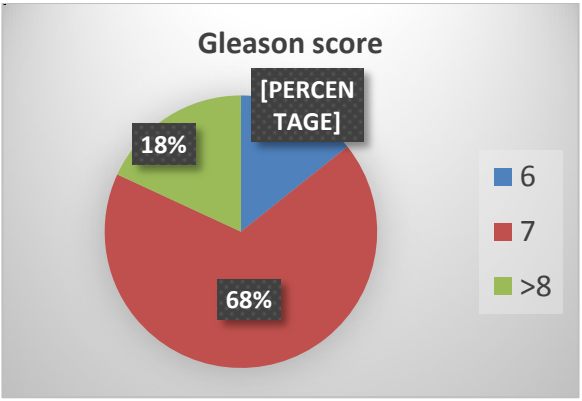
Descriptive Statement: This is a retrospective study looking into the perioperative parameters following robotic assisted radical prostatectomy and the final prostate specimen pathologies of the first 106 cases performed at the American University of Beirut Medical Center (AUBMC).

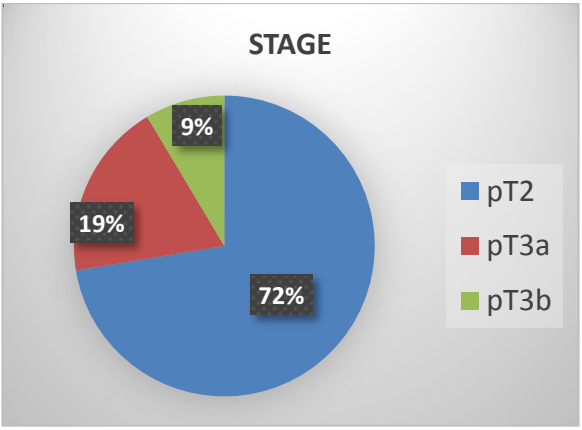
Introduction: Robotic-assisted radical prostatectomy (RARP) program was started at AUBMC in July 2013 and since then, it has been adopted as the primary approach. The literature in the Middle East lacks publications on the oncologic and functional outcomes of RARP. The objective of this study is to report the early outcomes of the largest RARP experience in the Middle East.

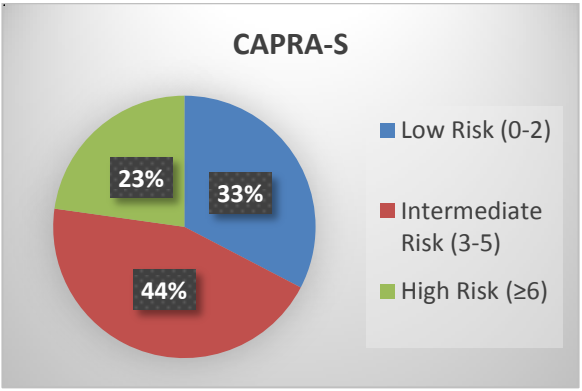
Methods: We collected retrospective data from 106 patients who underwent RARP at the division of urology in AUBMC, from July 2013 to December 2016.
Multiple perioperative parameters were collected and final specimen pathologies analyzed using capra-s score.

Results: The data of 106 patients were evaluated. All procedures were completed robotically with none converted to open. Mean age was 63.4 [48-77] and mean BMI was 29.09 [22.86-57.47]. The mean estimated blood loss was 258ml±150ml with one patient requiring blood transfusion. There were 2.8% minor (Clavien II) postoperative complications (3/106), and no mortalities. Mean hospital stay was 2 days. On final pathology 71.4% were organ confined pT2, and 75% were specimen confined (negative surgical margins). Pathological Gleason score ≥7 accounted for 85.6% of cases. Pelvic lymph node dissection was performed in 68.8% of the cases with lymph node yield of 13 on average (3-37). Lymph node involvement was found in 6.6% of the cases and Capra-S score was High risk (≥6) in 22.3% of the cases.

Conclusion: Our initial experience at AUBMC shows that robotic radical prostatectomy is associated with short hospital stay, low complications and excellent oncological outcomes. These results are comparable with the published literature on robotic surgery which supports the value of the robotic program at our institution.


Gleason score
[PERCENTAGE]
18%
68%
6
7
>8


STAGE
9%
19%
72%
pT2
pT3a
pT3b


CAPRA-S
23%
33%
44%
Low Risk (0-2)
Intermediate Risk (3-5)
High Risk (≥6)

Abstract # 91

Does Ki-67 expression at the margin influence biochemical recurrence after radical prostatectomy?

Shahait M[1], Mansour M[1], Mailhac A[5], Haddadeh O[4], Bulbul M[1], Khauli R[1], Mukherji D[2], Abou Kheir W[4], Tamim H[5], Nassif S[3], El Hajj A[1]

[1]Department of Surgery, Program and Division of Urology American University of Beirut, Beirut, Lebanon, [2]Department of Internal medicine, Division of Hematology-Oncology, American University of Beirut, Beirut, Lebanon, [3] Department of Pathology and Laboratory Medicine, American University of Beirut, Beirut, Lebanon, [4]Deparment of Anatomy, Cellular Biology and Physiologic Science, Faculty of Medicine, American University of Beirut, Beirut, Lebanon, [5] Clinical Research and Biostatistics Unit, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Albert El Hajj, MD
E-mail: ae67@aub.edu.lb

Funding source: MPP fund

Keywords: Prostate cancer, Biochemical recurrence, surgical margins, Ki67

Descriptive Statement: This study looks into the role of a simple and cheap marker Ki67 in predicting recurrence in prostate cancer patients with positive surgical margins after radical prostatectomy.

Introduction: background and aims Positive surgical margin (PSM) is a predictor of biochemical recurrence (BCR). Attempts to stratify PSM based on linear length, Gleason score, location and number have failed to add to predictive models using margin status alone. We evaluated the prognostic significance of Ki-67 expression at the margin.

Methods: Immunohistochemical staining for Ki-67 was done on prostatectomy specimens from 117 patients who had a PSM. Patients were dichotomized based on Ki-67 expression into three groups. Group 1 with no Ki-67 expression, Group 2 with Ki-67 ≤2 %, and Group 3 with Ki-67 ≥3%. To eliminate the impact of the adjuvant treatment (AT) on the outcome, data were analyzed by the Cox proportional hazards in which AT was Considered as a time-dependent covariate.

Results: The discordance rate of Ki-67 expression between matched index lesion and margin specimens was 44/117(37.6). High Ki-67 expression at the margin showed a trend toward significant association with higher risk of BCR (HR:2.06,(0.97-4.43),P=0.06). However High Ki67 expression in the deep tumor was strongly correlated with BCR (HR:4 (1.96-9.80),P=0.002)

Conclusion: We found that high Ki-67 expression in deep tumor is highly associated with BCR. On the other hand, High Ki67 expression at the surgical margin may correlate with BCR in patients with PSM following radical prostatectomy. Our findings need to be validated in larger cohort.

Figure 1: Prostatic adenocarcinoma {upper left}, While the margin exhibits high Ki-67 expression {upper right}, the deep tumor barely stained for ki 67{lower}

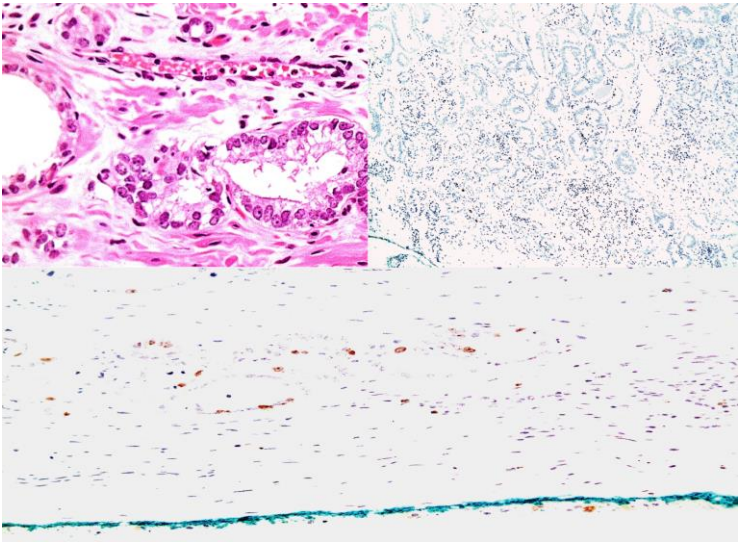


Table 1. Characteristics of the prostate cancer patients underwent RP who had PSM.

			PSA Failure		
Age	Mean (±SD)	62.01 ± 6.06	62.35 ± 5.98	61.65 ± 5.21	0.53
PSA-PRE surgery	0-10	69 (61.1)	42 (72.4)	27 (49.1)	0.04
	10-20	31 (27.4)	11 (19.0)	20 (36.4)	
	>20	13 (11.5)	5 (8.6)	8 (14.6)	
GS	6	16 (13.68)	9 (15.00)	7 (12.28)	0.39
	7	79 (67.52)	43 (71.67)	36 (63.16)	
	8	17 (14.53)	7 (11.67)	10 (17.54)	
	9	5 (4.27)	1 (1.67)	4 (7.02)	
EPE		52 (44.44)	23 (38.33)	29 (50.88)	0.17
SVI		23 (19.66)	11 (18.33)	12 (21.05)	0.71
Margin-length - categorical	<3mm	48 (41.38)	28 (46.67)	20 (35.71)	0.23
	>=3mm	68 (58.62)	32 (53.33)	36 (64.29)	
Margin-KI67 - categorical	1	64 (54.70)	31 (51.67)	33 (57.89)	0.42
	2	31 (26.50)	19 (31.67)	12 (21.05)	
	3	22 (18.80)	10 (16.67)	12 (21.05)	
Margin-Number	Single margin	55 (47.01)	30 (50.00)	25 (43.86)	0.51
	Multiple margins	62 (52.99)	30 (50.00)	32 (56.14)	
KI67-deep tumor - categorical	1	92 (78.63)	49 (81.67)	43 (75.44)	0.71
	2	11 (9.40)	5 (8.33)	6 (10.53)	
	3	14 (11.97)	6 (10.00)	8 (14.04)	
Adjuvant treatment		62 (52.99)	29 (48.33)	33 (57.89)	0.30

Table 2. Hazard ratio (HR) with 95% CI for PSA failure according to the ki67 expression at the margin and deep tumor, Length of the margin, and number of margin.

Variable	HR	95%CI	p
Ki 67 in deep tumor			
Group 1	Reference		
Group 2	1.41	(0.57 – 3.52)	0.46
Group 3	4	(1.64 – 9.80)	0.002
Ki 67 at margin			
Group 1	Reference		
Group 2	1.12	(0.55 – 2.31)	0.75
Group 3	2.08	(0.97 – 4.43)	0.06
Length of the margin			
<3mm	Reference		
>=3 mm	1.28	(0.70 – 2.37)	0.42
Number of margin			
Single Margin	Reference		
Multiple Margins	0.83	(0.45 – 1.51)	0.54

Abstract # 92

Demographics and Outcome of Meningioma Patients Treated at a Tertiary Care Center in the Middle East

*Lara Hilal MD[1], Ibrahim Abu Gheida MD[1], Fares Sukhon MD[2], Marwan Najjar MD[3], Ghassan Skaf MD[3], Fady Geara MD PhD[1], Maya Charafeddine MPH[2], Yasser Medlej MSc[2], Fadi Haddadin BSc[2], and Hazem Assi MD[2]**

[1]*Depatment of Radiation Oncology; American University of Beirut Medical Center; Beirut Lebanon*

[2]*Department of Internal Medicine; Hematology Oncology Division. American University of Beirut Medical Center; Beirut Lebanon*

[3]*Department of Surgery: Neurosurgery Division. American University of Beirut Medical Center; Beirut Lebanon*

Corresponding author: Hazem Assi – Assistant Professor of Clinical Medicine - E-mail: ha157@aub.edu.lb

Funding source: None

Keywords: Meningioma, demographics, Lebanon, Middle East

Descriptive Statement: Descriptive retrospective study concerning the characteristics and clinical outcomes of patients with meningioma, a brain tumor, treated at the American University of Beirut Medical Center (AUBMC)

Introduction: background and aims Meningioma is the most frequently diagnosed intracranial primary brain tumor. Many risk and prognostic factors have been previously reported from various centers in different parts of the world. To our knowledge, data from the Middle East region is lacking. We set to study the risk factors and outcomes of meningioma patients treated in a multidisciplinary tertiary-care center in the Middle East treating patients from the entire region.

Methods: Patients with pathologic diagnosis of meningioma from January 2005 to December 2015 at the American Univeristy of Beirut Medical Center (AUBMC) were included. Baseline demographics and risk factors where retrospectively collected and reviewed. Follow up and current disease status were then collected from the patients charts and updated by a specific questionnaire phone call interviews done by a third party.

