6TH ANNUAL AUB BIOMEDICAL RESEARCH DAY

Saturday, February 27, 2016

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
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- Hassan Zaraket, FM, Department of Experimental Pathology, Immunology and Microbiology
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- Ali Nabbouh, FM, Graduate Student Affairs


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Student Awardees of the 2015 AUB Biomedical Research Day

- **Ilige Hage**, FEA: *Distribution of Area Fraction of Pores in Cortical Bone's Pericortical and Intracortical Regions*

- **Dana Bazzoun**, FAS: *Effect of Connexin 43 Loss on Polarity and Initiation of Tumorigenic Pathways in the Phenotypically Normal Breast Epithelium*

- **Maamoun Abdul Fattah** and **Sara Al Ghadban**, FM: *Efficacy of Adalimumab Stored in Plastic Vials at Four Degrees Celsius*

- **Rola Hammoud**, FAFS: *Phosphorus Supplementation Abolished Weight Loss of Rats Maintained on Low Protein Diet*

- **Nadim Tawil**, FM**:** *Knock-out of the bradyzoite marker p18 in Toxoplasma gondii: insights towards a functional characterization during neurotoxoplasmosis*

2014 Farouk Jabre Award Recipients

- **Dr. Firas Kobaissy**, FM, **Dr. Hala Darwish**, FM and **Dr. Pierre Karam**, FAS: *Developing sensitive and specific biosensor for traumatic brain injury biomarkers*

- **Dr. Diana Jaalouk**, FAS, **Dr. Marwan Refaat**, FM and **Dr. Georges Nemer**, FM: *Insight into the deregulation of Hic-5 and Rbm20 in LaminA/C and emerin related cardiomyopathies*

- **Dr. Fadl Moukalled**, FM and **Dr. Samir Alam**, FM: *The development of a novel low computational cost non-invasive direct method to predict ischemia in human diseased coronary arteries*

- **Dr. Rihab Nasr**, FM and **Dr. Rabih Talhouk**, FAS: *miRNA as Circulating Biomarkers for Breast*

- **Dr. Md Anwarul Hasan**, FEA and **Dr. Ayad Jaffa**, FM: *Development of a biomimetic blood vessel using multilayered composite nano-microfiber scaffolds for cardiovascular tissue engineering*

List of jury members for the 5th Annual Biomedical Research Day

Faculty of Medicine

1. Hiba El-Hajj
2. Marwan Refaat
3. Marie Aouad-Maroun
4. Marwan Sabban
5. Mona Nabulsi
6. Elie Akl
7. Hala Darwish
8. Heinrich Burggraf Zu Dohna-Schlobi
9. Hassan Zaraket
10. Raya Saab

Faculty of Arts and Sciences

1. Youssef Mouneimne

Faculty of Agricultural and Food Sciences

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

Faculty of Engineering and Architecture

1. Elie Shammas
2. Ramsey Hamade

University of Balamand

1. Roula Abdel Massih

6TH ANNUAL AUB BIOMEDICAL RESEARCH DAY

Schedule of events

9:00 am - 9:30 am	Welcome note **Dr. Ayad Jaffa**, Assistant Dean for Graduate Studies and Interdisciplinary Programs 2016 Farouk Jabre Award Presentation *Dean Sayegh, Trustee Jabre (represented by his son Mr. Wissam Jabre)*
9:30 am - 10:15 am	Keynote speaker to be introduced by Dr. Kamal Badr, Associate Dean for Medical Education **Dr. Joao Lima**, Director of Cardiovascular Imaging, Professor of Medicine, Johns Hopkins University ***Title:*** *Cardiovascular Fibrosis: Lessons from MESA*
10:15 am – 10:55 am	Speakers to be introduced by Dr. Samia Khoury, Associate Dean for Clinical and Translational Research **Dr. Lokman Ibrahim Meho**, University Librarian and Associate Professor, AUB **Dr. Elie Akl**, Director of Clinical Research Institute ***Title:*** *AUB regional standing in biomedical and clinical research*
11:00 am – 2:00 pm	Poster viewing followed by lunch, award presentation for the top 10 posters and closing

Objectives

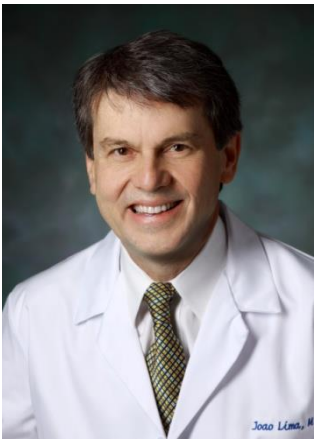
- serve as a platform to bring together the research community of different AUB faculties and to showcase the biomedical research performed at AUB
- provide an intellectual environment for scientific exchange among the various researchers at AUB
- provide a platform for students, postdoctoral fellows 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

Dr. Joao Lima



Dr. Lima has concentrated professional effort on clinical investigation and clinical scholarship as well as in academic teaching. His primary contribution to the advancement of cardiovascular medicine has been the development of MRI methods to measure infarct size and the extent and severity of microvascular obstruction in patients with acute myocardial infarction. Dr. Lima's initial work was focused on the pathophysiology of the left ventricular remodeling after myocardial infarction using non-invasive techniques such as MRI tagging and echocardiography to evaluate regional left ventricular function after myocardial infarction. He was one of the first investigators to measure infarct size by MRI. More recently he has developed MRI and CT imaging methods to measure atherosclerosis in comparison with invasive angiography and in response to statin therapy in patients with coronary artery disease.

Dr. Lima has been directly involved in applying imaging phenotyping methods in population research. His involvement in the Multi-Ethnic Study on Atherosclerosis (MESA) has been concentrated on the investigation of myocardial damage and dysfunction among asymptomatic individuals of different ethnicities living in the United States. His studies as a MESA investigator have concentrated on the determinants of incident heart failure and progressive ventricular dysfunction as a consequence of sub-clinical atherosclerosis and hypertensive heart disease. Dr. Lima has also developed contrast enhanced MRI methods to predict sudden death in patients who suffered myocardial infarction. The majority of Dr. Lima's clinical efforts have been dedicated to clinical scholarship and program development at the Johns Hopkins Hospital. He directed the

Echocardiography Laboratory at Hopkins for several years and spearheaded pioneering programs in cardiovascular MRI and cardiac CT. His leadership in mentoring cardiology and radiology trainees in cardiovascular imaging has also been significant both clinically and in clinical investigation.

Speakers

Lokman Ibrahim Meho, PhD

Lokman I. Meho (AUB 1991 and 1996) completed his Ph.D. in Information and Library Science in December 2001 from the University of North Carolina at Chapel Hill. Before joining AUB in 2009 as the University Librarian, he was a tenured Associate Professor and Director of the Master of Library Science program at the School of Library and Information Science at Indiana University Bloomington. Dr. Meho is author of several articles that deal with research assessment and scholarly communication and is a recipient of a number of teaching and international research awards.

Elie Akl, MD, MPH, PhD

Elie joined AUB in 2012 after practicing as a general internist for 8 years in the US. He currently directs the Clinical Research Institute, the AUB GRADE center, and co-directs the Center for Systematic Reviews in Health Policy and Systems Research (SPARK). His research interests include systematic review methodology, development and adaptation of practice guideline, conflicts of interest in health research and in clinical practice, and dealing with missing data in meta-analysis. He has published more than 200 peer-reviewed papers, including in the top general medical journals. He has acted as the methodologist and/or co-chair for a number of guidelines by North American professional societies and a dozen of guidelines by the World Health Organization.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ABSTRACTS

Abstract # 1

Gene expression profiling of breast cancer in Lebanese women

Joelle Makoukji[1], Nadine J. Makhoul[1], Maya Khalil[2], Sally El-Sitt[1], Ehab Saad Aldin[3], Mark Jabbour[4], Fouad Boulos[4], Emanuela Gadaleta[5], Ajanthah Sangaralingam5[4], Claude Chelala[5], Rose-Mary Boustany[¶*1,6], Arafat Tfayli[¶7]

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¶ Co-senior authors

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Funding source: MPP grant to R-MB MPP320046 and MPP grant to AT MPP320061

Keywords: Gene expression profiling, breast cancer, Lebanese women, microarray data analysis, mRNA fingerprint

Descriptive Statement: Gene expression profile of fresh breast tissue samples were analyzed using microarray technologies, in order to extract a unique mRNA fingerprint of breast cancer in Lebanese women.

Introduction: background and aims Breast cancer is the most common cancer in women worldwide. Elucidation of its underlying biology and molecular pathways is necessary for improving therapeutic options, hence, improving clinical outcomes. As molecular alterations in breast cancer are complex and involve cross-talk between multiple cellular signaling pathways, the application of gene expression profiling using microarray technologies provides a window to compare expression patterns across multiple samples from different populations. The aim of this study is to extract a unique mRNA fingerprint of breast cancer in Lebanese women.

Methods: Gene expression profile of 94 fresh breast tissue samples (84 cancerous and 10 non-tumor samples) were analyzed using GeneChip Human Genome U133 Plus 2.0 arrays. Quantitative real-time PCR was subsequently carried out to validate candidate genes.

Results: Differentially expressed genes between breast cancer and non-tumor control tissues were screened. Significant differences in gene expression between breast cancer and normal non-tumor tissues were established for COL11A1, COL10A1, MMP1, COL6A6, DLK1, S100P, CXCL11, SOX11, LEP, ADIPOQ, OXTR, FOSL1, ACSBG1, and C21orf37. Relevant pathways and diseases representing the genes were retrieved and linked using PANTHER® and Pathway Studio®. The analysis revealed that many of the deregulated genes are associated with extracellular matrix, inflammation, angiogenesis, metastasis, differentiation, cell proliferation, and tumorigenesis.

Conclusion: These findings add a better understanding of molecular mechanisms in breast cancer, particularly in Lebanese women. More importantly, key genes were uncovered which could serve as potential biomarkers or novel drug targets for breast cancer.

Abstract # 2

Caregiver Burden: Results from a Cross Sectional Study on Dementia in Lebanon

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]

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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: caregiver, care burden, dementia, elderly, Lebanon

Descriptive Statement: in a culture where caring for older adults is mostly confined to the family, measuring the mental burden of caregiving and understanding its causes are crucial steps towards providing proper support systems in the absence of a governmental plan.

Abstract

Introduction: In Lebanon, the proportion of elderly (≥ 60 years) is expected to reach 26% in 2050 indicating higher demand for elderly care. Families assume the primary responsibility of caregiving. The mental wellbeing of caregivers – in particular dementia caregivers – is scarce in the Arab Region. The study aims to assess the psychological distress and burden of care among a sample of elderlies' caregivers in Lebanon.