Results: One-hundred and ninety-five patients were analyzed. The mean overall survival (OS) and Progression free survival (PFS) for the entire cohort was 49 and 30 months respectively. Patients' area of residence (city VS country side), occupation, alcohol use, oral contraceptive use, family history of meningioma, previous head trauma, exposure to radiation head/brain imaging, cell phone use, and finally their current meningioma's Ki-67 stain were examined in univariate analysis and found not to correlate with survival outcome. On the other hand, intermediate/high grade and subtotal resection were significant predictors of worse PFS. Multivariate analysis showed that subtotal resection and intermediate/high grade tumors were significant independent predictors of poor survival.

Conclusion: In conclusion, our findings coincide with other results reported in the literature from other regions. Complete surgical resection and low-grade disease remain the two most important prognostic factors for patients diagnosed with meningioma.

Abstract # 93

Effectiveness of Ursodeoxycholic Acid Use in the Prevention of Gallstone Formation after Sleeve Gastrectomy: A Prospective Randomized Multicenter Placebo-Controlled Trial

Amr Al Abbas[1], Salim Rahal[1], Haytham Fawwal[2], Bassem Safadi[1], Ramzi Alami[1]
[1]Deparment of Surgery, Division of General Surgery, American University of Beirut, Beirut, Lebanon
[2]Department of Surgery, Division of General Surgery, Makassed General Hospital, Beirut, Lebanon
Corresponding author: Dr. Ramzi Alami – Assistant Professor - E-mail: ra204@aub.edu.lb

Position: Postdoctoral Research Fellow in General Surgery

Funding source: MPP Grant

Keywords: Sleeve Gasrtrectomy, Bariatric Surgery, Morbid Obesity, Ursodeoxycholic Acid, Gallstones, Cholecystectomy

Descriptive Statement: A Randomized Double Blinded Multicenter Trial of Ursodeoxycholic Acid versus Placebo in Prevention of Gallstone Formation Following Laparoscopic Sleeve Gastrectomy in Morbidly Obese Patients.

Introduction: Bariatric surgical procedures have become a mainstream treatment for morbid obesity. Of the different operations available, Sleeve Gastrectomy is one of the newer options offered. It has been shown to be an effective and safe options and is increasing in popularity. Gallstone formation is a known side effect of bariatric surgery. Among the more established bariatric procedures, ursodeoxycholic acid therapy has been shown to reduce the incidence of gallstone formation postoperatively. There are no prospective trials comparing the incidence of gallstone formation after sleeve gastrectomy among patients receiving ursodeoxycholic acid therapy to those receiving placebo.

Methods: 100 patients, with no evidence of gallstones, undergoing sleeve gastrectomy will be randomized into two groups. Patients in group A will receive a dose of 500 mg of Ursodeoxycholic acid in two divided doses for 6 months while patients in group B will not receive any therapy. Patients will undergo ultrasonographic screening of the gallbladder pre-operatively, at 6, 12 and 18 months post operatively.

Results: The Study is still in the recruitment phase.

Conclusion: The Study is still in the recruitment phase.

Abstract # 94

Total Body MRI-Based Distribution of Active Bone Marrow in Young Children

Ibrahim Abu-Gheida MD[1], Arwa Al-Zaghal MD[2], Lena Naffaa MD[2], and Phillip J Taddei Ph.D[1]*
Departments of [1]Radiation Oncology, and [2]Diagnostic Radiology, AUBMC

Purpose/Objectives: Survivors of pediatric radiation therapy have been shown to be at risk for radiation-induced hematological malignancies, and these risks are related to the dose deposited in active red bone marrow (RBM). Physiologic conversion of RBM into yellow bone marrow (YBM) occurs at a different rate in various body parts. For this reason, the percentage of RBM irradiated depends the age of the patient. Although measurements have been made for neonates and adults, no measurement-based analysis has been performed to estimate the percentage of RBM in various body parts for children in the pediatric age group. This is of crucial importance since this measurement aids clinicians to predict the risk of secondary hematological malignancies in pediatric radiation therapy survivors. The purpose of this study was to use magnetic resonance imaging (MRI) to measure percentage RBM in regional sub-volumes within the bodies of young children of various ages and both sexes.

Materials/Methods: We retrospectively collected all T1-weighted pediatric total body MRI (TB-MRI) sets of high resolution and dated from January 2005 to July 2015. Strict inclusion and exclusion criteria were followed to maintain high quality images and sampling from the healthy RBM population. For example, patients with bone marrow disease and composition-alternated risk were excluded. RBM was delineated and contoured manually on reconstructed coronal slices using our treatment planning system (TPS) commissioned for clinical service. Anatomical landmarks where used to segment the following regional sub-volumes of RBM: cranium & mandible, scapulae, sternum & clavicles, ribs, upper extremities, lower extremities, and pelvis & vertebrae. A board-certified pediatric radiologist verified all contours. Finally, in each TB-MRI set, the volumes of regional RBM were calculated using the TPS, and the percentage of RBM of each body region was determined by dividing its volume by the total RBM in the body measured on MRI. These percentages were compared to linear interpolations between matched ages from the most widely accepted mathematical models.

Results: Out of the 55 high-resolution pediatric TB-MRI sets that were found in our clinical database, only ten passed our inclusion and exclusion criteria. Of those, eight were males and two were females of ages between 4 to 60 months. Percentages of RBM in sub-volumes for these children are listed in table1. We observed a gradual shift of RBM towards the central skeleton with aging in the pediatric population. Compared to our measured data, the mathematical model slightly underestimated the percentage RBM in the cranium & mandible and sternum & clavicles, overestimated the percent RBM in the upper extremities, ribs, and pelvis & vertebrae. Trends and rates of change in RBM percentage were consistent between our measured data and the mathematical model for these sites. Finally, despite that our RBM percentage measurement was similar to the mathematical model one for the lower extremities and scapulae, trend and rate of change were different.

Table1: Percentage (%) volumes of RBM in each anatomic location of every subject based on high-resolution TB-MRI.

Body Site:		Cranium & Mandible	Lower Extremity	Upper Extremity	Sternum & Clavicle	Scapula	Ribs	Pelvis & Vertebrae
Subject Number	Age (Months)	RBM %						
1	4	38.97	22.82	7.14	2.06	2.34	9.23	17.56
2	7	39.52	19.13	6.43	1.46	2.14	7.69	24.15
3	10	32.65	23.57	6.67	1.81	4.46	8.88	21.97
4	10	38.14	20.42	7.40	0.88	0.87	6.70	26.35
5	10	28.87	20.28	8.60	1.92	1.38	15.73	22.21
6	13	38.80	23.04	5.35	1.15	1.99	4.99	24.67
7	19	29.17	26.48	8.17	2.15	2.68	6.55	24.79
8	24	28.08	26.33	10.09	3.15	1.54	7.54	23.29
9	60	30.54	14.10	4.14	3.63	4.76	7.73	35.22
10	60	23.47	21.69	6.11	3.00	3.33	6.35	36.08
Average		32.9	21.8	7.0	2.1	2.6	8.2	25.6
Standard Deviation		5.6	3.6	1.7	0.9	1.3	2.9	5.8

Conclusions: In conclusion, we found that the percentages of RBM in sub-volumes of young children measured in TB-MRI did not adequately match those of the most widely accepted mathematical model for most of the body parts. This study marks the first measurement-based evaluation of RBM percentages in body parts in young children of various ages. Despite the limited number of available subjects for this study, we were able to verify or point out inconsistencies between measured and modeled trends and rates of RBM changes based on TB-MRI. Further studies of high-resolution pediatric TB-MRI should be performed as highly-efficient acquisition of TB-MRI is becoming clinically manageable.

Abstract # 95

Parcellation of human auditory cortex using functional and structural 7-Tesla MRI.

Julien Besle[1,2], Olivier Mougin[3], Susan Francis[3] and Katrin Krumbholz[2]
[1]Department of Psychology, American University of Beirut, Beirut, Lebanon
[2]Institute of Hearing Research, School of Medicine, University of Nottingham, Nottingham, United Kingdom
[2]Sir Peter Mansfield Imaging Centre, School of Physics and Astronomy, University of Nottingham, Nottingham, United Kingdom
Corresponding author: Julien Besle – Assistant Professor - E-mail: julien.besle@aub.edu.lb

Funding source: Medical Research Council (UK)

Keywords: Human; Hearing; Auditory cortex; Brain imaging; MRI

Descriptive Statement: We delineated different areas in human auditory cortex using functional and structural MRI measures and compared the obtained functional organization to that of non-human primates.

Introduction: background and aims: The functional organization of human auditory cortex is still poorly understood and there is no accepted method to delineate distinct functional auditory areas *in vivo* in human volunteers using brain imaging. In animals models (in particular the macaque), functional subdivision has been obtained using a combination of invasive functional (topographical organization of cells preferred frequency, or tonotopy, and frequency tuning), structural (cyto-, myelo and chemo-architecture) and connectivity criteria. Here we measured some of these functional and structural markers non-invasively *in vivo* in 12 human volunteers using ultra-high field magnetic resonance imaging (MRI) to try and delineate different human auditory cortical areas.

Methods: We estimated preferred frequency and frequency selectivity using functional MRI (sparse 2D GRE EPI sequence, 1.5 mm resolution, phase-corrected for B0-related distortions) and trains of narrowband noises at 7 centre frequencies spaced on a cochlear filter scale. Preferred frequency and frequency tuning were estimated at each voxel as the centroid and spread of the voxel's frequency response. In addition, we estimated intra-cortical myelination using a semi-quantitative measure of R1, the longitudinal relaxation rate (3D PSIR sequence, 0.6 mm resolution). All structural and functional measures were projected onto a flattened model of the supra-temporal cortex, segmented from the high-resolution processed PSIR volume.

Results: In both hemispheres of all volunteers, we identified 2 mirror-symmetric gradients of preferred frequency (tonotopic gradients) oriented orthogonally to Heschl's gyrus (HG), with a gradient reversal just posterior to the long axis of HG. This pattern is similar to the tonotopic pattern observed in non-human primates. In contrast to other primates however, the frequency selectivity and intra-cortical myelination measures showed an increase along the long axis of HG that mainly overlapped the most anterior of the tonotopic gradients.

Conclusion: By combining structural and functional MRI, it is possible to delineate primary auditory areas on the temporal lobe of human volunteers. To our surprise, the functional organization of human auditory cortex follows different principles than that of other non-human primates. Delineating functionally equivalent cortical areas in different volunteers is a first step towards more meaningful group studies of the role of these different cortical areas in hearing and in hearing impairment.

Abstract # 96

Outcomes of Patients with Malignancy Admitted to the Intensive Care Units (ICU): a Prospective Study

Fares Sukhon[1], MD, Vicky Nahra, MD[2], Pierre Bou Khalil, MD[3], Deborah Mukherjee[1], MD, Imad Bou Akl[3], MD, Yasser Medlej[1], BSc, Rita Assi[1], MD, Nour Moukaddem[1], MD, Maya Charafeddine[1], MSc, Nour Abdul Halim[4], BSc, Christopher Mouhayyer[4], BSc, Hazem Assi[1], MD

[1] *Department of Internal Medicine; Hematology Oncology Division. American University of Beirut Medical Center; Beirut Lebanon*

[2] *Department of Internal Medicine; American University of Beirut Medical Center; Beirut Lebanon*

[3] *Department of Internal Medicine; Pulmonary and Critical Care Division. American University of Beirut Medical Center; Beirut Lebanon*

[4] *American University of Beirut; Beirut; Lebanon*

Introduction An important aspect of improving outcomes for patients with malignancy is the provision of critical care during periods of acute deterioration. Decisions regarding whether advanced cancer patients should be admitted to the ICU is based on a complex suite of considerations, including short- and long-term prognosis, quality of life, and therapeutic options to treat cancer. We set to describe demographic, clinical, and survival data and to identify factors associated with short- and long-term mortality in critically ill advanced cancer patients with unplanned admissions to general ICUs.

Material and Methods Critically ill adult (≥18 year old) cancer patients non-electively admitted to the intensive care units at the American University of Beirut Medical Center (AUBMC) between July 2015 and July 2016 were included. Demographic, clinical, and laboratory data was prospectively collected from first day of ICU admission up to 30 days after discharge. This study was strictly observational and clinical decisions were left to the discretion of the ICU team and attending physician.

Results Ninety patients were enrolled in the study, with 41 patients passing away while in the ICU. Cox regression analysis showed that malignancy status (stable versus active), and multi-organ failure (MOF) development in the ICU to be the major predictors of poor prognosis. Those with active progressive malignancies were 1.7 times more likely to die, and death was 2.2 times more likely if MOF was developed in the ICU.

Thirty days post-ICU discharge, 12 patients died, while 7 patients were lost to follow-up. Thirty days overall survival post-ICU discharge for patients under curative treatment plans were 4.9 times more likely to survive. Patients with hematological malignancies were more likely to develop invasive fungal infections ($p<0.018$). However, cancer type, stage, recent chemotherapy, radiotherapy, antibiotic use, and dialysis were not significant factor for prognosis.

Mean overall survival was estimated at 137 days, with a median OS of 31 days since date of admission to the ICU.

Conclusion Those with active progressive malignancies and those who develop MOF in the ICU seem to be more likely to die in the ICU. There is a need to develop criteria regarding decisions to admit a patient with advanced and uncontrolled malignancy to the ICU.

Abstract # 97

Alginate sulfate enhances growth factor binding and affects the growth of rat aortic smooth muscle cells (RASMC)

Moustafa Houmani[1] and Rami Mhanna[2]

[1] Department of Chemical Engineering, Faculty of Engineering and Architecture, American University of Beirut, Lebanon

[2] Biomedical Engineering Program, Faculty of Engineering and Architecture, American University of Beirut, Lebanon

Corresponding author: Rami Mhanna - Assistant Professor – E-mail: rm136@aub.edu.lb

Funding source: This work was supported by the Lebanese National Council for Scientific Research (CNRS).

Keywords: rat aortic smooth muscle cells (RASMC), podocytes, insulin-like growth factor-I (IGF-I), fibroblast growth factor-II (FGF-II), sulfated glycosaminoglycans (GAGs), biomimetics

Descriptive Statement: In this study, rat aortic smooth muscle cells (RASMC) and podocytes were incubated with sulfated alginate in the presence/absence of insulin-like growth factor-I (IGF-I) or fibroblast growth factor-II (FGF-II). This system was used to evaluate the effect of the degree of sulfation on growth factor binding and subsequent RASMC and podocyte proliferation.

Introduction: Growth factors, such as insulin-like growth factor-I (IGF-I) and fibroblast growth factor-II (FGF-II), bind to rat aortic smooth muscle cells (RASMC) and regulate their proliferation and migration. Binding of IGF-I and FGF-II to RASMC and their bioavailability are influenced by extracellular sulfated glycosaminoglycans (GAGs) such as heparin. In this study, the aim is to determine the possibility of using biomimetic sulfated polysaccharides such as alginate sulfate to regulate the proliferation/migration of RASMC. FGF-2 also appears to be mitogenic to podocytes as long-term treatment of rats with FGF-2 leads to mitotic figures in podocytes. Moreover, maturing podocytes up-regulate FGF-2 expression essential for cytoskeletal transformation and formation of podocyte actin-based foot processes. Bio-mimetic sulfated polysaccharides can be used examine the possibility of regulating podocyte differentiation and process creation. This becomes vital in diseases such as the "Minimal Change Disease" where there is loss of foot processes and loss of the negative charge barrier leading to proteinuria. The highly sulfated biomimetic GAGs can thus be used for regaining the negative charge barrier.

Methods: Alginate was synthesized with different degrees of sulfation (0.8 and 2.7). Binding of the sulfated biomimetic materials was assessed with ELISA. The sulfated biomimetic materials were incubated with RASMC cells or Podocytes in the presence/absence of IGF-I or FGF-II. Proliferation and migration of cells were quantified using the MTT assay and ImageJ image analysis tool respectively.

Results: Binding of FGF-II to the sulfated alginates increased with increasing their degree of sulfation. Moreover, cell proliferation was consistently higher when biomimetic materials were used compared to controls without any sulfated materials. However, no correlation between the degree of sulfation and cell proliferation could be made. This is possibly due to the experimental set-up. Currently, we are optimizing cell numbers and serum concentration (which are believed to have significant effects on the outcome of the study).

Conclusion: The degree of sulfation of natural GAGs has significant effects on the binding of growth factors to cells and subsequently on cell behavior. The engineering of sulfated biomimetic polysaccharides such as alginate sulfate will bring forth new biomaterials to precisely control cell behavior.

Abstract # 98

Engineering biomimetic sulfated substrates for enhanced growth factor binding

Diana El Hajj[1], Waddah Malaeb[2] and Rami Mhanna[1]

[1] Biomedical Engineering Program, Faculty of Engineering and Architecture, American University of Beirut, Lebanon

[2] Department of Mechanical Engineering, Faculty of Engineering and Architecture, American University of Beirut, Lebanon

Corresponding author: Rami Mhanna - Assistant Professor – E-mail: rm136@aub.edu.lb

Funding source:

This work was supported by the American University of Beirut University Research Board (URB) grant and the Centre National de la Recherche Scientifique (CNRS).

Keywords:

Glycosaminoglycans, biomimetic, sulfation, growth factors, nanofilms, biotin-streptavidin interactions

Descriptive Statement:

In the current work, the effect of the degree of sulfation of polysaccharides on FGF-2 binding was studied. This allows for the preparation of custom-made substrates with controllable growth-factor affinities, which can be used to induce predefined cell responses such as proliferation, migration and differentiation.

Introduction:

Glycosaminoglycans (GAGs) are extracellular polysaccharides that play key roles in various molecular and physiological processes. Although sulfation codes, or sulfation arrangements of GAGs have been shown to be responsible for their differential binding to growth factors, few mechanisms that regulate such interactions have been elucidated. Understanding the regulatory capacity of sulfated moieties will enable the development of substrates that could ultimately be used in the treatment of various diseases.

Methods:

The layered structure of the substrate is based on the non-covalent bond between streptavidin and biotin, where the binding of FGF-2 to biotinylated polysaccharides (heparin and sulfated alginate) is minimally affected. Sulfated alginate was prepared with different degrees of sulfation ranging from 0 to 2.7. The binding of FGF-2 to the custom-made substrates was measured using quartz crystal microbalance with dissipation monitoring (QCM-D), and will be validated using ELISA. The engineered substrates will then be used to study the response of cells.

Results:

Variations in the frequency and dissipation outputs of the QCM-D indicate related changes in the mass and stiffness of the substrates. As such, the binding of FGF-2 to the sulfated substrates was found to increase with increasing degrees of sulfation. Moreover, the binding of the growth factor to biomimetic polysaccharides (sulfated alginate) was found to be higher than its binding to glycosaminoglycans (heparin).

Conclusion:

The ability to prepare sulfated substrates with controlled sulfation levels has strong implications in the biomedical field. In particular, it can be used to induce different levels of growth factor binding and subsequently result in differential effects on cells seeded on these substrates.

Abstract # 99

Designing a multivariate tissue engineering bioreactor

Waddah Malaeb[1], Ramsey Hamadeh[1] and Rami Mhanna[2]

[1]Department of Mechanical Engineering, Faculty of Engineering and Architecture, American University of Beirut, Lebanon

[2]Biomedical Engineering Program, Faculty of Engineering and Architecture, American University of Beirut, Lebanon

Corresponding authors: Ramsey Hamadeh – Professor - E-mail: rh13@aub.edu.lb and Rami Mhanna – Assistant Professor - E-mail: rm136@aub.edu.lb

Funding source: This work was supported by the American University of Beirut University Research Board (URB) grant and the Mechanical Engineering department.

Keywords: Bioreactor, tissue engineering, cartilage, mechanical stimulation, oxygen tension, mechanotransduction.

Descriptive Statement: In this research, a 4-chambered bioreactor was engineered to test for the performance of cartilage substrates under mechanical signaling, oxygen tension, and pH changes.

Introduction *(background and aims)*: Articular cartilage is a stratified tissue with distinct layers of various cell morphologies and protein types/amounts. Compression, hydrostatic pressure, and hypoxic conditions give articular cartilage the properties of its middle and bottom layers, while surface motion and normoxic conditions induce a superficial zone phenotype. The aim of the bioreactor is to test for the response of cartilage constructs to changes in these parameters enabling a better tissue engineered cartilage.

Methods: A four-chamber bioreactor was built to simultaneously control compressive, shear, and torsion forces, hydrostatic pressure, and oxygen tension. Mechanical simulation is applied using a gear-rack mechanism, while oxygen tension is controlled by electric valves. The bioreactor is coded and controlled (with the help of oxygen and pressure sensors) using Arduino. The precision of the applied mechanisms was tested using Matlab-based computer vision tests. Injurious and proliferation tests were carried on cartilage substrates to find the ideal conditions under which the bioreactor is effective. The cartilage substrates were comprised of chondrocytes seeded on alginate-based scaffolds.

Results: Results of the precision tests showed a 4% error for each displacement of 1 mm. Results of the injurious tests showed significant numbers of dead cells that endured compressive forces greater than 10 MPa.

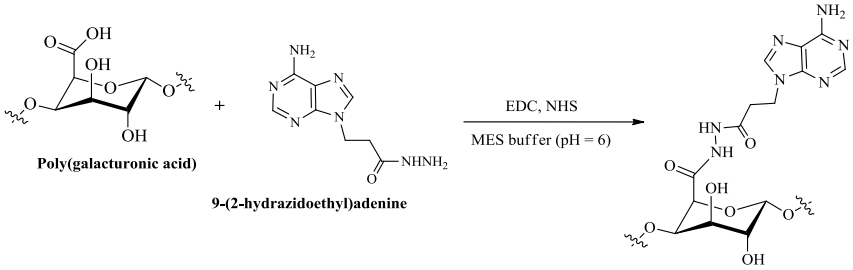
Conclusion: This novel system provides a platform to test for the ideal conditions required for the development of cartilage tissue. In future work, the bioreactor may also be used for other mechanoresponsive tissues (e.g. bones, muscles, blood vessels), and the precision of the bioreactor will be improved by adopting a cam-follower mechanism.

Abstract # 100

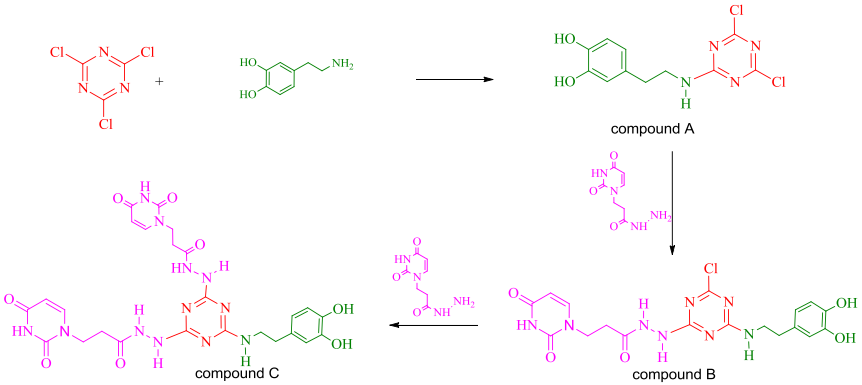
Synthesis and characterization of nucleic base functionalized triazine-based molecules as potential precursors for stimuli-responsive hydrogels

Sandrine Lteif, Ghassan Sonji, Rana Mezher, Antranik Jordenian, Kamal Bouhadir
Department of Chemistry, American University of Beirut, Beirut, Lebanon

Background and Aims: An increasing interest in stimuli-responsive materials has been developed over the last two decades. In particular, responsive hydrogels emerged as novel components for biomedical applications including drug delivery and tissue engineering. We are interested in the design and preparation of hydrogels responsive to an external stimulus such as an alternating magnetic field. Three main components are necessary for these systems: functionalized polymer, cross-linker and magnetic nanoparticles. We report herein the preparation of the functionalized polymer (polygalacturonic acid) and the cross-linker (triazine-based derivative). Poly(galacturonic acid) was decorated with the nucelic base (adenine) that was coupled to the carboxyl group on the polymer backbone. On the other hand, the triazine-based cross-linker is composed of dopamine, and two molecules of uracil hydrazide. The dopamine group is incorporated to enhance adsorption to particle surface (silica or magnetite). While, the uracil groups are incorporated into the cross-linker to form H-bonds with the complimentary base (adenine) that is coupled to the polymer backbone. Our ultimate goal is the synthesis of potential precursors for stimuli-responsive hydrogels that would incorporate hydrogen-bonding between the nucleic bases.



Methodology and Results: Adenine was coupled to poly(galacturonic acid) using water-soluble carbodiimide chemistry. The synthesis of the triazine-based cross-linker was initiated with cyanuric chloride that was reacted with dopamine in THF:acetone:water at 0ºC to yield compound **A** that was coupled to uracil hydrazide in methanol at room temperature to obtain intermediate **B**. Compound **B** was allowed to react with another uracil hydrazide under reflux conditions to yield the triazine-based cross-linker (compound **C**). The characterization of the intermediates and the final product was performed utilizing ^{1}H-NMR and ^{13}C-NMR, HPLC-MS and FTIR. All the spectral results supported the structure of the proposed molecules.