Methods: A cross-sectional study of 502 elderly was conducted in Lebanon in 2013 to assess dementia prevalence. Information on caregiving of the elderly was collected from 502 informants and included socio-demographic characteristics, type of caregiving (when applicable), mental health using the Self-Reporting Questionnaire (SRQ) – a WHO screening scale to detect cases of mental disorder based on a validated cutoff – and caregiving burden, when applicable, via the Zarit Burden Interview (ZBI) – a validated instrument commonly used to measure caregiver burden. Mean scores for SRQ and ZBI were computed. Binary logistic regression was performed to determine factors associated with being an SRQ case.

Results: 64 (12.7%) of elderly needed care. All informants of these 64 elderly were involved in care provision either as main caregivers (80%) or as partial care providers. Caregivers (n=64) had

significantly higher SRQ mean scores than non-caregivers. Among caregivers, those involved in hands-on care scored significantly higher on SRQ and ZBI compared to others. Being an SRQ case was associated with elderly's anxiety and not having a source of income (ORs 10.2 and 38.5 respectively). Dementia, although not significant due to small sample size, increased the OR of SRQ case by 2.2.

Conclusion: The study indicates the importance of considering the economic status and mental health of elderlies' caregivers. Financial and psychosocial support could alleviate the burden of psychological distress. Research is needed on appropriate interventions to address burden of caregiving.

Abstract # 3

Exogenous Galactosylceramide (GalCer) as potential treatment for CLN3 disease

Sally El-Sitt[1], Jihane Soueid[1], Nadine J. Makhoul[1], Joelle Makoukji[1], Rose-Mary Boustany[1, 2]
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Funding source: The work is supported by a generous grant from OpenMinds.

Keywords: CLN3 disease, galactosylceramide (GalCer), *Cln3Δ$^{ex7/8}$* mouse model, subunit C

Descriptive Statement: This work aims at investigating the impact of GalCer supplementation on the biochemistry, neuropathology and the behavior of homozygous Cln3$^{\Delta ex7/8}$ mice.

Introduction: background and aims Juvenile Neuronal Ceroid Lipofuscinosis (JNCL) or CLN3 disease, a disease that affects mainly children, leads to visual failure at an early age followed by seizures, motor decline and death at an early age. Pathological hallmarks include accelerated apoptosis and accumulation of autofluorescent material with subunit C of mitochondrial ATP synthase as its main protein component in neurons in the brain and other organs. The ~1 kb deletion eliminating exons 7/8 of the CLN3 gene represents the most common human mutation responsible for JNCL. CLN3 encodes a protein (CLN3p) consisting of 438 amino acids. Important roles of this protein are that it is antiapoptotic, and that it facilitates transport of galactosylceramide (GalCer), a crucial sphingolipid component of lipid rafts to plasma membrane, from its site of synthesis in Golgi via early endosomes. The mutated CLN3p results in disrupted anterograde transport of GalCer resulting in its retention in Golgi and recycling endosomes without localization to lipid rafts (LRs). To compensate, an increase in ceramide levels ensues, most likely aggravating apoptosis and resulting in massive neuronal loss. The *Cln3$^{\Delta ex7/8}$* knock-in mouse harbors the most common JNCL mutation and manifests a number of biochemical, neuropathologic and behavioral changes consistent with JNCL and, hence, is a good model to test therapeutic strategies.

Methods: An expanded mouse clinical trial with treatment over 44 weeks, and including a larger number of GalCer vs. vehicle treated mice is now underway to assess the impact of prolonged GalCer treatment on different aspects of the disease. This will be accomplished by assessing ceramide levels before and after GalCer injections in serum and brain, staining brain and organs for subunit C, examining for brain microglial activation and gliosis, and apoptotic indices. More importantly, the impact of GalCer administration on motor function and exploratory behavior of *Cln3$^{\Delta ex7/8}$* mice will be determined using a battery of behavioral tests comprising wire hanging, grip strength meter measures, pole climbing, rotarod and T-maze performance.

Results: Injections of GalCer in the *Cln3Δ$^{ex7/8}$* mouse for 44 weeks reduced subunit C accumulation in brain specifically in the cerebellum. Moreover, GalCer improved locomotor activity in affected mice.

Conclusion: GalCer daily injections will lead to improvement in the neuropathology of GalCer treated vs. vehicle treated mice with diminished gliosis and subunit C staining, decrease in apoptosis and ceramide levels, as well as an enhanced behavioral outcome. This will lay the groundwork for future clinical trials in humans.

Abstract # 4

Whole-exome sequencing in Lebanese families identifies novel causes of autism spectrum disorder

Jihane Soueid[1], Dikran Richard Guisso[1], Maria Chahrour[2], Rose-Mary Boustany[1]
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Corresponding author: Jihane Soueid - Postdoctoral fellow - E-mail: js61@aub.edu.lb

Funding source: The work is supported by a generous grant from OpenMinds.

Keywords: ASD; Whole-exome sequencing; GABRB2; HUWE1

Descriptive Statement: By using whole exome sequencing, we identified two novel mutations in genes implicated in neurodevelopmental disorders, but new to autism.

Introduction, background and aims. Autism spectrum disorders (ASDs) are a group of neurodevelopmental disorders with high heritability. In Lebanon, ASD prevalence in the greater Beirut and Mount Lebanon areas is 1/66 children (Chaya et al, 2015 JADD). Recent findings by our group (Soueid et al, Scientific Reports, NPG, Jan 2016) support a highly heterogeneous genetic etiology, including rare *de novo* and inherited mutations, chromosomal rearrangements, as well as double hits.

Methods: We performed whole-exome sequencing (WES) in 4 families having 1 or 2 affected children in order to identify novel causative genes and autism susceptibility variants. Validation of WES results was accomplished by Sanger sequencing in the families and in normal Lebanese controls (n=104).

Results: We identified 2 potentially causative genes in 2 out of 4 families analyzed. These variants are intronic substitutions in GABRB2 and HUWE1 genes, less than 100 base pairs away from the exon. They might alter splicing sites, or transcriptional regulatory elements causing a dysregulation of the pre-mRNA splicing process and dysfunction at the protein level. Mutations were successfully validated by Sanger sequencing in the family and were absent in 104 controls.
GABRB2 encodes for the β2 subunit of the γ-aminobutyric acid type A (GABAA) receptor, one of three main classes of receptors activated by GABA, the principal inhibitory neurotransmitter in the central nervous system. Mutations in genes encoding various subunits of this receptor are implicated in a number of neurological and developmental disorders, including epilepsy and autism. To date, genetic studies have implicated mutations in GABRB2 with intellectual disability and epilepsy, but not autism.
HUWE1 is an X-linked gene and encodes a protein that functions as an E3 ubiquitin ligase. HUWE1 is required for the ubiquitination and subsequent degradation of the BCL2-related anti-apoptotic protein MCL1, the p53 tumor suppressor, core histones, and DNA polymerase beta. Defects in HUWE1 cause mental retardation of the syndromic X-linked Turner type (MRXST). Recently, a de novo missense variant in HUWE1 was identified in a male ASD proband, but not in the proband's less severely affected brother.

Conclusion: WES analysis has proven to be an efficient strategy to identify de novo and inherited mutations that can contribute to ASD risk in the Lebanese. We were able to identify two novel variants in GABRB2 and HUWE1. Future functional studies in cellular models are underway to determine the contribution of these mutations to pathogenicity in autism.

Abstract # 5

PATTERNS AND DETERMINANTS OF MAMMOGRAPHY SCREENING IN LEBANESE WOMEN

Nadia Elias, MD[1]; Ibrahim R. Bou-Orm, MD, MPH[2,3]; Salim M. Adib, MD, DrPH[2,3]

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[2]Department of Epidemiology and Population Health, [3]Faculty of Health Sciences, American University of Beirut, Beirut, Lebanon
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Funding source: Roche International

Keywords: breast cancer, Health Belief Model (HBM), psychosocial factors, husband support, Arab, Middle-East.

Descriptive Statement: The aim of the study is to optimize the educational content of advertisement messages which accompany the annual national breast awareness campaigns by promoting a cognitive status in favor of annually repeating the screening mammography.

Introduction: The decision to engage in ever using and/or repeating a mammography test may be associated with psychosocial and socio-demographic factors. These associations were measured in 2014 among Lebanese women ≥40.

Methods: A cross-sectional sample of 2400 women was selected to represent the target population across Lebanon. All variables that showed significance in the bivariate analysis were analyzed in a multivariate logistic model.

Results: Of the total, 105 women (4.4%) had never heard of mammography as a tool for screening and early detection of breast cancer. Among 2295 women who had ever heard of it, 45% had ever used it, of whom 10% had obtained it for the first time within the year preceding the survey. Among 926 women who had the time opportunity to repeat the test, 67% had ever done so (Median life-time frequency: 2 mammograms). Older age, higher SES and living within the metropolitan Beirut area were significantly associated with ever-use. Perceived susceptibility, perceived benefits, ease of access and husband's attitude were also significant determinants. Only 4% reported opposition from husbands to their mammograms. For ever-repeating the mammography, higher education emerged as a significant socio-demographic determinant in addition to older age and higher SES. Perceived susceptibility remained significantly associated with repeating the mammography. Comfortability of the previous test was a significant determinant of re-use.

Conclusions: Socio-economic disadvantage affects the life-time performance of a mammogram. Providing the service free-of-charge at least during the campaigns may alleviate some obstacles. Women who perceived themselves as susceptible tended to repeat the test, which indicates the importance of continuously stressing that good test results one year do not make the cancer less likely or the test less important for the future. The comfortability of mammography testing should continue to be improved to ensure repetition.

Abstract # 6

Smoking among Lebanese Medical Students: Prevalence and Attitudes

Amanda Chidiac, MD[a]; Hani Tamim, PhD[a], Mohamad Kanso, MD[a] ; Arafat Tfayli, MD[a]

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Funding source: PI fund

Keywords: Smoking, Medical students, Tobacco, Smoking cessation

Descriptive Statement: A cross-sectional study investigating the prevalence of smoking among Lebanese medical students and the effect of their smoking habits on their clinical behavior.

Introduction: The tobacco epidemic is a major public health threat facing the world. Tobacco dependence is recognized as the greatest preventable cause of disease and death. Medical students are in key position influencing future tobacco cessation programs. The primary objective of this study is to evaluate the prevalence of smoking among medical students across Lebanon and their smoking attitudes. It also investigates their attitude towards smoking, showing where they really stand on this major public health issue. This study helps better tackle anti-smoking campaigns among both physicians and patients.

Methods: This cross-sectional study was conducted by sending a questionnaire to currently enrolled medical students at all seven medical schools in Lebanon. The 32-item questionnaire and comprised of three sections assessing socio-demographic characteristics, smoking habits, and attitudes towards smoking among Lebanese medical students. The questionnaire was launched online on Limesurvey in order to retain anonymity. The data was then transferred to SPSS for analysis. Data was expressed as percentages for discrete variables and as mean ± SD for continuous variables.

Results: 163 complete responses remained out of the 182 obtained responses. 42 of the total 163 students identified themselves as either daily or occasional smokers yielding a prevalence of 25.8%. Smokers were less likely to ask patients about their smoking habit and to counsel them about smoking cessation. Almost one third of smokers felt they had no obligations towards the society

Conclusion: Approximately 1 in 4 Lebanese medical students is a smoker. Students who smoke are less likely to ask patients about their smoking habits and to counsel them on smoking cessation. This is a major drawback in the fight against tobacco. This calls for better education of our future doctors on smoking cessation to decrease the smoking burden on our Lebanese society and worldwide.

Abstract # 7

Short relative telomere length (RTL) in peripheral blood is associated with breast cancer risk in the Lebanese

Sleiman F[1], Awada Z[1], Nasr R[2], Tfayli A[3], Boustany R[4], Makoukji J[4], Zgheib, NK[1]*

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

Keywords: Breast cancer, RTL, association study

Descriptive Statement: Relative telomere length that is critical for maintaining genomic stability is significantly shorter in breast cancer patients when compared to non-breast cancer controls.

Background: Telomeres play a critical role in maintaining genomic stability. Previous studies linked relative telomere length (RTL) with several cancer types. However, clinical studies on the association between blood RTL and breast cancer showed inconsistent results. Hence, more studies are required to solve this inconsistency.

Aims: Herein, we aim to address the following three questions: Is RTL in whole blood of breast cancer patients significantly different from that of non-breast cancer female controls? Is RTL altered in breast cancer tissues when compared to normal adjacent tissues? Is RTL in breast cancer tissues congruent with RTL in whole blood and circulating tumor DNA?

Methods: Lebanese breast cancer patients (n=87) of different IDC stages and grades have already been recruited at our institution, the American University of Beirut Medical Center (AUBMC), between 2012 and 2013. Peripheral blood and tissues were collected before treatment initiation and stored at -80°C. In addition, and after signing an informed consent, 501 Lebanese subjects, of whom 328 were females and older than 18 years of age were recruited from Greater Beirut between February and June 2014, and blood was stored. Telomere and single copy gene (human beta-globin) in peripheral blood were amplified by real-time polymerase chain reaction (RT PCR).

Results: RTL in peripheral blood of breast cancer patients was significantly shorter from that of non-breast cancer female controls (Mean RTL ± SD: 0.405 ± 0.099 vs. mean RTL ± SD of 0.93 ± 0.6, P= 0.000). Further work is in progress on cancerous and normal adjacent breast tissues, as well as on circulating tumor DNA to detect whether RTL is a biomarker for breast cancer development, severity, and outcome.

Conclusion: This is the first study to show that RTL is significantly shorter in Lebanese breast cancer patients when compared to non-breast cancer Lebanese controls. Analysis is ongoing to adjust for factors such as age, body mass index, known risk factors of breast cancer, smoking status, alcohol consumption, and complete blood count with % neutrophils.

Abstract # 8

Association between bisphenol A (BPA) levels and estrogen receptor alpha (ERα) promoter methylation in a cohort of Lebanese individuals

Awada Z[1], Akika R[1], Mogharbel N[1], Nasrallah M[2], Nakhoul N[2], Nasreddine L[3], Mouneimne Y[4], Abiad M[3], Koleilat L[3], Ismaeel H[2], Tamim H[2], Zgheib, NK[1]*

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

Keywords: BPA, ERα methylation, association study

Descriptive Statement: Urinary BPA levels may be associated with *ERα* promoter methylation in whole blood in a cohort of Lebanese individuals.

Background: Bisphenol A (BPA), a monomer of plastics, is an essential component of hard polycarbonate plastics and epoxy resins that are used in many consumer products. BPA has been shown to mimic estrogen in several in-vitro and in-vivo studies. Besides, BPA levels were shown to be associated with an increase in estrogen receptor alpha (ERα) gene expression levels in peripheral blood leukocytes, however no study investigated the association between BPA and *ERα* promoter methylation.

Aim: Herein, we aim to test the hypothesis that BPA is associated with *ERα* promoter hypomethylation, which may explain reported BPA-associated increase in ERα expression.

Methods: After signing an informed consent, 501 Lebanese subjects older than 18 years old were recruited from Greater Beirut between February and June 2014. A fasting urine sample was collected in a glass container to avoid any BPA contamination for BPA measurement. Peripheral whole blood was collected and stored at -80°C. Urinary BPA was measured using HPLC-MS and a C18 column with acetonitrile mobile phase. *ERα* promoter in peripheral blood was amplified from bisulfite converted DNA and sequenced using Sanger sequencing. Sequencing analysis of the methylation percentage of 5 CpG sites in *ERα* promoter was carried out using the epigenetic sequencing methylation software (ESME).

Results: The mean ± SD urinary BPA was 3.67 µg/L ± 4.76. Most participants had hypomethylated *ERα* promoter sites, and the mean methylation % ± SD was 5.25 ± 9.84. Besides, preliminary results showed that extremely high urinary BPA levels were associated with low average methylation % in *ERα* promoter, and that extremely high *ERα* promoter methylation % levels were associated with low urinary BPA levels.

Conclusion: This is the first study to evaluate the association between urinary BPA levels and *ERα* promoter methylation levels in peripheral blood. We suggest that *ERα* promoter hypomethylation is implicated in the previously reported BPA-associated increase in ERα expression, which may be the mechanism behind the potential association of BPA exposure with breast cancer risk. Further analysis is ongoing to adjust for factors such as age, body mass index, sex, glomerular filtration rate, menopausal status, and last menstrual period.

Abstract # 9

Association between bisphenol A (BPA) levels and relative telomere length (RTL) in a cohort of Lebanese individuals

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

Keywords: BPA, RTL, association study

Descriptive Statement: Urinary Bisphenol A may be associated with altered relative telomere length in whole blood in a cohort of Lebanese individuals.

Background: Bisphenol A (BPA), a monomer of plastics, is an essential component of hard polycarbonate plastics and epoxy resins that are used in many consumer products. BPA has been shown to mimic estrogen in several in-vitro and in-vivo studies. It has been reported that environmental chemicals and estrogen are correlated with relative telomere length (RTL) in peripheral blood. However, no study previously evaluated the association between the xenoestrogen BPA and blood RTL.

Aim: Herein, we aim to test the association between urinary BPA levels and blood RTL

Methods: After signing an informed consent, 501 Lebanese subjects older than 18 years old were recruited from Greater Beirut between February and June 2014. A fasting urine sample was collected in a glass container to avoid any BPA contamination for BPA measurement. Peripheral whole blood was collected and stored at -80°C. Urinary BPA was measured using HPLC-MS and a C18 column with acetonitrile mobile phase. Telomere and single copy gene (human beta-globin) in peripheral blood were amplified by real-time polymerase chain reaction (RT PCR).

Results: The mean ± SD urinary BPA was 3.67 µg/L ± 4.76. RTL has so far been measured in 249 blood samples with mean RTL ± SD of 0.93 ± 0.66. Further RTL measurement is in progress on this cohort. Preliminary results showed that extremely high urinary BPA levels were associated with short RTL, and extremely long RTL were associated with low BPA levels.

Conclusion: This is the first study to evaluate the association between urinary BPA levels and RTL in peripheral blood. We suggest that short RTL may be implicated in the potential association of exposure to high BPA levels with breast cancer risk. Further analysis is ongoing to adjust for factors such as age, sex, body mass index, glomerular filtration rate, smoking status, and alcohol consumption.

Abstract # 10

Half Dose Sugammadex combined with neostigmine is non-inferior to full dose sugammadex for reversal of rocuronium-induced deep neuromuscular blockade: a cost-saving strategy.

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Funding source: Institutional Funding.

Keywords: Combined reversal, half dose sugammadex, cost saving.

Descriptive Statement: Low dose sugammadex and neostigmine for cost saving.

Introduction: background and aims Sugammadex reverses the effect of rocuronium more rapidly and effectively than neostigmine, especially from deep levels of neuromuscular blockade (NMB). However, its cost is prohibitive. The combination of half dose sugammadex with neostigmine would be non-inferior to full dose sugammadex for the reversal of deep NMB. This approach would reduce the cost of sugammadex while preserving its efficacy.

Methods: Patients were randomly allocated to receive sugammadex 4 mg/kg (Group S) or sugammadex 2 mg/kg with neostigmine 50 µg/kg and glycopyrrolate 10 µg/kg (Group NS) for reversal of rocuronium-induced deep NMB. The primary outcome was the percentage of patients who recovered to 90% Train of Four (TOF) ratio within 5 min. The time to achieve full recovery (TOF ratio > 0.9) and the time to extubation were secondary outcomes. The non-inferiority margin was set at 10%.

Results: Twenty eight patients were enrolled in each group. The number of patients who reached 90% TOF ratio within 5 min was 27 out of 28 (96%) in group S versus 25 out of 28 (89%) in group NS by intention-to-treat analysis (Psup=0.6, difference: 7%, 95% CI of the difference: -9% to 24%). The number of patients who reached 90% TOF ratio within 5 min was 26 out of 26 (100%) in group S versus 23 out of 25 (92%) in group NS by per-protocol analysis (Psup=0.2, difference: 8%, 95% CI of the difference: -6% to 25%).

The time to achieve TOF ratio of 0.9 was 180.9±96.8 sec in group S and 228.2±83.9 sec in group NS (Psup=0.06, difference: 47.3 sec, 95% CI of the difference: -95.9 to 1.2 sec). The time from reversal to extubation was 504 ± 186 sec in group S and 544 ± 176 sec in group NS (Psup=0.5, difference: 29.6 sec, 95% CI of the difference: -126 to 66.8sec).

Conclusion: Sugammadex 2 mg/kg with neostigmine 50 µg/kg was at worst 9% and 6% less effective than sugammadex 4 mg/kg by intention-to-treat and by per-protocol analysis respectively, hence was non-inferior to the recommended dose of sugammadex.

Abstract # 11

Detection of Furfural and 5-hydroxymethyl Furfural in the aerosol of electronic cigarettes

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Funding source: Research was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Number P50DA036105 and the Center for Tobacco Products of the U.S. Food and Drug Administration.

Keywords: Electronic cigarette (ECIG), sweet flavored e-liquids, furan compounds (furfural and 5-Hydroxymethyl furfural (HMF))

Descriptive Statement: Electronic Cigarette (ECIG) is designed to deliver nicotine, flavorings, water and humectants like propylene glycol (PG) and/or glycerol (VG) in the form of aerosols. Unlike conventional cigarette, ECIG uses a heating coil to heat the e-liquid in the absence of combustion. However; the thermal degradation still delivers different toxicants depending on the chemical composition of the e-liquid. The aim of this study is to discuss the degradation of sugar additives in ECIG.
Position: Graduate Student

Introduction: The diversity of sweet flavorings has been immensely attributed to the use of ECIG among youth. The composition of sweet e-liquids includes the basic sugar components: glucose, sucrose and sorbitol which can lead to furans upon heating. In this study the aerosol generated from prepared sweet e-liquids were assessed for the formation of furan compounds under variable battery outputs and puff durations.