Conclusion: We have successfully functionalized the backbone of the poly(galacturonic acid) with adenine and prepared a triazine-based cross-linker as potential precursors for stimuli responsive hydrogels. Future plans include evaluating the H-bonding between the polymer and the cross-linker followed by the adsorption of the cross-linker onto magnetite nanoparticles.

Keywords: hydrogel, nucleic bases, hydrogen bonding, nanoparticles
Emails: kb05@aub.edu.lb-**Corresponding Author:** Kamal Bouhadir

Sandrine Lteif is a Master's student in chemistry.

The authors are grateful to the University Research Board (URB) at AUB for funding this project.

Abstract # 101

Stress distribution during movement of palatally impacted canines: A finite element analysis

Kinan G. Zeno1, Samir Mustapha1, Georges Ayoub2, Joseph G. Ghafari1
1American University of Beirut, 2University of Michigan-Dearborn
Corresponding author: Kinan Zeno – MS candidate – E-mail: kz12@aub.edu.lb

Funding source: Not present

Keywords: palatally impacted canine, virtual alignment, finite element analysis.

Descriptive Statement: An analytical engineering tool, Finite Element Analysis, is used after reconstructing oral anatomy in patients with palatally impacted canines for a non-invasive analysis of orthodontic treatment mechanics. The analysis is applied for the first time taking into account individual variation. Initial force application in various directions leads to differential responses and important clinical implications.

Background: Palatally impacted canines (PIC) require significant time to align in the dental arch and may cause irreparable side effects (root resorption).
Aims: 1-determine PIC severity by projecting its virtual final alignment in the arch (VAC) through the angle PIC/VAC; 2-simulate in a finite element analysis (FEA) model the initial movement of PIC in various directions.

Methods: Part 1: PIC from 38 CBCT images were stratified into severe (PIC/VAC>30^{o}) and less severe (PIC/VAC<30^{o}) groups. Part 2: 30 CBCT PIC images from 21 patients were processed through standardized steps into a FEA model. Forces were applied at the PIC crown level in vertical, buccal and distal directions. Induced stresses (Von Mises) were recorded at different levels of the PIC root. Statistics comprised analysis of variance for group differences and correlations for associations among variables.

Results: PIC angulation to midline was significantly ($p<0.001$) correlated to PIC/VAC ($r=0.85$), cusp-tip deviation ($r=0.67$), and cusp tip to midline ($r=-0.86$). Significant predictors of PIC/VAC were: PIC vertical position, angulation to midline and to palatal plane. Distal and buccal forces resulted in higher stress (S=6.64KPa, 6.41 KPa respectively) compared to the vertical force (S=5.97KPa), but were not statistically significantly different in stresses generated at the cervical level and over the whole root. Stresses at the mid-root level with the vertical force direction correlated with PIC/VAC ($r=-0.73$) and most positional measures. Simulated clinical appliances indicated highest stresses on the adjacent lateral incisor and first premolar with a buccal force.

Conclusion: 1. PIC/ reflects an effective measure of impaction severity. 2. A differential stress distribution was found with different force directions, the distal and vertical yielding the highest and least amount of stress, respectively. 3. Novel in FEA studies, the inclusion of individual variations determined trends of responses to initial force application and ensuing clinical implications.

Abstract # 102

Effect of cortical bone stiffness and thickness on two orthodontic distalization modalities: A finite element analysis study

Makram J. Ammoury1, Samir Mustapha1, Georges Ayoub2, Paul Dechow3, Joseph G. Ghafari1
1American University of Beirut, 2University of Michigan-Dearborn, 3Texas A&M University

Corresponding author: Makram Ammoury – MS candidate – E-mail: ma322@aub.edu.lb

Funding source: Not present

Keywords: distalization, miniimplants, finite element analysis, cortical bone.

Descriptive Statement: Specific but common orthodontic modalities were evaluated through an analytical engineering tool, Finite Element Analysis, after reconstructing oral anatomy of the dental arch for a non-invasive assessment of the treatment. The analysis was applied for the first time taking into account individual variation. Insight on the role of the compact bone around the teeth indicated important clinical implications.

Background: Orthodontic minimplants are used to correct distoclusions via direct anchorage (direct pull from miniimplant to the teeth) and indirect anchorage (teeth pulled against other teeth anchored by the minimplants).

Aims: Evaluate the effect of cortical bone stiffness and thickness on initial tooth movement in the two distalization modalities. Our hypothesis was that cortical bone quality and quantity influence the rate of tooth movement in both approaches.

Methods: A 3D model of the maxilla containing the different components (teeth, PDL, trabecular and cortical bones) was generated from a CT scan and material properties were assigned to each component. Cortical bone, the study variable, was divided into several masks. Stiffness and thickness data measured in 11 cadavers were incorporated into the initial model to simulate individual variation of cortical bone at the different locations. Subsequently, a finite element analysis was applied to simulate the different distalization modalities. Statistics included analyses of variance for group differences and correlations for associations among variables.

Results: In response to initial force application, higher stresses (0. KPa) and more displacement (=0.—mm) were on the canine, decreasing progressively to the last molar, in the direct mode. Indirect anchorage resulted in the highest stresses (=---KPa) and displacement (0.---mm) at the first molar. The greatest number of high and significant correlations between stress and bone properties was observed with stiffness at the molar ($0.67<r<0.75$) in the indirect mode, but not with thickness.

Conclusion: The results suggest that stiffness more than thickness of the cortical bone impacts tooth movement. Steering the teeth away from the stiff cortical bone decreases resistance to displacement. Accordingly, effective treatment modalities should be chosen on the basis of individual anatomy not only on force magnitude and vector, to generate the least amount of side effects.

Abstract # 103

Interarch elastics and corresponding stress on the temporomandibular joint: A finite element analysis

Joe El Helou[1], Samir Mustapha[1], Georges Ayoub[2], Paul Dechow[3], Joseph G. Ghafari[1]
[1]American University of Beirut, [2]University of Michigan-Dearborn, [3]Texas A&M University

Email of corresponding author: (Joe El Helou) *je40@aub.edu.lb - elheloujoe@gmail.com*

Keywords: Orthodontic Interarch Elastics – Finite Element Analysis – Temporomandibular Joint

Descriptive Statement: During the course of orthodontic treatment, elastics from one jaw to the other are sometimes needed to help correct malocclusions of the teeth. We use the finite element analysis to quantify the stresses that are dissipated on the teeth and the temporomandibular joint, in an attempt to simulate real-time occurrences on a numerical model.

Position: MS candidate in the Division of Orthodontics and Dentofacial Orthopedics

Funding Source: N/A

Introduction: Orthodontic interarch elastics (IE) are commonly used in the correction of malocclusions during orthodontic treatment. However, they exhibit side effects on neighboring teeth (e.g. undesirable movement of teeth) and temporomandibular joints [TMJ] (e.g. pain, clicking).

Aims: 1- Quantify the stress and strains transmitted by the different configurations of orthodontic inter-arch elastics onto the teeth and condyle; 2- Identify the different stress patterns when applying different bone stiffness and thickness according to specific patient variation.

Method: An initial numerical patient model was constructed from a CBCT. Subsequently, variations were introduced representing the anatomical characteristics of 10 different cadavers previously evaluated for bone characteristics and material properties. The individual variations in thickness were introduced using an image processing software (Simpleware®), and variations in stiffness were included by the solver software (Abaqus®) for the different segments of the bone. The models were then analyzed for stress/strains generated through the application of different forces on the individual specimens.

Results: Stress patterns were similar across the different bony stiffness distribution. However, of both elastic configurations, with Class II IE (from posterior mandibular teeth to maxillary anterior teeth) more displacement was produced on the teeth versus the Class III IE (reverse direction from Class II IE). More stresses were transmitted on the condyles by the Cl II elastics than Cl III elastics.

Conclusions: Cl II sagittal interarch elastics provide a greater potential of stress generation on condyles concomitant with the displacement of mandibular teeth in a mesial direction compared with Cl III elastics. The FEA model helped elucidate TMJ functional mechanical characteristics in ways not achieved by other means.

Abstract # 104

Community Involvement in Out of Hospital Cardiac Arrest: A Cross-Sectional Study Assessing Cardiopulmonary Resuscitation Awareness and Barriers Among the Lebanese Youth

Ali Shams, MD[1,2], Mohamad Raad, MD[2], Nour Chams, MD[2], Sana Chams, MD[2], Rana Bachir, MPH[3], Mazen J. El Sayed, MD, MPH[3*]

1- Department of Emergency Medicine, William Beaumont Hospital, Royal Oak, Michigan, USA
2- American University of Beirut, Lebanon
3- Department of Emergency Medicine, American University of Beirut Medical Center, Lebanon

*** Corresponding Author**

Email address of corresponding author: Dr. Mazen El Sayed melsayed@aub.edu.lb

Presenter: Dr. Rayan El Sibai (postdoctoral fellow)

Funding source: Research not funded

Descriptive Statement: This study looks at the CPR knowledge among university students and identifies its potential barriers.

Abstract

Background: Out of Hospital Cardiac Arrest (OHCA) is a leading cause of death worldwide. Developing countries including Lebanon report low survival rates and poor neurologic outcomes in affected victims. Community involvement through early recognition and bystander Cardiopulmonary resuscitation (CPR) can improve OHCA survival.

Objectives: This study assesses knowledge and attitude of university students in Lebanon and identifies potential barriers and facilitators to learning and performing CPR.

Methods: A cross sectional survey was administered to university students. The questionnaire included questions regarding the following data elements: Demographics, knowledge and awareness about sudden cardiac arrest, CPR, Automated External Defibrillator (AED) use, prior CPR and AED training, ability to perform CPR or use AED, barriers to performing/learning CPR/AED and preferred location for attending CPR/AED courses. Descriptive analysis followed by multivariate analysis was carried out to identify predictors and barriers to learning and performing CPR.

Results: A total of 948 students completed the survey. Participants' mean age was 20.1 (± 2.1) years with 53.1% females. Less than half of participants (42.9%) were able to identify all the presenting signs of cardiac arrest. Only 33.7% of participants felt able to perform CPR when witnessing a cardiac arrest. Fewer participants (20.3%) reported receiving previous CPR training. Several perceived barriers to learning and performing CPR were also reported. Significant predictors of willingness to perform CPR when faced with a cardiac arrest were: earning higher income, previous CPR training and feeling confident in one's ability to apply an AED or perform CPR. Lacking enough expertise in performing CPR was a significant barrier to willingness to perform CPR.

Conclusion: University students in Lebanon are familiar with the symptoms of cardiac arrest, however they are not well trained in CPR and lack confidence to perform it. The attitude towards the importance of bystander CPR and the need to learn CPR is very positive. Interventions should focus on public awareness campaigns regarding the importance of initiating bystander CPR while activating EMS and on making CPR training more available.

Keywords: University students, knowledge and attitude, CPR, barriers, Beirut-Lebanon

Abstract # 105
Seizure Onset and Propagation Analysis Toolbox

Karen Adam[1], Hassan Dbouk[1], Hassan Hmedi[1], Fadi Karameh[1]
[1]Department of Electrical and Computer Engineering, American University of Beirut, Beirut, Lebanon
Corresponding author: Karen Adam - Student - E-mail: kma48@mail.aub.edu

Funding source: No Funding

Keywords: brain surgery, seizure onset zone, toolbox.

Descriptive Statement: Seizure Onset and Propagation Analytics (SOPA) is an in-house toolbox that is being developed to aid physicians in detecting and visualizing seizure onset zones in epilepsy patients based on recorded brain electric activity. SOPA is a user friendly add-on that neurologists can utilize to improve on their decision-making prior to cortical resection.

Introduction: background and aims People who suffer from epileptic seizures are often prescribed a decent amount of medication that has a long term effect on their quality of life. A surgical option is only valid when the clinician can clearly identify the seizure focus and the area of the brain to be removed doesn't control a critical function like language, sensation, or movement. The motivation behind this project is to provide an in house toolbox for AUBMC to help improve pre-surgery assessment when it comes to localizing the seizure and studying its propagation.

Methods: The toolbox is based on the analysis of electrocorticogram (ECoG) recordings using multivariate analysis techniques coupled with data reduction paradigms. The toolbox provides a user friendly and intuitive Graphical User Interface to help the user understand the obtained results without the technical jargon involved.

Results: SOPA is comprised of an array of state-of-the-art algorithmic tools for detecting causal relationships between brain areas as these undergo ictal (seizure) activity. It also implements innovative plotting techniques that allow intuitive and interactive visualization of the results. The first uses arrows which allow plotting connectivity strength and directionality between different channels. The second uses a heat map that shows the probability of a brain portion being the seizure onset zone.