Methods: Liquids of varying concentrations were prepared by adding aqueous solutions of glucose, sucrose or sorbitol to a 70/30 PG/VG solution. Aerosols were generated using a commercially available ECIG operating at 4 and 10 Watts, using puff durations of 4 and 8 s. Aerosols were trapped on filter pads and extracted and purified using solid phase extraction (SPE) technique. Quantification of furfural and 5-Hydroxymethyl furfural (HMF) was achieved using a novel gas chromatography/mass spectroscopy (GC/MS) technique.

Results: Furfural and HMF were found in aerosols under all conditions. Furan emissions increased with sweetener concentration, electric power, and puff duration, and for some conditions the per-puff yields exceeded values previously reported for combustible cigarettes.

Conclusion: The addition of sweeteners to ECIG liquids likely increases ECIG user exposure to furans. The obtained results call into question the safety of flavors in e-liquids.

Abstract # 12

Clinical Profile of Amblyopia across Age Groups

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Keywords: Amblyopia; age groups; clinical profile.

Descriptive Statement: Amblyopia (lazy eye) can be caused by many eye conditions, namely strabismus (eye misalignment), anisometropia (different prescription in each eye), deprivation (media opacities obscuring the visual axis), or by any combination of the above causing underdevelopment of the visual pathway in the affected eye due to sensory deprivation. Treatment is only possible during the sensitive period of visual development (8-9 years of age), after which visual loss is irreversible. Causes of amblyopia and treatment outcomes thus vary by age groups.

Introduction: background and aims: In Lebanon, there is scarce literature on the clinical characteristics of amblyopia. A survey done in 1996 on children aged 5-12 years showed that 5% of subjects screened had refractive error, suggesting that the burden of amblyopia may be underestimated. It was thus important to conduct this study to further characterize the epidemiology of amblyopia in the Lebanese population across different age groups and compare it to similar reports from other countries.
The aim of the current study was to look at the clinical profile of patients with amblyopia in the ophthalmology service at the American University of Beirut Medical Center in the past 6years across different age groups. Eye examination parameters (including visual acuity, motility and refractive errors), causes of amblyopia and treatment outcomes were compared across age groups.

Methods: This study was a retrospective chart review of all patients diagnosed with amblyopia at the pediatric ophthalmology service, American University of Beirut Medical Center (AUBMC) between September 2009 and September 2014. The study was approved by the Institutional Review Board of the American University of Beirut and informed consent was waived.

Results: Mean age at diagnosis and follow-up time were 6.3±6.1years(y) and 13.5 ±21.8 months (m) respectively. The two main causes of amblyopia were anisometropia (36.1 %), which was significantly more prevalent in patients diagnosed at ages 3-7 y ($p=0.03$) and 8-15 y ($p<0.001$), and strabismus (33.2%), which was common among patients diagnosed <3 y ($p<0.001$). Strabismus and anisometropia were equally prevalent in those detected ›15 y. Visual acuity was better in anisometropes compared to strabismic patients. A significant difference between baseline and final visual acuity was noted among patients in age groups: 3-7y ($p‹0.001$) and 8-15 y($p=0.04$). Treatment success was significantly associated with anisometropic amblyopia as compared to strabisimic and mixed types.

Conclusion: Strabismus was the main cause of amblyopia below 3 years of age, while anisometropia accounted for amblyopia in older children (3-15 years) as it could go unnoticed. With more than a quarter diagnosed late (after 8 years of age), the need to screen earlier is essential to attain better visual outcomes. Early and standardized amblyopia screening is needed as anisometropia can be asymptomatic; urgent referral as soon as suspicion of amblyopia arises is of paramount importance to prevent irreversible visual morbidity.

Abstract # 13

Sensory Characterization of Bowel Cleansing Solutions

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Funding source: This research received no specific funding.

Keywords: laxatives; sensory evaluation; taste; preparation; acceptability; colonoscopy

Descriptive Statement: To evaluate the sensory characteristics of commercial bowel cleansing solutions.

Introduction: background and aims Bowel preparation is an important quality indicator in colonoscopy. Patient adherence may be significantly affected by the unpleasant taste of purgative solutions and patients may suffer from several reported side effects including abdominal bloating, nausea and vomiting. To date, no major studies have investigated the sensory properties of bowel cleansing solutions using comprehensive sensory evaluation techniques.

Methods: Descriptive analysis was conducted with trained panelists (n=14) for 4 commercial bowel cleansing solutions [polyethylene glycol electrolyte solution (PEG), PEG + ascorbic acid (PEG-Asc), sodium picosulfate (SPS), and oral sodium sulfate (OSS)] using a 15-cm line scale with the Compusense at-hand® software, to create a sensory profile for the solutions. Acceptability testing (n=80) was conducted with untrained panelists (n=80) using the 9-point hedonic scale. Moreover, a Just-About-Right (JAR) scale was included for the four basic tastes to determine their intensity compatibility with acceptability levels in the products.

Results: Samples were significantly different on descriptive analysis for all attributes ($p<0.05$) except sweetness. SPS received the highest ratings for turbidity, viscosity-appearance, orange odor and flavor; PEG-Asc for citrus odor and flavor; OSS for sweetener taste, sweet aftertaste, bitterness, astringency, mouthcoating, bitter aftertaste and throatburn, and along with PEG-Asc, the highest ratings for saltiness, sourness and adhesiveness. Acceptability results showed significant differences between the samples ($p<0.05$). SPS received significantly higher ratings for overall acceptability, taste, and mouthfeel ($p<0.05$). Ratings on the JAR scale showed that PEG and PEG-Asc were perceived as slightly too salty; SPS and OSS were slightly too sweet, while SPS, PEG-Asc and OSS were slightly too sour and OSS slightly too bitter.

Conclusion: Further improvements are needed to enhance the sensory profile and optimize consumer acceptability for better compliance with bowel cleansing solutions.

Abstract # 14

Flupirtine Analogue Structure-Activity Relationships for Treatment of Batten Disease

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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.

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 flupirtine derivatives were tested by establishing growth curves under pro-apoptotic conditions of etoposide treatment assessed by trypan blue and Propidium Iodide. Flupirtine derivatives with desirable activity at the optimum concentration were evaluated by Trypan blue staining after siRNA knockdowns of CLN3 gene in PC12 cells.

Results: Three of the flupirtine analogues with specific chemical substitutions proved to be neuroprotective after the application of etoposide to PC12 cells. After knocking down the CLN3 gene in PC12 cells, the same three drugs prevented neuronal cell death. These drugs had a better neuroprotective effect than 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.

Abstract # 15

Nanohybrid conjugated polyelectrolytes: highly photostable and ultrabright nanoparticles

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Funding source: This work was supported by TWAS ,the Lebanese National Council for Scientific Research and the University Research Board at the American University of Beirut (AUB).

Keywords: Fluorescence, Conjugated polyelectrolyte, Amphiphilic polymer, Photophysical properties, Brightness, and Photostability

Descriptive Statement: we present a straightforward one-step approach to enhance the photophysical properties of conjugated polyelectrolyte (poly [5-methoxy-2-(3-sulfopropoxy)-1,4-phenylenevinylene](MPS-PPV) upon complexing it with an amphiphilic polymer (polyvinylpyrrolidone)(PVP).

Introduction: Conjugated polyelectrolytes are remarkable class of material with a wide range of applications ranging from light emitting diodes to biosensing and bioimaging. However, despite their huge potential, they still suffer from photo-blinking, irreversible photo-bleaching and low quantum yield which limits their implementation into various applications. In this work, we aim at improving the photophysical properties of commercially available conjugated polyelectrolyte (MPS-PPV) by tuning their microenvironment through complexing them with amphiphilic polymer (PVP).

Methods: A solution of MPS-PPV was mixed with different molecular weights of PVP to form nanohybrid particles. To probe the interaction between MPS-PPV and PVP, the fluorescence emission of MPS-PPV was monitored upon adding incremental amount of PVP. To further understand the interaction between MPS-PPV and PVP, a series of quenching experiments was conducted. We next focused our attention on studying the nanohybrid photostability at ensemble and single molecular levels, MPS-PPV/PVP nanohybrid particles was subjected to continuous excitation at 450nm and 488nm respectively.

Results: A 23 folds increase in the fluorescence emission of MPS-PPV was achieved accompanied with a red shift in the emission spectra upon complexing it with PVP. A nanohybrid system with improved photostability and with brightness that is ca. 450 times higher than conventional organic dyes was achieved.

Conclusion: The intimate interaction between MPS-PPV and PVP results in the deaggregation of conjugated polymer backbone. As a result, the interchain energy transfer is inhibited and thus enhanced the emission intensity and the quantum yield of MPS-PPV. In addition, PVP provides a protection shell against the interchain impact between freely diffusing polyelectrolyte which consequently led to enhancing their photostability.

Abstract # 16

Tunable Nanothermometer Based on Short Poly(phenylene ethynylene)

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Funding source: Lebanese National Council for Scientific Research (LCNRS #102901), University Research Board (URB #102848 and #103009)

Keywords: Conjugated polyelectrolyte, temperature sensing, nanothermometer, ratiometric fluorescent

Descriptive Statement: We report a self-referencing ratiometric fluorescent nanothermometer based on a short conjugated polyelectrolyte (CPE) complexed with a large amphiphilic polymer.

Introduction: Precise thermal sensing at the nanoscale is essential for various nanotechnological and nanomedical applications; however, such applications have posed a significant challenge that traditional contact-based thermometers have failed to meet. Ideal thermometry at this scale should be simple and non-invasive and provide swift readout with minimal signal calibration over time. Ratiometric fluorescent nanothermometry can satisfy these conditions. We report a highly reproducible single-component ratiometric fluorescent probe that is tunable over three important aspects: thermal sensitivity, time response, and isoemission point.

Methods: The probe was prepared by complexing poly (phenylene ethynylene) carboxylate (PPE-CO_2-7) with 10K, 55K, and 360K polyvinylpyrrolidone (PVP) in 10mM HEPES and 150mM NaCl buffer solution (pH=7.3). Steady-state fluorescence spectroscopy was carried out using Thermo Fisher Lumina spectrometer equipped with a temperature controller unit. To maintain a homogeneous temperature, the solution was continuously stirred at 400 rpm. Fluorescence emission spectra were acquired upon excitation at 420 nm, and the solution was allowed to stabilize for three minutes before each measurement.

Results: PPE-CO_2-7 complexed with each of the three PVP molecular weights displayed highly accurate and reproducible thermal sensitivities within a useful temperature range (15.0 ^{o}C - 70.0 ^{o}C). The PVP destabilizes the CPE π-π stacking, which makes it possible to shift the equilibrium between the less emissive destabilized state and the more emissive dissolved chains of the CPE within the temperature range. With increasing PVP molecular weight, the sensitivity for the probe increased while the corresponding response time decreased. In addition, the isoemission point was found to be dependent on the PVP concentration, thus it may also be tuned accordingly.

Conclusion:

We believe the reported nanothermometer will prove instrumental in ongoing efforts to accurately map and investigate heat production and dissipation at the nano level. This system displays the highest sensitivity of any single-component, ratiometric nanothermometer to our knowledge, with highly versatile tunability, therefore making the PPE-CO_2-7/PVP system readily applicable for mapping thermal fluctuations at the nanoscale.

Abstract # 17

Towards an Ultrasensitive Detection of Traumatic Brain Injury Biomarkers

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Funding source: Farouk Jabre Biomedical Research Grant

Keywords: Traumatic Brain Injury (TBI) - Sandwiched Assay- Differential Pulse Voltammetry (DPV) - Flow Cytometry

Introduction: The call for an early and consistent detection of traumatic brain injury is escalating as the number of victims, caused mainly by motor vehicle use, is dramatically increasing. Therefore, having an ultrasensitive testing device for protein biomarkers will facilitate a more routine clinical assessment for molecules that are signs of the disease. As such, we aim at developing a biosensor platform based on electrochemical and fluorescent methods that would allow us to detect trace amount of biomarkers specific for TBI.

Methods: The electrochemical scheme includes fabrication of nanostructured gold micro-electrodes using amperiometry, functionalization of antibodies specific for TBI biomarkers and building of a sandwiched assay of antigen-antibodies coupled with silica nanoparticles. The sensing strategy depends on monitoring the current at each step using differential pulse voltammetry. Whereas, the fluorescent scheme includes the use of gold-coated polystyrene beads, functionalization of antibodies specific for TBI and building of a sandwiched assay of antigen-antibodies coupled with labeled liposomes. The sensing strategy depends on monitoring the fluorescence shift using flow cytometry.

Results: We succeeded in getting high sensitivities of antigen concentration (ng/ml) and low signal-to-noise ratios.

Conclusion: We have reached an advanced stage in the development of an ultrasensitive approach for the detection of traumatic brain injury.

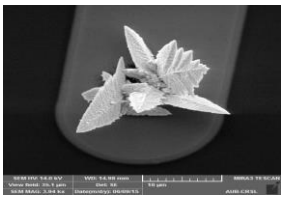

Figure1. SEM image of a nanostructured gold microelectrode

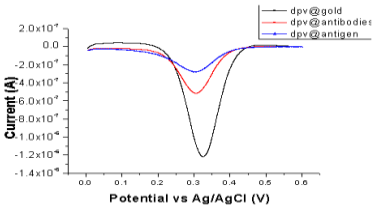

Figure 2.Differential Pulse Voltammogram showing the signal decrease after each incubation

Abstract # 18

Conjugated Polyelectrolyte a Tool for Cellular Imaging and Cellular Targeting

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Funding source: Lebanese National Council for Scientific Research (LCNRS #102901), University Research Board (URB #102848 and #103009)

Keywords: nanohybrid conjugated polyelectrolytes, fluorescence imaging, cell targeting

Introduction: Conjugated polyelectrolytes (CPEs) consist of two parts; a π-conjugated backbone and a water-soluble ionic side chain. These properties make CPEs useful for biomedical applications. Moreover, complexing poly[5-methoxy-2-(3-sulfopropoxy)-1,4-phenylenevinylene] (MPS-PPV); an anionic conjugated polyelectrolyte, with an amphiphilic macromolecule polyvinylpyrrolidone (PVP) makes its feasible to functionalize our system for imaging purposes as well as specific cell targeting. Our aim is to characterize the interaction between the nanohybrid CPE (MPS-PPV/PVP) and Hela cells. As a proof of concept, we functionalized PVP with folic acid for targeting cancer cells overexpressed with folate receptors.

Methods: We used flow cytometry to study the uptake of the nanohybrid CPE. Confocal fluorescence imaging was used to verify the location of the nanohybrid CPE. CellTiter-Blue assay was used to monitor cell viability.

Results: Our results showed that MPS-PPV demonstrated a higher brightness and specificity towards Hela cells compared to MPS-PPV/PVP55K. We also used different molecular weights of PVP (10K, 29K, 55K, 360K, and 1300K) where MPS-PPV/PVP 10K showed the highest fluorescence intensity. Confocal fluorescence imaging showed that MPS-PPV are internalized inside Hela cells, however, complexing it with PVP55K prevented it from efficiently entering the cell. Furthermore, cell viability was evaluated by using cell titer blue assay, and showed that MPS-PPV and MPS-PPV/PVP55K has no effect on HEK cells viability. To target specific cells we decided to functionalize PVP with folic acid and tested them against Hela cells that are known to be over-expressed with folate receptors. MPS-PPV/PVP folic acid showed higher brightness compared to MPS-PPV/PVP10K, suggesting the specific targeting and internalization of MPS-PPV/PVP folic acid into Hela cells.

Conclusion: Nanohybrid conjugated polyelectrolytes presents a powerful tool for cellular imaging due to their high brightness and exceptional photostability. Moreover complexing CPE with PVP opens up new domains for cell targeting and possibly drug delivery through functionalizing PVP.

Abstract # 19

Pleurobiliary Fistula from Iatrogenic Cosmetic Liposuction

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Keywords: *Liposuction; Biliary fistula; Laparoscopy*; *liver trauma*

Funding: None

Descriptive statement: Liposuction is generally a safe aesthetic procedure which sometimes can be associated with serious morbidity and mortality. We report a case of a 26-year-old female patient who was referred to our institution from a cosmetic clinic with shortness of breath and abdominal pain post body liposuction.

Background: Liposuction is the one of most frequent aesthetic procedure performed in plastic surgery. It can be associated with major complications when performed by inexperienced physicians. The limited training of personnel and the limited setup may be associated with lethal postoperative complications. The aim of this paper is to present a serious complication from liposuction.

Methods: In this case report, literature was reviewed on liposuction complications. Clinical presentation and diagnostic studies were reported. The surgical management was elaborated.

Results: 26 year old female patient underwent extensive liposuction in an outpatient cosmetic center. Postoperatively, the patient complained of worsening dyspnea that was left unnoticed on outside basis. She presented 5 days later to our emergency room. Chest X ray showed significant right pleural effusion. Thoracocentesis revealed bilious fluid suggestive of bilothorax. Exploratory laparoscopy was performed and revealed multiple bilious collections, 2 holes in the diaphragm with 2 corresponding liver lacerations and a perforation at the gallbladder tip. Drainage of the collections was performed with a cholecystectomy and intraoperative cholangiogram. The patient did well postoperatively and was discharged home after 2 days.

Conclusion: Despite our reported complication, liposuction remains a safe procedure that will be performed by many physicians. To lower the complication rate, physicians should obtain and maintain adequate surgical and esthetic training. In addition, extensive liposuction should be performed in a medical center with adequate resources and backup rather than a cosmetic center. To our knowledge, this is the first reported case of iatrogenic bilothorax secondary to liposuction.

Abstract # 20

Surgical Training at the American University of Beirut Medical Center: From a Resident Perspective

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Keywords: *Surgical education; Residency; Training*

Review of the surgical training program at the AUBMC using a survey

Ghina El Nounou: Research Assistant

Funding: None

Introduction: The history of the American University of Beirut Medical Center (AUBMC) and the Department of Surgery dates back to 1867. It started in a small building in Beirut which turned into a 200-bed hospital few years later to become a state-of-the-art medical center in 1970. Up-to-date surgical education and training is one of the main targets of the university and department.

Background and Aims: Surgical residency training is continuously undergoing changes. Finding the specific strengths and weakness of our program might help to improve the current curriculum, and input changes that are relevant and address the perceived strengths, weakness, and concerns of the residents in that specialty. The aim of this study is to identify all weaknesses and make a plan to improve the program.

Methods: An anonymous, cross-sectional, web-based survey was sent to all surgical residents. The questions are primarily closed ended, multiple choice and consisted of Likert scales. Descriptive and correlative statistics will be used to analyze the responses among residents.

Results: There was an 85% (57/67) response rate to the survey. The responders are from various surgical specialties at the AUBMC, 93% of which were males. 30.4% belonged to the age group 20-25, 62.5% 26-30, and the rest were 31-35. The survey covered the subjects of study habits, satisfaction with facilities provided, their participation in the operations and satisfaction with attending' teaching, attitude towards research, along with many others teaching and educational tasks.

Conclusion: Many challenges and weaknesses have been identified in our programs; we suggest several solutions and present a moral obligation of gargantuan proportions to this generation of surgeons and at the same time a unique opportunity to shape the future of our profession and the way we serve our patients. Change takes time, but it begins with acceptance of the need for change. We need to educate in what we practice and certify by what we do.

Abstract # 21

Collaborative Storage and Research Use of Human Biospecimens between MSKCC and AUB

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Keywords: *Human Biospecimens; Collaborative storage, tissue bank*

Introduction to the tissue bank project conducted at AUB in collaboration with MSKCC

Ghina El Nounou: Research Assistant

Funding: None

Introduction: In order for biomedical research to help in advancing knowledge about diseases, and developing new treatments and preventive measures, the creation of repositories of human biospecimens is imperative. Research laboratories at AUB (American University of Beirut) and MSKCC (Memorial Sloan-Kettering Cancer Center) conduct studies on cell development and function. For this reason, AUB and MSKCC strive to maximize the number of biospecimens in their repositories that are made available for future research.

Background and Aims: As biospecimens are ultimately institutional resources, biologic specimens-tissue, blood or other body fluids- with benign or malignant disease that are left over after all intended diagnostic tests for clinical care are stored at our facilities. This project aims to procure and maintain a repository of human biological specimens for distribution to investigators, while maintaining confidentiality of patients.

Methods: Left over biospecimens are procured and stored in the pathology department by the Tissue procurement service in a manner consistent with high standards for the protection of human participants in research. Patients are approached by consenting professionals to obtain the consent as part of the informed consent process. The objective and nature of the study is explained, as well as the voluntariness of the process.

Results: In the course of 2 years, over 270 samples were collected from the patients to perform research studies. The sample types vary, the organ from which samples were procured include among others: thyroid samples, breast, brain, stomach, pancreas, liver, intestine, colon, and rectum. They include a vast variety of pathologies.

Conclusion: The stored biospecimens will play a vital role in the development of anticancer interventions benefitting from the size, diversity, and richness of demographic and clinical information linked to the specimens. Our repository of human biospecimens has grown and will continue to grow as more samples are being stored daily.