Conclusion: The work proposes a toolbox that is tailored to the detection of seizure onset zones, employs powerful algorithmic advancements for analyzing and simplifying data-handling, and presents the final results in a user-friendly manner that is so far unique to this toolbox. When integrated with other modalities, such as MRI and PET imaging, SOPA can arguably augment the evidence that neurologists seek to obtain regarding pathological seizure-prone tissue in epilepsy patients.

Abstract # 106

Electrospun Absorbable Surgical Mesh for Hernia Repair

Sara Assi[1,2], Rakan Nasser Eldine[1], Marwan El-Sabban[3], Ali Tehrani[2] and Ramzi Alami[1]
[1]Department of Surgery, Faculty of Medicine; [2]Department of Chemical Engineering, Faculty of Engineering and Architecture; [3]Department of Anatomy, Cell Biology and Physiology, Faculty of Medicine; American University of Beirut, Beirut, Lebanon

Corresponding authors: Marwan El-Sabban, Ali Tehrani and Ramzi Alami
E-mails: me00@aub.edu.lb; at711@aub.edu.lb; ra204@aub.edu.lb

Funding source: Farouk Jabre

Keywords: Surgical mesh, tissue engineering, Electrospinning, Nanofibers, Absorbable polymers

Descriptive Statement: Electrospun polymeric nanofibers have the potential to provide an economical mesh and become the standard of care in hernia repair.

Introduction: Hernia repair surgery is among the most common general surgical procedures performed. The current tenants of hernia repair are based on tension free repair, which requires the use of a reinforcing mesh. The majority of the surgical meshes currently used are stable and non-absorbable synthetic polymers. Thus, they stay in place permanently. Although this decreases the chance of recurrence, it may cause discomfort, movement restriction and chronic pain. The ideal mesh incorporates the attributes of tissue incorporation, giving it strength, thereby minimizing the risk of recurrence, with absorbability, which eliminates physical discomfort and complications of harboring a foreign body. Thus, the search for an ideal mesh is of significant importance to the patient. The aim of this study is to develop a biologically absorbable mesh by electrospinning technique, impregnated with cells, for hernia repair.

Methods: A series of medically approved polymers such as poly DL lactide (PDL) and copolymers of L lactide and DL lactide (PLDL) were used. The morphology of electrospun nanofibrous meshes was examined by Scanning Electron Microscopy (SEM). The *in-vitro* degradation rate of PLDL and PDL nanofibrous meshes was studied from weight loss (%) in buffer solution at 37°C over a period of time. The surface properties of the meshes were studied by optical tensiometry. The pore size distribution of the meshes was determined by Porometer. NIH3T3 fibroblast cells were seeded on the scaffolds for variable time intervals and observed by SEM.

Results: The average fiber diameter of the electrospun PDL and PLDL meshes was in the range of 400-500 nm. No significant weight loss (%) or morphological changes were observed by SEM over one month. NIH3T3 fibroblast cells adhered and proliferated on the fibers.

Conclusion: This is an ongoing project and work is underway to study the mechanical strength, pore size distribution, surface properties, cell infiltration *in vitro* and resistance to bacterial infection. Absorbable meshes that meet criteria for clinical applications will be tested *in vivo*.

Abstract # 107

Patterns and predictors of ambulatory health services utilization among elderly people – Lebanon, 2013

Monique Chaaya[1], Kieu Phung[2], Samir Atweh[3], Khalil Asmar[1], Georges Karam[4], Rose Mary Khoury[5], Lilian Ghandour[1], Husam Ghusn[6], Sarah Assaad[1], Martin Prince[7], Gunhild Waldemar[2]

[1]Department of Epidemiology and Population Health, Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon

[2]Department of Neurology, Danish Dementia Research Center, The Neuroscience Center, University of Copenhagen, Copenhagen, Denmark

[3]Department of Neurology; [5]Department of Surgery, Division of General Surgery; and [6]Depatment Of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon

[4]Department of Psychiatry and Clinical Psychology, St. George Hospital University Medical Center, Beirut, Lebanon

[7]Department of Health Service and Population Research, Institute of Psychiatry, King's College London, London, UK

Corresponding author: Monique Chaaya – Professor – E-mail: mchaaya@aub.edu.lb

Presenter: Sarah Assaad – Research Assistant – E-mail: sa225@aub.edu.lb

Funding Source: the Fogarty International Center, American National Institute of Health and National Institute of Aging, grant number 1R21AG039333-01 under the program "Brain Disorders in the Developing World: Research across Lifespan (BRAIN)"

Keywords: Aged; Health Status; Health Services Underutilization; Health insurance; Dementia.

Descriptive Statement: in Lebanon, the use of ambulatory health services by elderly is low and more pronounced for public services compared to private ones. This was related to demographic and socio-economic characteristics of the elderly in addition to self-perceived health and health insurance status. These factors, especially the latter one, should be considered when developing and implementing a needed comprehensive health-care plan for elderly.

Abstract

Introduction: Elderly in Lebanon constitute at least 10% of its population, have one of the highest prevalence of non-communicable diseases in the region, but have a weak pension system. Recently, the government increased hospitalization coverage for elderly to 100% with no efforts to address ambulatory care. This study aims at identifying the patterns and predictors of ambulatory health services utilization among a representative sample of elderly in Lebanon that could serve as a baseline cohort for future comparisons and provide evidence needed for development of relevant programs and policies.

Methods: This is based on analysis of secondary data from a cross-sectional study of 508 elderly conducted in 2013 to assess dementia prevalence in Beirut, and two semi-urban and rural districts. The Anderson model for health services utilization was considered to determine predictors of use classified into predisposing, enabling and need factors. Bivariate and multivariable analyses of two major outcomes were considered: use of private physician services and use of public services including health-care centers, physicians and other health professionals.

Results: Utilization was low, ranging from 2% for 'dental' to 5% for 'public' and 23% for 'private services. Use of Public services was significantly higher for those residing in semi-urban and rural areas, among low educated and never married elderly. Private physician services were significantly more commonly used by elderly with health insurance and those with lower self-perception of health.

Conclusion: There is an underutilization of ambulatory health services by Lebanese elderly with regional disparities. Improving accessibility to and availability of health services outside the capital might balance the use of services between private and public sector. Yet, providing health insurance as part of a comprehensive health-care plan for elderly would have the highest impact.

Abstract # 108

DETERMINANTS OF WATERPIPE TOBACCO SMOKING AMONG LEBANESE WOMEN

Karim N. Daou, MD, MPH[1]
Ibrahim R. Bou-Orm, MD, MPH[1]
Salim M. Adib, MD, DrPH[1]
[1] *Department of Epidemiology and Population Health, Faculty of Health Sciences, American University of Beirut, Lebanon*
Corresponding author: Karim N. Daou, MD, MPH (Student), E-mail: knd04@mail.aub.edu

Funding source: None

Such research paper would have practical implications in terms of public and women's health. There seems to be an urgent need to emphasize the specific health dangers of WTS without mixing the information with more general "smoking" information messages.

Abstract:
Introduction. Waterpipe tobacco smoking (WTS) has become a serious public health threat in the Middle-East and beyond. Uptake of the behavior is increasing among women, compared to cigarette smoking. Adverse health effects may be more serious in women than men.

Methods. A secondary analysis of data on women's health obtained in a national survey conducted in 2010, estimated the prevalence rates of cigarette and WTS and described the risk profiles associated with each of those two behaviors.

Results. Of 2255 selected women, 78% reported no or long-term past WTS. Among 12% who were regular smokers, 40% were light users (mean of 3 waterpipe heads weekly), while 60% were heavy users (mean of 11 heads). About 70% were never or long-term past cigarette smokers. Younger age, location within Greater-Beirut (GB) and having a professional activity were significantly associated WTS. As for cigarettes smoking, older age, GB location, lower education and ever-married status remained significant covariates.

Conclusions. Risk profiles confirm that WTS is becoming a socially normative behavior among increasingly empowered professional women, who can spare the time and expenses to engage in this behavior in easily accessible cafés. Results highlight differences with the risk profile of cigarette smoking women.

Keywords: Water pipe; hookah; narghile; Arab; Middle-East; determinants.

Abstract # 109

Requirements of Health Policy and Services journals for authors to disclose financial and non-financial conflicts of interest: a cross-sectional study

Assem M. Khamis[1], Maram B. Hakoum[2], Lama Bou-Karroum[3], Joseph Habib[4], Ahmed Ali, MD,[1], Gordon Guyatt[5], Fadi El-Jardali[1,3,5], Elie A. Akl[2, 3, 5, 6]

[1]Faculty of Health Sciences, [2]Clinical Research Institute, [3]Center for Systematic Reviews for Health Policy and Systems Research (SPARK), [4]Faculty of Medicine, [6]Department of Internal Medicine - American University of Beirut, Beirut, Lebanon; [5]Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada

Primary author: Assem Khamis, MD, MPH – Research Fellow – mk88@mail.aub.edu

Corresponding author: Elie A. Akl, MD, MPH, PhD – Professor of Medicine – ea32@aub.edu.lb

Funding source: This project was funded by the AUB FM's Medical Practice Plan (MPP) funds.

Keywords: conflict of interest, health policy and services, cross-section

Descriptive Statement: This is a cross sectional study to investigate the conflict of interest policies in Health Policy and Services Journals.

Introduction: The requirements of the Health Policy and Services (HPS) journals for authors to report their financial and non-financial conflicts of interest (COI) are unclear. The objective of this study was to assess the requirements of HPS journals for authors to disclose their financial and non-financial COIs.

Methods: We included journals indexed by the Web of Science (WOS) under the category of "Health Policy and Services". We reviewed the "instructions for authors" on the journal website and then simulated the submission of a manuscript to obtain any additional relevant information made available during that step. We abstracted data in duplicate and independently using a standardized form.

Results: Out of 72 eligible journals, 67 (93%) had a COI policy. All 67 policies required a COI disclosure of authors; fewer required it for reviewers (34%) and editors (18%). A minority of policies (34%) described how the disclosed COIs of authors would impact the editorial process. None of the policies had clear-cut criteria for rejection based on the content of the disclosure. About a fifth of policies (21%) explicitly stated that inaccurate or incomplete disclosures might lead to manuscript rejection or retraction. No policy described whether the journal would verify the accuracy or completeness of authors' disclosed COIs. Most journals' policies (93%) required the disclosure of at least one form of financial COI. While the majority asked for specification of source of payment (71%), a minority asked for the amount (18%). Eighty-one percent of policies explicitly required disclosure of non-financial COIs.

Conclusion: A majority of HPS journal policies required the disclosure of authors' financial and non-financial COIs, but few required details on disclosed COIs. Only a small minority specified how the disclosed COIs would impact the editorial process or required COI disclosure for reviewers and editors.

Abstract # 110

Measuring the Quality of anesthesia care at AUBMC from patients' perspective: adoption, translation and validation of a short questionnaire

Mariam Batakji MD, Marie Aouad Maroun MD
Department of Anesthesiology, American University of Beirut, Beirut, Lebanon
Corresponding author: Marie Aouad Maroun MD, E-mail: mm01@aub.edu.lb Research Assistant: Lama AbdelKhalek MS
Funding source: Departmental Funding
Position: CA3 anesthesiology resident
Keywords: quality of anesthesia care, questionnaire, patient care

Descriptive Statement: Anesthesia care perception from patients' perspective

Introduction:

Background: AUBMC is committed to provide patient care that focuses on quality and strives to improve patient satisfaction. The surgical population is growing and the operating room is one of the busiest facilities of the medical center. Patients usually place particular importance on anesthesia care and consider it as one of the most critical component of the overall care. Therefore, we thought that it would be useful to have a valid tool that can be used to measure the patients' perceptions regarding the quality of the anesthesia care provided.

Aim: The primary objective of the study was to adopt, translate into Arabic and validate a short psychometric questionnaire that tackles patients' perceptions regarding the anesthesia care provided at our medical center. A secondary objective was to analyze the factors that might affect patients' perceptions.

Methods: A short questionnaire was adopted from an article entitled "Measuring the Quality of Anesthesia from Patient's Perspective" published in the *British Journal of Anesthesia*. The questionnaire was then translated and back translated into Arabic. The Arabic version was piloted at first then tested for validation. For the Process of validation, 150 adult patients undergoing surgery at AUBMC were enrolled and were asked to fill the questionnaire the following day after their surgery, during a 6 month period.