Abstract # 22

Laparoscopic management of Primary Splenic Hydatid Disease

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Keywords: Laparoscopic surgery, Echinococcus, Hydatid disease

Hussein Nassar: Medical Student year IV

Funding: None

Descriptive statement: Hydatid disease is caused by infection with the tapeworm Echinococcus. It is a common disease in agricultural societies and in endemic areas in the Middle East. While approximately 50% of detected cases occur in asymptomatic patients, many more cases remain undiagnosed or are found incidentally at autopsy.

Background: Primary splenic hydatid disease is very rare. Usually,it is secondary to spontaneous spread of cysts or after operations involving hydatidosis in other organs. The rare contamination of the spleen is related to the anatomy of the portal vein system and the flow of the embryos of the tapeworms. We report a very rare case of isolated splenic hydatid cyst managed with laparoscopic cystectomy.

Methods: This case report includes literature review about primary splenic hydatidosis and the management of such a rare entity. The clinical presentation of the patient is elaborated with emphasis on the role of laparoscopic cystectomy.

Results: A 50 year-old male patient presented with multiple episodic dyspnea associated with angioedema and hypotension on outside basis. Workup revealed a splenic hydatid cyst and was started on albendazole. He underwent laparoscopic partial cyst de-capsulation with preservation of the spleen. Patient did well with no intraabdominal spillage or anaphylactic reactions and was discharged home 2 days postoperatively.

Conclusion: Although laparoscopic management of splenic hydatid disease is established worldwide, however there is reluctance to perform it probably because of the concern of spillage predisposing to anaphylaxis and recurrence. Laparoscopic partial splenic resection might be the best procedure for treating cysts located deep in the splenic parenchyma when most or the entire cyst wall is covered by splenic tissue.

Abstract # 23

Update on Liver Transplantation: A Single Center Experience from 1998 to Present

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Keywords: liver transplantation; cadaveric donation; living donor graft; Lebanon

Randa Raad: Clinical Transplant Coordinator

Funding: None

Introduction: Liver transplantation is the treatment of choice for patients with cirrhosis, decompensated disease, acute liver failure and other liver diseases. At AUBMC, liver transplantation numbers increased due to the establishment of a specialized unit and adjusted logistics.

Background: The aim of this study is to review all liver transplants performed at the American University of Beirut Medical Center from 1998 to present.

Material/Methods: From 1998 to present, 24 liver transplants were performed at AUBMC. Of these, 17 were adults and 7 were children. Indications for adult transplants : 2 alcoholic liver cirrhosis, 2 hepatitis B, hepatitis C with HCC, 1 sub-acute liver failure, 1 budd-chiari syndrome, 1 biliary cirrhosis secondary to iatrogenic common bile duct injury, 1 multiple hydatid disease of the liver, 5 autoimmune hepatitis, and 1 vanishing bile duct syndrome. Pediatric transplant indications: 3 cryptogenic liver cirrhosis, 1 extrahepatic biliary atresia, 1 familial hypercholesterolemia, 1 familial intrahepatic cholestasis, and 1 congenital hepatic fibrosis. Of the 23 transplants, 7 were living related.

Results: Patient survival was 74% at 1, 5 and 10 years. There were 6 deaths at a median of 9 days (range 1-56) post-transplantation. The causes of death: 2 primary non-functions, 2 intraoperative cardiac arrest, 1 portal and hepatic artery thrombosis, and 1 severe cellular rejection. There were 2 biliary complications and 2 major vascular complications. All 18 survivors are well, with normal liver function tests at a median follow-up time of 93 months (range 10-185) post-op.

Conclusions: Cadaveric organ donations should be encouraged to increase the number of transplants. Living related liver transplant is an important alternative source of organs, but shouldn't replace cadaveric donation. The broadening gap among organ provision and the waiting list is the main restraint.

Abstract # 24

Pancreaticoduodenectomy in the Middle East: A Single Center Experience

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Keywords: Pancreaticoduodenectomy, Pancreatic Cancer, Tumor.

Hussein Nassar: Medical Student year IV

Funding: None

Descriptive Statement: Pancreatic cancer is one of the leading causes of cancer death because of short-term survival time, regardless of the stage. It is mostly seen in the elderly population, and the overall 5-year survival rate is below 5%.

Background: Pancreatic cancer is the fourth leading cause of death from cancer among men and women. Radical surgical approach is still the only hope to cure it. Since most patients present with an advanced stage, only 20% of patients can be resected. We are presenting our 20-years' experience in pancreaticoduodenectomy.

Materials and Methods: A retrospective data analysis review was performed for all patients who underwent pancreaticoduodenectomy at our institution from January 1994 to December 2014. Clinicopathological data as well as variables such as age, gender, post-op complication day, and presentation were retrieved from the medical records. The aim of this study was to evaluate the prevalence of pancreatic cancers, surgical complications, morbidity and mortality rates, and to compare the overall outcomes between past and present to improve surgeons' performances and patients' outcomes.

Results: From January 1994 to December 2014, 370 patients underwent pancreaticoduodenectomy at our institution. Of the 370, only 256 charts could be retrieved from the medical records. Out of the 256, 167 male and 89 female patients with a median age was 60 years (range 13-84). The most presenting symptoms were jaundice and abdominal pain. The median levels of Ca 19.9 were 90.1 (0.6-45707). Pancreatic adenocarcinoma was the most common pathology (47%). The median length of hospital stay was 13 days (range 4-89 days).Of the 256, 153 were alive at 3 months and 103 at 1 year. Post-operative complications were: Pancreatic fistula in 13%, bile leak in 2% and delayed gastric emptying in 18%.

Conclusion: Pancreaticoduodenectomy is the only chance of cure, but it has significant mortality and morbidity even in high volume centers. At AUBMC, the number of patients has been increasing annually with good results in terms of morbidity and mortality.

Abstract # 25

Antibacterial activity of Polyvinylpyrrolidone coated with silver nanoparticles

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Funding source: This work was supported by TWAS

Keywords: Antibacterial activity, silver nanoparticles, polyvinylpyrrolidone

Descriptive Statement: The well-known bactericidal capacities of silver were coupled with the stabilizing properties of polyvinylpyrrolidone (PVP) to create a stable complex able to completely inhibit bacterial growth at very low concentrations of silver.

Introduction: Bacterial attachment to a surface leads to the formation of a biofilm that is difficult to treat clinically. The hazardous of the formation of such biofilms spreads over a large scale, from disturbances to industrial setups to creation of health hazards. The growing resistance of microorganisms to traditional antibiotics is making them difficult to treat, increasing the mortality rate of such drug resistant infections. Hence the need of a new and effective antimicrobial agent. PVP was employed for its rough and porous morphology which enhances bacterial adhesion, which was then coated with silver nanoparticles as bactericidal agents. The system formed thus acts like a trap, attracting the bacteria by its nanostructured surface, only for that bacteria to be killed upon contact with silver. The antibacterial activity of the complex formed was studied.

Methods: two assays were employed to test for the antibacterial activity of silver: a TTC assay and a life/dead cell assay. The TTC assay is based on the capacity of live bacteria to reduce triphenyltetrazolium chloride (TTC) into red formazan. The live/dead cell assay helps separate and quantify live and dead cells by fluorescence signal using a flowcytometer.

Results: both assays proved the antibacterial activity of PVP-Ag. Bacterial growth was completely inhibited at a remarkably low concentration of 80µg/ml. more importantly, it was shown that PVP alone is able to enhance bacterial growth.

Conclusion: Results suggest that the PVP-Ag complex can act as a tuning agent of bacterial growth, enhancing or inhibiting bacterial growth by changing silver concentration. Such properties can open vast prospects of research and application.

Abstract # 26

Phosphorus supplementation improved growth rate of rats maintained on gluten diet.

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Funding source: -

Keywords: *Phosphorus, Weight gain, Growth, Gluten, cereal protein, Lysine*

Abstract:

Introduction: Wheat gluten is the major protein source in many developing countries. Gluten lacks some essential amino acids, primarily lysine, and, accordingly, can't foster optimal growth. Further, wheat is known to contain limited amounts of available phosphorus. In rats, the addition of phosphorus to a low complete protein diet (10%) was reported to yield a weight gain comparable to normal protein (20%) diet. This study investigates the effect of phosphorus addition to low incomplete protein diets on growth.

Methods: Forty male rats were randomly divided into four groups and maintained on diets containing 10% protein as wheat gluten (G) with added lysine (L) or phosphorus (P) or lysine plus phosphorus (L+P). Body weight and food intake were measured 2 times/week for 9 weeks.

Results: The L and P groups had similar weight gain, food intake and energy efficiency, and these were lower than that of the L+P group, but higher than that of the G group

Groups	G	L	P	L+P	p-value*
Weight gain (g/d)	0.152 ± 0.245^{a}	1.013 ± 0.382^{b}	0.859 ± 0.314^{b}	3.915 ± 0.905^{c}	<0.001
Food intake (g/d)	17.36 ± 2.28^{a}	20.37 ± 3.34^{b}	19.17 ± 2.37^{ab}	25.54 ± 2.73^{c}	<0.001
Energy efficiency (g/100kcal)	0.213 ± 0.335^{a}	1.199 ± 0.432^{b}	1.064 ± 0.351^{b}	3.627 ± 0.478^{c}	<0.001

*One way analysis of variance (ANOVA), Groups with different subscripts are significantly different using Fisher test

Conclusion: The addition of phosphorus to a diet based exclusively on wheat gluten lacking in lysine exhibited similar effects on weight and food intake as diets supplemented with lysine. The data suggest that both phosphorus and lysine are needed to sustain growth of rats fed low quality protein diets.

Abstract # 27

Increased postprandial energy expenditure following the addition of phosphorus to a high carbohydrate meal.

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Funding source: URB

Keywords: Diet induced thermogenesis (DIT), postprandial energy expenditure, adenosine triphosphate (ATP), phosphorus.

Descriptive Statement: Phosphorus is required for ATP production and is known to be involved in energy metabolism. However, it's not clear whether phosphorus ingestion with meal can affect energy expenditure.

Introduction: background and aims: Both overweight and obesity are increasing globally and recognized to cause main health problems nowadays. Weight gain results from an imbalance between energy intake and energy expenditure. Diet induced thermogenesis (DIT) accounts for 5-15% of total energy expenditure and is mainly related to ATP production that depends on phosphorus (P) availability. Our objective was to determine the effect of P ingestion with high carbohydrate meal on postprandial energy expenditure. We hypothesized that P ingestion increases postprandial thermogenesis of the subjects.

Methods: A cross over study was conducted on six lean male subjects. Subjects received a 500 Kcal high carbohydrate meal with (500 mg of P) or without P. Energy expenditure was measured at baseline and at 30 minute intervals for 4 hours following meal ingestion using a ventilated hood and canopy system COSMED QUARK CPET unit.

Results: Postprandial energy expenditure of meal containing P was significantly higher than that of placebo ($p=0.007$). This increase was associated with a significant rise in fat oxidation (%) ($p= 0.022$), while carbohydrate oxidation (%) was decreased ($p= 0.023$).

Conclusion: P was able to increase postprandial energy expenditure mainly due to increased fat oxidation. This data may have promising effect for the management of obesity.

Abstract # 28

TPEN induces DNA damage in human colon cancer cells: Role of Chk1/2 and DNA-PK

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Keywords: Metal chelation; redox cycling; copper; ROS; anticancer

The statements made herein are solely the responsibility of the authors.

Maamoun Fatfat: Postdoc

Funding source: This work was funded by NPRP grant # 09-047-3-012 from the Qatar National Research Fund.

Abstract

Background: The cell permeable and high affinity zinc chelator TPEN has been shown to induce apoptosis in many cancer cell lines; however, its DNA damage potential and mechanism has not been studied before. We have recently shown that the zinc chelator TPEN increases the generation of ROS which selectively kills colon cancer cells. We have also provided evidence that the redox cycling of copper is responsible for TPEN anticancer effects. In this study, we investigated if TPEN induces DNA damage and deciphered the signaling pathways involved in DNA damage in response to TPEN. **Methods**: DNA damage response to TPEN was investigated by cell viability assays, comet assays, reactive oxygen species by DCFH, gene knockout by siRNA transfection, apoptosis by Annexin assays, Immunocytochemistry by flow cytometry, and protein expression by western blot. **Results:** We show that cell death by TPEN is associated with significant DNA damage, an effect that was dependent on ROS generation and on the redox cycling of copper, as evidenced by reversal of DNA damage in the presence of antioxidants (NAC, CAT) or the copper chelator Neocuproine (Neo). DNA damage was associated with increased expression of γ-H2AX and a significant activation of ATM/ATR signaling molecules. Pre-incubation of cells with inhibitors of ATM and DNApk reversed DNA damage caused by TPEN. The involvement of DNApk and ATM/ATR pathways in TPEN-mediated effects was further confirmed by the fact that silencing DNApk and Chk1 reversed DNA damage caused by TPEN. **Conclusion:** This study shows for the first time the involvement of DNApk and Chk1 in TPEN-induced DNA damage and confirms our previous findings that the redox cycling of copper is the main mechanism by which TPEN induces cell death in human colon cancer cells.

Abstract # 29

The Loss of Connexin 43 Induces Breast Cancer Initiation Presumably by Positive Regulation of the Wnt/β-catenin Pathway

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

Keywords: Breast cancer, Connexin 43, Gap junction complex, Wnt/β-catenin pathway

Descriptive statement: The loss of connexin 43 (Cx43) induces disassembly of gap junction (GJ) complex and releases β-catenin from membrane sequestration, a mechanism through which it possibly activates the Wnt/β-catenin pathway and drives breast cancer initiation.

Introduction: background and aims Reduced expression of connexin 43 (Cx43) reported in breast cancer, suggests a tumor suppressive role. Silencing Cx43 in HMT-3522 S1 cells (S1 cells hereafter), non-tumorigenic breast epithelial cell line, induced phenotypic changes indicative of breast cancer initiation. This study aims to delineate the mechanism through which Cx43 loss induces breast cancer initiation.

Methods: S1 and Cx43 shRNA-transfected counterparts were cultured under 2-dimensional (2-D) and 3-D conditions. Proliferation and cell cycle progression were monitored by trypan blue exclusion (2-D) or measurement of acini (3-D) and flow cytometry. Invasiveness was assessed using cell invasion assay. Expression of β-catenin, c-Myc and cyclin D1 and Cx43-β-catenin association were assessed by Western blotting and co-immunoprecipitation.

Results: Silencing Cx43 enhanced proliferation of S1 cells in 2-D, as shown by increased cell counts on days 6 and 10. Likewise, Cx43-knockdown S1 cells in 3-D exhibited increased acinar size on days 4, 6, 9 and 11, suggesting enhanced proliferation. Silencing Cx43 enhanced cell cycle progression of S1 cells in 2-D (days 4, 6, 9 and 11) and 3-D (days 4 and 11), as shown by reduced percentage of cells in G0/G1 and increased percentages of cells in S and G2/M. Furthermore, silencing Cx43 induced invasiveness of S1 cells, as demonstrated by increased number of matrigel-invading cells. c-Myc and cyclin D1 were consistently upregulated in 2-D cultures of Cx43-knockdown S1 cells on days 4, 6 and 9, demonstrating enhanced proliferation and cell cycle progression. Preliminary data showed that Cx43-silenced S1 cells exhibit increased nuclear β-catenin in 2-D (day 9), suggesting activation of Wnt/β-catenin pathway. Silencing Cx43, however, did not alter total β-catenin throughout 2-D cultures (days 4, 6, 9 and 11) of S1 cells. Cx43-β-catenin association in 2-D cultures (days 6 and 9) of S1 cells suggests release of β-catenin into the cytoplasm as a consequence of gap junction (GJ) complex disassembly at the membrane in Cx43-knockdown counterparts, thereby enhancing β-catenin nuclear translocation.

Conclusion: We propose the involvement of GJ complex disassembly in activation of Wnt/β-catenin pathway and breast cancer initiation downstream of Cx43 loss in mammary epithelium.

Abstract # 30

Clinical and Epidemiologic Characteristics of Norovirus Gastroenteritis in Lebanon among Hospitalized Children Less than Five Years Old

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Funding source: This study was supported by the University Review Board (URB) Grant at the American University of Beirut and partially by an investigator-initiated research grant from Merck Sharpe and Dohme (MSD).

Keywords: Norovirus; RT-PCR; Sequencing; GI; GII; Lebanon

Descriptive Statement: This study aims to determine the incidence of Norovirus gastroenteritis in Lebanon as well as the distribution of their genotypes among hospitalized children less than five years of age.

Introduction: background and aims Norovirus (NoV) is responsible for at least 50% of all gastroenteritis outbreaks worldwide. NoVs are classified into six different genogroups (GGI- GGVI) based on the viral capsid protein with NoV genogroup II genotype 4 (GGII.4) being the predominant strain causing human diseases. This study aims to determine the incidence of Norovirus gastroenteritis in Lebanon as well as the distribution of their genotypes among hospitalized children less than 5 years old.

Methods: Stool samples were collected from six major hospitals in different regions of Lebanon during a period of 30 months. A total of 739 samples were eligible. Viral RNA was extracted from stool samples using the QIAamp Viral RNA Mini Kit (Qiagen, Germany). RT-PCR was used to test for NoV. Nucleotide sequencing of the major capsid protein gene was performed and phylogenetic tree was inferred to determine the extent of diversity and evolution among detected viruses.

Results: 11.2% of the samples tested positive for NoV. Our data show that NoV infection can occur throughout the year with the highest number of cases detected during the hot months. GII.4 was predominantly isolated from children less than 5 years old hospitalized due to gastroenteritis in Lebanon. Within GII, 68% of positive cases were attributed to GII.4. A JB-15/KOR/2008 GII.4 Apeldoorn 2008-like variant strain circulated in 2011. This strain was replaced between 2012 and 2013 by a variant sharing homology with the Sydney/NSW0514/2012/AUS GII.4 Sydney 2012 and the Sydney 2012/FRA GII.4 strains. Among GI samples, 80% were designated GI.3 and 20% as GI.4.

Conclusion: We report the results of a large-scale study on NoV-associated gastroenteritis in Lebanon. To our knowledge, this is the first study to assess the frequency of NoV infections among hospitalized children less than five years old. Our results are compatible with globally reported ones whereby the majority of viral gastroenteritis outbreaks are attributable to GII.4 and co-circulating with other genotypes. The co-circulation of several GII.4 lineages is well described and has been suggested to be a mechanism of positive selection of mutations to generate new NoV variants. NoV remains an understudied causative agent of acute gastroenteritis in the developing countries. Future studies to assess NoV infection among other age groups including immunocompromised individuals along with seroprevalence studies are clearly needed to support intervention strategies.

Abstract # 31

HIV and Viral Hepatitis among High-Risk Groups: Understanding the Knowledge Gap in the Middle East and North Africa (MENA) Region

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Funding source: None

Keywords: Human immunodeficiency virus; Hepatitis B virus; Hepatitis C virus; Men who have sex with men; Female sex workers; Injecting drug users; Prisoners

Descriptive Statement: This review highlights the available data on human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) and their co-infections in the Middle East and North Africa (MENA) countries with specific focus on high-risk groups: men who have sex with men (MSMs), female sex workers (FSWs), injecting drug users (IDUs) and prisoners.

Introduction: background and aims Despite the availability of preventive and control measures, co-infection of HIV-positive individuals with HBV and/or HCV is a global health problem of significant and increasing magnitude. While the potential of worse HIV outcomes are suggested to be associated with viral hepatitis, it is still yet to identify the populations in the MENA region with dual infections (HIV-HBV or HIV-HCV) or triple co-infections with HIV, HBV and HCV. The aim of this study is to identify gaps in the existing knowledge on single, dual and triple infections of HIV, HBV and HCV in the MENA region among MSMs, FSWs, IDUs and prisoners.

Methods: We performed an extensive literature search on articles published on the topic in the 25 countries of the MENA region between 2005 and 2015. PubMed database was used as the main search engine. The World Health Organization (WHO), Centers for Disease Control and Prevention (CDC), Joint United Nations Programme on HIV/AIDS (UNAIDS), World Bank and MENA National AIDS Programs websites were also checked for any updated data on the distribution of any of these infections. Original articles and reviews dealing with the prevalence of HIV, HBV and HCV and their co-infection were included. Case reports, case series, qualitative studies, editorials, commentaries, authors' replies and animal studies were excluded. Data on population type, sample size, age and markers of infections were extracted from the relevant studies.

Results: Limited number of studies exists in the MENA region on the status of HIV, HBV and HCV and their co-infections among IDUs, prisoners, MSMs and FSWs. The prevalence of HIV among prisoners as reported during the last decade in these countries ranged from 0% to 42.5% with Iran reporting the highest prevalence rate followed by Libya (18.2%). Studies on the seroprevalence of HIV and viral hepatitis were reported from Iran, Cyprus, Israel, Lebanon, Libya, Palestine and Saudi Arabia. A common feature between the MENA countries reporting on IDUs is the predominance of male participants. Dual and triple infections were rarely reported in the MENA countries. Evidence supports the continued increase of the HIV epidemic among MSMs. In addition to the lack of studies on MSMs and FSWs in the MENA region, our review highlights the

lack of data on the practices, characteristics, or the status of HIV infection and viral hepatitis among male sex workers selling or exchanging sex for money.