Results: The scores of the 15 different questions which collected feedback regarding the anesthetic journey were analyzed using SPSS version 20. Cronbach's alpha was calculated and showed values ranging between 0.35 and 0.73 with a mean of 0.61. Hence, we could not validate the Arabic version of the quality questionnaire. Most of the patients (81%) underwent general anesthesia with the remainder receiving spinal anesthesia. Seventy three percent believed that anesthesia poses no risk to their health. None of the patients reported awareness. The majority of patients was satisfied with the postoperative pain management plan and had a good interaction with their anesthesiologist, whereby they rated their anesthesiologist as skillful, gentle and kind. Of note, female and sicker patients (ASA III and IV) were more anxious than male and healthier patients (ASA I and II) regarding their anesthetic care.

Conclusion: We enrolled a diversified sample of surgical patients in terms of demographic characteristics and surgical procedures. However, we believe that a common cultural perception prevents patients from expressing negative comments toward their treating physicians. Patients were predominantly grateful and positive toward their anesthetic journey. Therefore, the patients' perceptions were skewed to one side and lacked the variability needed for the validation process.

Abstract # 111

Reporting of financial and non-financial conflicts of interest in systematic reviews on Health Policy and Systems Research: a methodological survey

[1]Lama Bou-Karroum, [2]Maram B. Hakoum, [3]Mira Z. Hammoud, [4]Assem Khamis, [5]Mounir Al-Gibbawi, [4,5]Sanaa Badour, [5]Divina Justina Hasbani, [6]Luciane Cruz Lopes, [5]Hebah El-Rayess, [1,4,7]Fadi El-Jardali, [7]Gordon Guyatt, [2,7,8]Elie A. Akl

[1]Center for Systematic Reviews for Health Policy and Systems Research (SPARK), American University of Beirut, [2]Clinical Research Institute, American University of Beirut Medical Center, [3]Department of Psychiatry, Massachusetts General Hospital, United States of America, [4]Faculty of Health Sciences, American University of Beirut, [5]Faculty of Medicine, American University of Beirut, [6]Pharmaceutical Science Master Course, University of Sorocaba, São Paulo, Brazil, [7]Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada, [8]Department of Medicine, American University of Beirut Medical Center

Primary author: Lama Bou Karroum, MPH – Research Assistant – lb25@aub.edu.lb

Corresponding author: Elie A. Akl, MD, MPH, PhD – Professor of Medicine – ea32@aub.edu.lb

Funding source: This project was funded by the American University of Beirut Faculty of Medicine's Medical Practice Plan (MPP) funds.

Keywords: conflict of interest, systematic review, health policy, health systems

Descriptive Statement: This is a methodological survey to assess the frequency and different types of conflicts of interest reported by authors of systematic reviews on Health Policy and Systems Research (HPSR).

Introduction: Health policymakers are increasingly relying on systematic reviews to inform their decisions in a variety of policy areas including tobacco control, traffic safety, alcohol control and perinatal care. As in other forms of research, conflicts of interest (COI) – defined by the Institute of Medicine as "a financial or intellectual relationship that may impact an individual's ability to approach a scientific question with an open mind" - can influence the conduct and reporting of systematic reviews resulting in misguided public policies and systems level decisions. The objective of this study was to assess the frequency and types of COI that authors of systematic reviews of HPSR report.

Methods: We conducted a methodological survey using standard systematic review methodology. We searched the Health Systems Evidence database of McMaster Health Forum for systematic reviews published in 2015. We extracted information regarding the characteristics of the systematic reviews and the associated COI disclosures. We conducted descriptive and regression analyses.

Results: Eighty percent of systematic reviews included COI disclosures of authors. Of the 160 systematic reviews that included COI disclosures, 15% had at least one author reporting at least one type of COI. The two most frequently reported types of COI were individual financial COI and individual scholarly COI (11% and 4% respectively). Institutional COIs were less commonly reported than individual COIs (3% and 15% respectively) and non-financial COIs were less commonly reported than financial COIs (6% and 14% respectively). The regression analysis showed a positive association between the 'inclusion of a COI disclosure statement' and 'journal requiring a COI disclosure' (odds ratio = 27.048).

Conclusion: Uniform inclusion of COI statements in all systematic reviews in the health policy field, use of a standard disclosure form, and attention to editors' and reviewers' conflict, would increase transparency and allow readers to judge whether conflicts have influenced review conduct, authors' conclusions, and the decision to publish the review.

Abstract # 112

Most adapted health-related guidelines did not report using published adaptation methods, and their adaptation quality was variable

Rima A. Abdul-Khalek, PharmD, MSc. [1], *Andrea J. Darzi, MD, MPH* [1], *Mohammad W. Godah, MD, MPH* [1,2], *Holger Schünemann, MD, PhD* [3], *Elie A. Akl, MD, MPH, PhD* [1,2,3,4]

[1] *AUB GRADE Center, Clinical Research Institute, American University of Beirut, Beirut, Lebanon,* [2] *Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon,* [3] *Department of Medicine, McMaster University, Canada,* [4] *Department of Internal Medicine, American University of Beirut, Beirut, Lebanon,*

Corresponding author: Elie Akl – Professor of Medicine - E-mail: ea32@aub.edu.lb

Funding source: The study was not funded.

Keywords: guidelines, adapted guidelines, ADAPTE, AGREE II

Descriptive Statement: Most guidelines adaptations published in peer-reviewed journals did not report using a published method for adaptation. Therefore, guideline adaptation projects need to improve on the reporting of their methods.

Introduction: Background: Adaptation refers to the systematic approach for considering the endorsement or modification of recommendations produced in one setting for application in another as an alternative to de novo development. **Aim:** Our objective was to describe and assess the methods used for adapting health-related guidelines published in peer-reviewed journals, and to assess the quality of the resulting adapted guidelines.

Methods: We searched Medline and Embase up to June 2015. We assessed the method of adaptation, and the quality of included guidelines.

Results: Seventy-two papers were eligible. Most adapted guidelines and their source guidelines were published by professional societies (71% and 68% respectively), and in high-income countries (83% and 85% respectively). Of the 57 adapted guidelines that reported any detail about adaptation method, 34 (60%) did not use a published adaptation method. The number (and percentage) of adapted guidelines fulfilling each of the ADAPTE steps ranged between 2 (4 %) and 57 (100%). The quality of adapted guidelines was highest for the “scope and purpose” domain and lowest for the “editorial independence” domain (respective mean percentages of the maximum possible scores were 93% and 43%). The mean score for “rigor of development” was 57%.

Conclusion: Most adapted guidelines published in peer-reviewed journals do not report using a published adaptation methodology, and their adaptation quality was variable.

Abstract # 113

Reporting of financial and non-financial conflicts of interest by authors of 200 randomized controlled trials: a methodological survey

[1]Nahla Jouni, [2]Maram B. Hakoum, [3]Eliane A. Abou-Jaoude, [4]Divina Justina Hasbani, [5]Elias Abou-Jaoude, [6]Luciane Lopes, [7]Mira Z. Hammoud, [4]Mounir Al-Gibbawi, [8]Sirine Anouti, [9]Gordon Guyatt, [10]Elie A. Akl

[1]Faculty of Agriculture and Food Sciences, American University of Beirut, [2]Clinical Research Institute, American University of Beirut Medical Center, [3]Department of Internal Medicine, SUNY University at Buffalo, United States of America, [4]Faculty of Medicine, American University of Beirut, [6]Pharmaceutical Science Master Course, University of Sorocaba, São Paulo, Brazil, [8]Department of Epidemiology and Population Health, American University of Beirut, [9] Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada, [10]Department of Medicine, American University of Beirut Medical Center

Presenter: Nahla Jouni, BS – Student – naj12@mail.aub.edu
Corresponding author: Elie A. Akl, MD, MPH, PhD –Professor of Medicine – ea32@aub.edu.lb

Funding source: This project was funded by the American University of Beirut Faculty of Medicine's Medical Practice Plan (MPP) funds.

Keywords: financial conflict of interest, non-financial conflict of interest, randomized controlled trial

Descriptive Statement: This is a methodological survey of randomized controlled trials (RCT) to assess disclosures of conflicts of interest (COI).

Introduction: There is evidence that COIs may influence author's conclusions in RCTs. The objective of this study was to assess whether and what COIs authors of RCTs report.

Methods: We conducted a survey using standard systematic review methodology. We searched Medline's 119 Core Clinical Journals for RCTs published in 2015. We defined a COI disclosure as the reporting of whether a COI exists or not, and based our classification of COI on a comprehensive framework of the types of COI that exist in healthcare research, including individual COIs (financial, professional, scholarly, advocatory, personal) and institutional COIs (financial, professional, scholarly, and advocatory). We conducted descriptive and regression analyses.

Results: Of the 200 RCTs, 188 (94%) reported authors' COI disclosures, mostly in the main document and several in online ICMJE forms. Of these 188 RCTs, 57% had at least one author reporting at least one type of COI in addition to at least one author reporting individual financial COI. In contrast, only 3% of RCTs reported non-financial COIs. Institutional COIs were less commonly reported than individual COIs. Trials that reported contribution by a medical writer did not report the medical writers' COI disclosures. Regression analyses showed a positive association between reporting individual financial COI and a higher journal impact factor, a larger number of authors, being an author affiliated with an institution from a high-income country, and for trials on a pharmacological intervention.

Conclusion: More than half of published randomized controlled trials report that authors have conflicts of interest, particularly financial types. Authors report individual and financial conflicts of interest more frequently than institutional and non-financial conflicts.

Abstract # 114

Vitamin D Replacement in Children, Adolescents and Pregnant Women in the Middle East and North Africa

A Systematic Review and Meta-analysis of Randomized Controlled Trials

Chakhtoura M[1,2], El Ghandour S[3], Shawwa K[2,3], Akl EA[2,3,4], Arabi A[1,2], Mahfoud Z[2,5], Habib R[2,3], Hoballah H[3], El Hajj Fuleihan G[1,2].

[1]Department of Internal Medicine, Calcium Metabolism and Osteoporosis Program, WHO Collaborating Center for Metabolic Bone Disorders, Division of Endocrinology, American University of Beirut Medical Center, Beirut, Lebanon. [2]Scholars in HeAlth Research Program (SHARP), American University of Beirut Medical Center, Beirut, Lebanon. [3]Department of Internal Medicine, American University of Beirut Medical center, Beirut, Lebanon. [4]Department of Health Research Methods, Evidence, and Impact (HE&I), McMaster University, Hamilton, Canada. [5] Department of Global and Public Health Weill Cornell Medical College, Doha Qatar

Corresponding author: Marlene Chakhtoura- Instructor of Clinical Medicine – E-mail: mc39@aub.edu.lb

Funding source:

Resource Plan at the American University of Beirut, Lebanon

This project was made possible thanks to the Scholars in HeAlth Research Program (SHARP), NIH Grant D43TW009118.

Keywords: Vitamin D, Middle East and North Africa, meta-analysis, pregnant women, children and adolescents.

Descriptive Statement: Hypovitaminosis D is a global public health problem, worldwide and more so in the Middle East and North Africa (MENA) region. This systematic review of vitamin D trials assesses the effect of supplementation on vitamin D status and other outcomes, in children, adolescents, and pregnant women.

Introduction: Hypovitaminosis D is prevalent in the MENA region. Our aim is to evaluate the effect of vitamin D supplementation on 25-hydroxyvitamin D [25(OH)D] level, and other skeletal and non-skeletal outcomes.

Methods: This is a systematic review of vitamin D trials in the MENA region. We conducted a literature search in 7 databases, until 2016. We calculated the mean difference (MD) and 95%CI of 25(OH)D level reached, when at least 2 studies were eligible in each comparison (low (<800IU), intermediate (800-2,000IU) or high (>2,000IU) daily dose of vitamin D, or placebo). We pooled data using RevMan version 5.3.

Results: We identified 15 eligible trials: 1 in infants, 4 in children/adolescents and 10 in pregnant women.

In children/adolescents, an intermediate vitamin D dose (1,901 IU/d), resulted in a mean difference in 25(OH)D level of 13.5 (95%CI 8.1;18.8) ng/ml, compared to placebo ($p < 0.001$), and allowed for 74% of children to reach a 25(OH)D level ≥20 ng/ml.

In pregnant women, supplementation started early or at the end of the second trimester, and continued until delivery. The MD in 25(OH)D level reached was 8.6 (95%CI 5.3-11.9) ng/ml ($p<0.001$), comparing the high (3,662IU/d) to the intermediate dose (1,836IU/d), and 12.3 (95%CI 6.4-18.2) ng/ml ($p<0.001$), comparing the high (3,399IU/d) to the low dose (375IU/d). Comparing the intermediate (1,832IU/d) to the low dose (301IU/d), the MD in 25(OH)D level achieved was 7.8 (95%CI 4.5-10.8) ng/ml ($p<0.001$). The proportion of pregnant women reaching a 25(OH)D level ≥20 ng/ml was 80-90%, 73%, 27-43% in the high, intermediate, and low dose groups, respectively.

Conclusion: In children, adolescents and pregnant women from the MENA, an intermediate vitamin D dose of 1,000-2,000IU/d seems necessary to allow for the majority of the population to reach the desirable 25(OH)D level ≥20 ng/ml.

Abstract # 115

The Global Evidence Synthesis Initiative (GESI) Secretariat at the American University of Beirut

Tamara Lotfi, Elie A Akl, Fadi El Jardali

Funding source: GESI is funded by Cochrane, the Campbell Collaboration, the International Initiative for Impact Evaluation (3ie), The Alliance for Health Systems and Policy Research (AHSPR), the EPPI-Center, the American Institutes for Research (AIR) and the Joanna Briggs Institute (JBI).

Keywords: Evidence Synthesis, Global, Systematic Reviews,

Descriptive Statement: The Global Evidence Synthesis Initiative (GESI) has chosen, through a competitive process, the Center for Systematic Reviews on Health Policy and Systems Research (SPARK) to host the Secretariat of the Global Evidence Synthesis Initiative. GESI aims to build capacity in Evidence Synthesis in Low & Middle-Income Countries.

Low and Middle-Income countries (LMIC) have less production and use of research synthesis to inform practice and policy-making, compared to High Income countries. A major reason for this imbalance is due to the low capacity of synthesizing evidence in LMIC. Thus, the Global Evidence Synthesis Initiative (GESI) was launched to enhance the capacity for research synthesis worldwide, and especially in LMICs.

A number of international research organizations, committed to the production and use of research synthesis to enhance practice, public policy, public service delivery and citizens' involvement, created GESI. These organizations aim to advance the preparation, quality assurance, dissemination and promotion of research syntheses. These include Cochrane (previously the Cochrane Collaboration), the Campbell Collaboration, the EPPI-Centre, the International Initiative for Impact Evaluation (3ie), the Alliance for Health Policy and Systems Research, and the Joanna Briggs Institute (JBI).

The goal of GESI is to increase the capacity to undertake research syntheses by establishing and supporting an initial ten GESI Centers in LMICs. GESI is interested in building capacity in evidence synthesis in multiple areas of public practice and policy and public service delivery, including but not limited to agriculture, crime and justice, economic development, education, food security, health and healthcare, hygiene, social protection and water sanitation.

GESI Secretariat

A Secretariat has been established to support and manage GESI functions, and is hosted by Center for Systematic Reviews on Health Policy and Systems Research (SPARK) at the American University of Beirut (AUB), Lebanon.

The secretariat will build a network of Evidence Synthesis Centers from LMICs to enhance collaboration and encourage sharing knowledge and experience. The Secretariat will also hold capacity building activities (e.g., workshops) in evidence synthesis in the different disciplines.

Abstract # 116

Screening for Guidelines on Refugees' Health: A Systematic Survey

Tamara Lotfi [1,2]; Mohamad Itani[2] ; Lama Kilzar [1]; Pamela Howeiss [3]; Nesrine Rizk [3]; Elie A. Akl [2,3,4]

[1] Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon, [2] Clinical Research Institute, AUBMC, Beirut, Lebanon, [3] Department of Internal Medicine, American University of Beirut, Beirut, Lebanon, [4] AUB GRADE Center, Clinical Research Institute, American University of Beirut, Beirut, Lebanon

Corresponding author: Elie A Akl – Associate Professor - E-mail: ea32@aub.edu.lb

Funding source: This paper did not receive any funding.

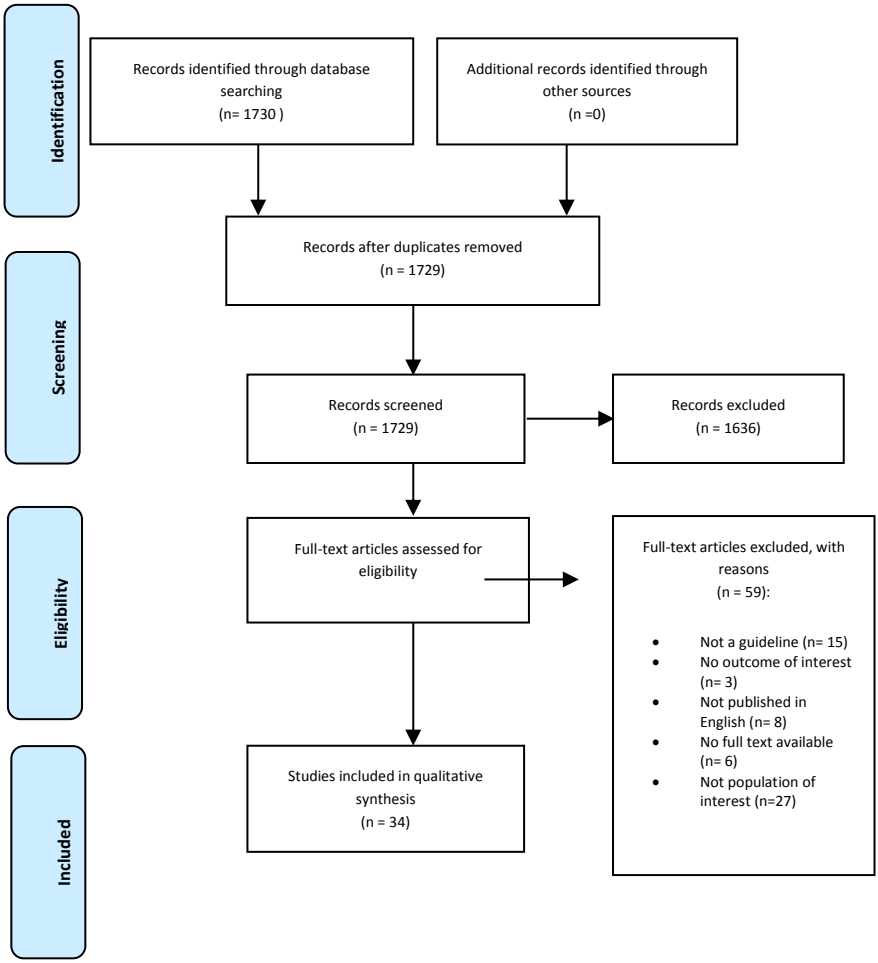
Keywords: Migrants, Refugees, Clinical, Practice Guidelines, Health

Descriptive Statement: This paper aims to survey the literature for guidelines targeting refugees and migrants' health.

Introduction: There is an increasing number of migrants and refugees worldwide, especially with the recent conflicts. This study aims to identify published guidelines related to health, clinical practice, public health and policy that target refugees' health.

Methods: We conducted a search on the electronic databases Medline, Embase, National Guideline Clearinghouse (NGC) and the Canadian medical Association's Clinical Practice Guidelines Database (CPGs). We also searched the World Health Organization's website for relevant guidelines. We included papers that responded to the WHO's definition of guidelines, whose target populations were refugees and/or migrants, and were published in the last ten years. Two reviewers screened in duplicate and independently the titles and abstracts of the citations found by the search, then they retrieved full texts of potentially eligible studies and screened them in duplicate and independently. They abstracted data in duplicate and independently for the following variables: publication date of the guideline, publishing organization, methodology used in the development, the disease group covered, the approach of the guideline (treatment, screening…) . They assessed, in duplicate and independently, the quality of the guideline using the AGREE-II tool and also assessed the reporting of the guideline using the RIGHT statement.

Results: Appendix 1 shows the results of the screening. We are currently finalizing the data synthesis.


Identification
Records identified through database searching (n= 1730)
Additional records identified through other sources (n =0)
Records after duplicates removed (n = 1729)
Screening
Records screened (n = 1729)
Records excluded (n = 1636)
Eligibility
Full-text articles assessed for eligibility
Full-text articles excluded, with reasons (n = 59):
Not a guideline (n= 15)
No outcome of interest (n= 3)
Not published in English (n= 8)
No full text available (n= 6)
Not population of interest (n=27)
Included
Studies included in qualitative synthesis (n = 34)

Abstract # 117

How are family-related factors associated with sexual and reproductive health, violence, and mental health of adolescents and youth? An overview of reviews

Mariana Yaafar Jaafar[1], Tamara Lotfi[2,3], Chaza Akik[4], Noura El Salibi[2], Jillian Grisel[1], Hala Najm[1], Caroline Zahm[3], Lilian Ghandour[2], Elie Akl[3,5], Rima Afifi[1]

[1]Department of Health Promotion and Community Health, Faculty of Health Sciences, American University of Beirut, [2]Department of Epidemiology and Population Health, Faculty of Health Sciences, American University of Beirut, [3]Department of Clinical Research Institute, American University of Beirut, [4]Center for Research on Population and Health, Faculty of Health Sciences, American University of Beirut, [5]Department of Internal Medicine, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

Corresponding author: Rima Afifi - Professor and Associate Dean - E-mail: ra15@aub.edu.lb

Funding source: University of Melbourne through a grant from the Bill and Melinda Gates Foundation.

Keywords: Family, youth, adolescents, sexual health, violence, mental health, overview of reviews

Descriptive Statement:

This paper describes the results of a research study that identified, summarized and synthesized published systematic and narrative reviews investigating the influence of family factors on the mental health, sexual/reproductive health, violence and mental health of adolescents and youth.

Introduction:

Research has indicated that families have both positive and negative effects on adolescent/youth health. A variety of frameworks describe the specific pathways of influence of families on adolescent/youth health. Our study aims to identify, synthesize and summarize the published systematic reviews assessing family influences on youth and/or adolescents' sexual/reproductive health, violence and mental health.

Methods: We searched the following electronic databases Medline (Ovid), Embase (Ovid) and Popline. Our inclusion criteria include all narrative reviews, meta-analyses, or systematic reviews that: 1) had quantitative and/or qualitative data; published between January 1990 and April 2015; (2) included at least one study where the outcome was measured in the 10-24 age group; (3) reported on at least one the following outcomes: mental health, sexual and reproductive health, or violence; (6) and assessed any family–related variable. Teams of two reviewers screened in duplicate and independently the titles and abstracts of the citations captured by the searches, and then the full texts of the potentially eligible studies. They abstracted data in duplicate and independently for the finally included papers. Moreover, they assessed the quality of eligible systematic reviews using the "A Measurement Tool to Assess Systematic Reviews" (AMSTAR) tool. This paper reports the results of the systematic reviews addressing observational studies.

Results: Our search identified 2867 articles of which 918 were assessed for eligibility, and 17 eventually included. Only 4/17 were of moderate-high quality. Five of the seven main pathways of family influence on youth health are evident in the quantitative and consistent results of the systematic reviews. The results of the reviews seem to point to one key variable of influence that cuts across all three health outcomes: parent-adolescent or family-adolescent communication and relations.

Conclusion: Richer and sharper conceptualizations, operationalization, and methods are urgently needed to strengthen our understanding of the influences of families, and the systems/communities/global environments they operate within, on young people's health outcomes.

Abstract # 118

Traumatic Brain Injury in a War Zone: A Systematic Review of its Epidemiology and Clinical Characteristics in Lebanon

Hiba Ghandour[1], Hussein Abou-Abbass[2], Hisham Bahmad[3], Natally Al-Arab[3], Rayyan Wazzi-Mkahal[3], Salah Ballout[3], Hala Darwich[4], Mazen J. El Sayed[5], Hayat Haraty[6], Hani Tamim[2] And Firas Kobeissy[3]*

[1] Faculty of Medicine, American University of Beirut, [2]Clinical Research Institue, Department of Internal Medicine, [3]Department of Anatomy, Cell Biology and Physiological Sciences, , [4]Faculty of Medicine-School of Nursing, [5]Department of Emergency Medicine, American University of Beirut Medical Center, Beirut, Lebanon. [6]Neuroscience Research Institute, Lebanese University.

Corresponding author: Dr. Firas Kobeissy – Assistant Professor - E-mail: firasko@gmail.com

Funding source: None

Keywords: Neuroepidemiology, Neuroscience, Traumatic Brain Injury, Lebanon

Descriptive Statement: Systematic Review about status of Traumatic Brain Injury in Lebanon.

Introduction: Although mild traumatic brain injuries - concussions - had previously been deemed unimportant and are often ignored, currently mTBI and its long term sequelae are being referred as the "signature injury" of war conflicts affecting both civilian and military personnel equally. Our aim is to systematically review the status of TBI in Lebanon – a Middle Eastern country with a weak health system in order to identify the present gaps in knowledge, direct future research initiatives and assist policy makers in planning progressive and rehabilitative policies.

Methods: OVID/Medline, PubMed, Scopus databases and Google Scholar were lastly searched on April 15th, 2016 to identify all published research studies on TBI in Lebanon. Studies that assessed Lebanese patients afflicted by TBI in Lebanon were warranting inclusion in this review. Case reports, reviews, biographies and abstracts were excluded. Reviewers worked independently and in duplicates during study selection, data abstraction and methodological assessment using the Downs and Black Checklist.

Results: In total, 11 studies were deemed eligible. Considerable methodological variation was found among the eligible studies. All studies, except for two that evaluated non-military injury mechanisms such as falls, motor vehicle accidents, etc. focused on TBI caused by combat related activities. A total of 682 TBI cases were confirmed in Lebanon from all the eligible reviewed articles. Age distribution of TBI victims revealed two peaks, young adults between 18 and 40 years, and older adults aged 60 years and above; males constituted the majority. Only three studies reported rates of mild TBI. Mortality, rehabilitation and systemic injury rates were rarely reported and so were the complications involved; infections were an exception.

Conclusion: Apparently, the status of TBI in Lebanon suffers from several gaps which need to be bridged through implementing more basic, epidemiological, clinical and translational research in this field in the future.

Abstract # 119

Prevalence, Awareness and Control Rates of Hypertension in Greater Beirut Area and the Respective Predictors: A Cross Sectional Study

Author: Aya Noubani [4]

Advisors: Hani Tamim[1], Hussain Ismaeel[2], Lara Nasreddine[3] and Abla Mehio Sibai [4]*

***Corresponding Author:** Hani Tamim - htamim@aub.edu.lb

[1]Department of Internal Medicine, AUBMC; [2]Division of Cardiology, Department of Internal Medicine, AUBMC; [3]Department of Nutrition and Food Sciences-FAFH-AUB; [4]Department of Epidemiology and Population Health-FHS-AUB

Position: Masters student in Epidemiology and population health

Funding: the data is secondary, no fund was needed

Abstract

Background and aim: Hypertension (HTN) has been identified as the leading risk factor for mortality, and the third cause of disability worldwide. Lebanon has witnessed a three-fold increase in the prevalence of HTN in the past decade. The timely exploration and detection of the factors contributing to a higher prevalence of the disease is fundamental. The objective of this study was to assess the prevalence, awareness and control rates of HTN in Greater Beirut Area and identify their respective predictors.

Methods: A representative sample of 501 participants aged between 18-79 years residing in Greater Beirut Area were examined. Data collection form was filled up, through interviews, physical exams, and lab tests. The analysis was done for 3 defined outcomes: Blood Pressure status (normal, prehypertension and hypertension), aware HTN and controlled HTN. These were compared for the various associated predictors.

Results: The sample consisted of 64.3% women and mean age 45.4 ±15 years and the subjects were predominantly from low socioeconomic status. The results showed that 36.4% of the study participants were hypertensive, 25.3% were pre hypertensive and 38.2% had optimal BP. The awareness and control rates were 65.4% and 61%, respectively. The independent predictors of HTN were: age, gender, marital status, diabetes, body fat, triglyceride (positive correlates) and income level (negative correlate). However, there was no significant association between dietary intake and HTN after adjustment. Moreover, the identified predictors were positively correlated to unaware HTN: age, gender, and obesity. Yet, we couldn't identify any factor related to uncontrolled HTN.

Conclusion: The prevalence of HTN in Greater Beirut Area was similar to that reported in the national study, yet, the awareness and control rates were higher. The predictors identified were similar to those traditional known associations. However, obesity was found to be common among HTN patients, especially those who are unaware. Public health measures on a national level are urgent to increase the level of awareness, achieve primary prevention and better control of the disease.

Abstract # 120

Non-Communicable Diseases in the Eastern Mediterranean Region (EMR): Overview of Reviews

Abla Mehio Sibai[1], Alaa Akkawi[1], Aya Noubani[1], Sara Jamali[2], Tamara Lotfi[1]*
[1] Department of Epidemiology and Population Health, Faculty of Health Sciences. American University of Beirut
[2] Faculty of Medicine, American University of Beirut
***E-mail address:** am00@aub.edu.lb

Keywords: Systematic reviews, meta-analysis, Non-communicable diseases, risk factors, Eastern Mediterranean Region (EMR).

Indicate your position: Masters in Public Health Student

Funding source: This work was carried out with the aid of a grant from the International Development Research Centre, Ottawa, Canada.

Introduction: In the Eastern Mediterranean Region (EMR), more than 1.7 million people die yearly from the four main types of Non-communicable diseases (NCDs): cardiovascular diseases, cancer, diabetes and chronic respiratory diseases. The health research productivity and quality in the EMR is bleak with critical deficits in different areas. The objective of this study is to identify, summarize and synthesize systematic reviews (SRs) and/or meta-analysis addressing NCDs and their risk factors in the EMR to critically appraise the research to assess the research focus on each outcome as well as the impact of the SRs on implementing policies.

Methods: We searched the electronic databases, Medline Ovid in April 2016, Cochrane Central in May 2016 and Epistemonikos in May 2016 to find the relevant SRs published between1996-2015 by using Montori et al., SR filter. We used MeSH and key terms for the topic of interest and the EMR countries. We screened and abstracted data independently and in duplicate and assessed the quality of the included SRs using AMSTAR tool.

Results: We found 2439 SRs and the final number included in the qualitative analysis is 105. The majority of the studies were conducted by one country and Iran has the highest level of publication. 43% SRs addressed CVDs as an outcome and 21% SRs addressed smoking as a risk factor. 85% of the studies were of low quality, which increased by year and with the collaboration with a non-EMR corresponding author.

Conclusion: More than 70% of the SRs addressed CVDs and DM. The focus on DM may/may not be appropriate. However, the analysis is still ongoing and we didn't finish the data synthesis.

Abstract # 121

The Use of Contrast Enhanced Ultrasound in the Confirmation of Central Venous Catheter Placement: A Systematic Review and Meta-Analysis.

Ralphe Bou Chebel[1], Shafeek Kiblawi[1], Christopher El Khuri[1], Nadine El Hajj[1], Rana Bachir[1], Roni Aoun[1]

[1]Department of Emergency Medicine, American University of Beirut Medical Center, Beirut, Lebanon

Corresponding author: Gilbert Abou Dagher – MD/Assistant Professor - E-mail: ga66@aub.edu.lb

Presenter: Dr. Shafeek Kiblawi (Resident: second year)

Funding source: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Keywords: Ultrasound, Contrast-Enhanced Ultrasonography, Central Venous Line Location, X-ray

Descriptive Statement: A systematic review and meta-analysis was conducted to culminate the current literature pertaining to the use of a specific technique in bed-side ultrasound to confirm correct placement of a central venous line catheter compared to standard X-ray.

Introduction: Multiple studies have been conducted to assess the use of ultrasound as an alternative to chest X-ray for the confirmation of central line placement. The objective of this paper was to determine the sensitivity, specificity, positive and negative predictive values of contrast enhanced ultrasound in confirming the tip location and placement of the central venous catheter in adult patients.

Methods: A systematic review of English articles was performed using electronic databases, and scanning reference lists of articles. The databases included Medline (1966-present), ClinicalTrials.gov, Cochrane, EMBASE, Pubmed, and Scopus. Inclusion criteria were studies conducted on adult patients receiving an internal jugular (IJ) or a subclavian (SC) central venous catheter (CVC) in the emergency department or in the intensive care unit. Furthermore, CVC tip location had to be checked with the use of agitated saline contrast enhanced ultrasonography (CEUS) technique as compared to chest X-ray.

Results: From 7306 preliminary papers, 4 articles and one abstract were included in the final analysis. CEUS showed a pooled sensitivity of 72% (95% CI, 44-91), pooled specificity of 100% (95% CI, 99-100), PPV of 92.1% and NPV of 98.5% when compared to chest X-ray for confirming the placement of IJ or SC central venous catheters.

Conclusion: In the setting of IJ or subclavian CVC placement, post-procedural contrast enhanced ultrasonography is safe, efficient and highly specific confirmatory test for CVC tip location when compared to chest X-ray.

Abstract # 122

Design Guidelines for a Therapeutic Roof Garden: Case of AUBMC Oncology Courtyard

Elias Nasser Karaan[1], Dr. Salma Talhouk[2,1], Dr. Sally Temraz[3]

[1]Department of Landscape Design and Ecosystem Management, [2]Program and Division of the Interfaculty Graduate Environmental Science Program, Ecosystem Management , American University of Beirut, Beirut, Lebanon

Corresponding author: Ms. Nayla Al-Akl- Research Assistant/Professor - E-mail: na143@aub.edu.lb

Funding source: [insert here]

Keywords: Design guidelines, therapeutic landscapes, stress relief, environmental perception, stress reduction theory, participatory approach

Descriptive Statement: The following thesis aims at identifying the natural, social and physical aspects of a garden that reduces stress.

Introduction: Nature has always been considered as a healer. Due to rapid growth of cities, green spaces became difficult to find. Presently, natural settings are regaining popularity in new complex architectural projects due to their scarcity in urbanized areas. Healing through exposure to nature is re-inserted and planners are re-inviting nature into their designs to promote effective healing. Green roofs are one of those concepts that are being used as therapeutic gardens in complex healthcare settings. The main goal of this thesis is to create a set of guidelines surveying social, physical and theoretical aspects to properly design a healing garden.

Methods:

1. Compiling a set of guidelines from existing literature using Ulrich's Stress Reduction Theory and its subcomponents as the main reference and how it is applied in other writings. This is mainly achieved using tables to demonstrate clearly the process.
2. Present a profile for the case study (AUBMC's 8th floor) and a detailed analysis of the site. Site analysis includes a social (ethnographic) and spatial (physical) study of the site and its users. Social analysis included mainly the use of a survey that investigated the users preferences of a garden.
3. General design guidelines are created from both the literature review analysis and the outcomes of the observation and information acquired from the survey.

Results: One important outcome of this research is that people value nature. AUBMC users were conscious of the importance of nature's effects in reducing stress. The methodology applied for this thesis came from an interdisciplinary approach. It linked the notion of stress reduction and medical environment to the concept of nature as a healing element, to the notion of potential spaces for healing and to creating design guidelines for these spaces. A crucial part of the methodology was the survey. Every person has a distinct perspective about what in nature is considered as stress relieving. Moreover, practice did prove theory right. It was through this thesis that design guidelines were generated from theoretical aspects and notions such as Ulrich's theory.

Conclusion: This study gave further insight on the natural, social and physical aspects in gardens that aid in reducing stress for the local community. It highlighted the most important aspects for the design of an effective therapeutic garden on the 8th floor: the strategic location, visibility, accessibility, climate and condition, use and activity, and natural/lightly maintained greenery.

Abstract # 123
Music and Self-Rated Health

Nour Gebara[1], Talar Telvizian[1], Halim Bou Daher[1], Hassan Nahouli[1], Sali Sarkis[1], Rana Al Barazi[2]
[1]Faculty of Medicine, [2]FHS, American University of Beirut, Beirut, Lebanon
Corresponding author: [Nour Gebara - E-mail: nourg@live.com, nyg00@mail.aub.edu

Funding source: None

Keywords: music, SRH, exercise

Descriptive Statement: *The relationship between music (listening and type of music) and Self-related health among university students at the American University of Beirut*

Introduction: Background and aims: Self Rated Health (SRH) is a subjective health scale adopted by the World Health Organization (WHO). It has been shown to be an accurate predictor of health, morbidity, mortality, and disease prognosis. Music is, for many, a self-administered therapy of the body and mind, and evidence suggests that it enhances parameters of health and improves lifestyle habits, which in turn affect SRH.

Methods: This is an analytical cross-sectional study using a quantitative survey method. The study population includes students at the American University of Beirut aged 18-24 from all majors and all levels. Self-administered questionnaires were distributed in a randomly selected manner to classes from a pool of common classes, both for undergraduates and graduates. Data was collected in February 2016. 425 students completed the 10-minute survey after giving oral voluntary consent. Data was analyzed using SPSS 20.00. Bivariate analysis using a two-tailed chi-square test was done to study the association between potential confounders. P-value of <0.2 was considered significant.
Next, multivariate logistic regression was performed while adjusting for the results found to be significant in the bivariate regression. P-value of <0.05 was considered significant.

Results: 87% AUB students reported a good/ very good/ excellent SRH. There was no significant association between SRH and the frequency or duration listened to music in this sample. From the music genres, metal music was significantly correlated with a poorer SRH. A particular finding with possible important clinical implications is that among the excessive alcohol drinkers, those who listened to music while exercising were more likely to report a higher SRH than the excessive alcohol drinkers who don't listen to music while exercising.

Conclusion: Future studies are needed to verify the findings of this study, and to determine the existence of a correlation between SRH and social and cultural capital other than music. Since most of the study participants listen to music, it is important to study its effects in different contexts and especially among different aged populations. Music is a readily available, accessible and a relatively cheap resource. With further research, music may even be incorporated in the new Arts-on-Prescription movement, which is using the arts as means to promote health.