Conclusion: This review highlights the paucity and the variability of existing data on high-risk groups and the status of HIV, HBV, HCV infections and co-infection in the MENA region. It is obvious that resources need to be allocated to inform strategic planning and policy of the silently creeping waves of HIV and viral hepatitis epidemics among these groups. The MENA countries are in urgent need of advanced research and strengthening of the data collection systems and reporting practices of these infections among key populations.

Abstract # 32

Curcumin as Molecular Probe to Study Influence of Rhamnolipids on Liposomes

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Funding source: University Research Board, AUB

Keywords: Curcumin, Liposomes, Rhamnolipids

Descriptive Statement: Fluorescence probing method is widely used in studying various physiological and physiochemical properties. In our lab we have established successfully curcumin as a fluorescence probe to study liposomes/phospholipids membrane properties.

Introduction: Rhamnolipids as a biosurfactant has increased interest due its various applications, especially in food and agriculture. It has also antibacterial activities. Influence of such amphipathic molecules on human health and toxicological impact is not yet clearly understood. Here, we have investigated modulation of physiochemical properties of liposomes/phospholipids membrane by amphipathic rhamnolipids.

Methods: Liposome was prepared by solvent evaporation method in which desired amount of phospholipids was dissolved in 2:1 chloroform:methanol, evaporated using a rotary evaporator above phase transition temperature and dried. The liposomes were mixed with enough phosphate buffers at pH 7.0. Desired amount of rhamnolipids anc curcumin was mixed.

Results: Rhamnolipids increased the fluidity of the liposomes. It also helped in stabilizing curcumin in alkaline medium. Lipid membranes are known to exist in different phase depending on the temperature. Curcumin fluorescence was found to be sensitive to temperature and could determine influence of rhamnolipids on phase transition temperature of both DPPC and DMPC liposomes.

Conclusion: Rhmnolipids modulate liposomes properties. Stability of curcumin could be improved using mixed rhamnolipids and liposome system.

Abstract # 33

Non-enzymatic Determination of Cholestrol: Improving Selectivity and Sensitivity of Fluorescence Probe by Nanocapsules

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Funding source: University Research Board, AUB

Keywords: Curcumin, Cholestrol, Nanosensor

Descriptive Statement: Analytical specificity has long been an intriguing topic that plays a crucial role during estimation for targeted biomedical species. Enzymatic reaction, base stacking (aptamers) and antigen-antibody linkers are few possibilities. Each of these possibilities has their own limitations.

Introduction: background and aims For cholesterol determination, enzyme based electrochemical biosensors require a development step to adapt and enhance the surface of the electrode followed by cholesterol oxidase immobilization. Fluorescence method can be an alternative approach, but fluorescence probe are sensitive to its environmental change and other chemical species.

Methods: To address this problem, as a proof of concept, we have designed nanosensor by self-assembly of curcumin (probe molecule)-chitosan oligosaccharide lactate (polyelectrolyte) on silica nanoparticle surfaces. Use of Si nanoparticles is vital to help association of curcumin with chitosan oligosaccharide lactate in neutral pH condition during estimation.

Results: The nanosensor explicitly enhances analytical specificity of cholesterol estimation without using any enzymatic reaction. The analytical selectivity in the presence of other foreign substances such as ascorbic acid, uric acid, etc. has been tested. Even interference from metal ions, which are well known fluorescence quencher for curcumin could be avoided because association of chitosan oligosaccharide lactate blocks the keto-enol (or diketo) group of curcumin that is responsible of metal ion binding.

Conclusion: The developed nanosensor shows a wider linear dynamic range from 1 □M to 10 mM for cholesterol estimation, which is comparable to other reported methods.

Abstract # 34

Burnout and depression among nurses in a Lebanese academic medical center

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Funding source: Self-funded

Keywords: Burnout, Depression, Healthcare providers, Nurses, Public Health, Mental Health

Descriptive Statement: A cross-sectional study on the prevalence of burn out and depressive symptomatology in nurses working at an academic medical center.

Introduction: We investigated the prevalence of depressive symptomatology and burnout among nurses in a Lebanese academic medical center (operating under international nursing standards) and their association with different factors. We hypothesized that there will be a high prevalence of burnout among nurses and that this prevalence will be associated with depressive symptomatology.

Methods: A cross-sectional study was carried out at American University of Beirut Medical Center (AUBMC) from August to October of 2013. A 68 question self-administered anonymous survey was developed and administered via e-mail. The survey consisted of three parts: demographic information, questionnaires about depression, burnout, anxiety, alcohol use, and substance abuse and supplemental questions regarding: family/social stressors, use of mental health services, and self-prescription of psychotropics.

Results: A total of 33 participants (36%) showed moderate to severe depressive symptoms on the PHQ-9. Depression was found to be significantly correlated with anxiety ($r = .50$, $p < .001$), burnout ($r = .48$, $p < .001$), and drug abuse ($r = .30$, $p = .001$). Anxiety ($ß = .30$, $p < .001$) and burnout ($ß = .27$, $p < .001$) were significant predictors of PHQ9 scores. A total of 48 (53%) participants had burnout on the BMS.
Burnout severity was found to be significantly correlated with depression severity ($r = .60$, $p < 0.001$), and anxiety scores ($r = .47$, $p < .001$). Anxiety ($ß = .45$, $p < .001$) and depressive symptomatology ($ß = .23$, $p < 0.001$) were significant predictors of burnout. Out of 91 participants, 12 (13%) reported illicit drug abuse. Drug abuse scores were significantly correlated with depression severity ($r = 0.13$, $p < 0.001$).

Conclusion: Our study showed that 36% of nurses reported severe depressive symptoms according to the PHQ-9. The nurses in our study who were in that same age group had a higher prevalence of depressive symptoms than in the age matched general population and higher than the reported prevalence in a regional study which reported depression at 20% among nurses surveyed. Burnout in our study was at 53%. A significant association between age and burnout was observed, with older nurses being more burned out. Nursing and health care leaders should routinely educate and raise awareness among nurses regarding depression and burnout, and provide accessible treatment options for at risk nurses.

Abstract # 35

SLEEP DISORDERS IN HOSPITALIZED PSYCHIATRIC PATIENTS

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Keywords: sleep disorders, psychiatric patients, co-morbid psychiatric conditions

Funding: Self-funded

Abstract: Sleep is an important part of an individual's health. In Lebanon and the Arab region there is a lack of data on the prevalence of sleep disorders in psychiatric patients. Our hypothesis aims to prove that there exists a high prevalence of multiple sleep disorders in the Lebanese psychiatric patients.

Introduction: A close relationship has been well established among some psychiatric and sleep disorders for some time. Sleep domains in psychiatric disorders have been restricted to broad descriptive terms such as decreased sleep or increased sleep.

There has been limited research in quantifying the presence of separate sleep disorders among the major psychiatric disorders.

Objectives: To quantify and describe the prevalence of sleep disorders in hospitalized psychiatric patients at an academic medical center and to investigate the correlations between psychiatric patient profile and potential sleep disorders.

Methods: Demographic information, psychiatric and general medical diagnoses, current psychotropic medication use, and history of substance abuse were collected. Questionnaires pertaining to insomnia, excessive daytime sleepiness, restless leg syndrome and sleep apnea were administered to 103 patients hospitalized for psychiatric disorders. Depressive and anxiety symptoms were also examined via questionnaires. Statistical analysis was conducted to detect the prevalence of sleep disorders among the participants to examine correlations and associations between psychiatric disorders and sleep disorders.

Results: 16.8% were found to have severe insomnia, 23.8% were found to have moderate insomnia and 27.7% were found to have mild insomnia which was associated with a diagnosis of schizophrenia/schizoaffective disorder and drug or alcohol addiction.

Insomnia was also associated with depressive symptomatology, anxiety symptoms and suicidal thoughts.

13.6% were found to have restless leg syndrome (RLS) ranging from mild to severe which was also found to be associated with higher depressive symptomatology, suicidal ideations and working nightshifts.

8.7% of patients were found to have an abnormal range of sleepiness.

49.5% were found to have a very high likelihood of sleep apnea based on the Berlin sleep questionnaire also associated with depressive symptoms and anxiety.

Conclusion: A great percentage (69%) was found to be suffering from insomnia which was found to be associated with a diagnosis of schizophrenia/schizoaffective disorder, substance use disorders, depressive as well as anxiety symptomatology and suicidal ideation.

46% of hospitalized psychiatric patients in this study were found to have a high likelihood of sleep apnea.

52% who had severe anxiety symptoms were found to have a high likelihood of sleep apnea (χ^2= 11.14, p=0.01).

The overall prevalence of RLS has been estimated at 5% to 10% which is lower than the prevalence in our study (13.6%).

Abstract # 36

Acid Sphingomyelinase does not Enhance the Propagation of Influenza A Virus in Human Lung Epithelial Cells

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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) is a major human respiratory pathogen causing annual epidemics as well as periodic pandemic. Lipid rafts, membrane microdomains enriched in sphingomyelin and cholesterol, have been shown to be important for IAV infection. Understanding the role of sphingomyelin pathway is necessary to identify novel host targets, such as sphingomyelinases, and the development of future anti-influenza virus therapeutics.

Introduction: Background and Aims: Sphingomyelinases (SMases) are enzymes that catalyze the hydrolysis of sphingomyelin (SM) into phosphocholine and ceramide. Attachment of some pathogens to their receptors at the plasma membrane can trigger the activation of acid sphingomyelinase (ASMase) and consequently the formation of ceramide-enriched membrane platforms, which are required for pathogen uptake. Although it has been previously shown that IAV utilizes lipid rafts during its entry and budding from the cells, the details of entry mechanism and the role of sphingomyelinases in IAV infection are not well understood. We aim to better understand the role of sphingomyelin pathway in IAV pathogenesis, and to investigate the role of ASMase in IAV replication.

Methods: Sphingomyelin depletion assay using exogenous ASMase was used to assess the requirement for sphingomyelin in IAV infection in A549 cells (human lung adenocarcinoma epithelial cell line). We also assessed the effect of desipramine (an ASMase inhibitor) treatment on replication of IAV in A549 cells. Additionally, virus replication in ASMase deficient fibroblasts

(NPD cells) and normal human fibroblasts was assessed. Viral titers were determined by either $TCID_{50}$ or plaque assay.

Results: Depleting plasma membrane SM by ASMase slightly reduced IAV replication in A549 cells, indicating that IAV requires SM at the plasma membrane. Pharmacological inhibition of ASMase by desipramine had no effect on production of IAV in A549 cells. On the other hand genetic deficiency of ASMase results in significant increase in production of infectious viral particles which may be due to accumulation of SM in plasma membrane of NPD cells.

Conclusion: Our data suggests that ASMase has no or slight effect on propagation of IAV in lung epithelial cells and that SM is an important modulator for viral replication. We further plan to investigate localization of ASMase upon inoculation of A549 cells with IAV and the role of nSMAse during IAV infection.

Abstract # 37

Self-perceived obesity is a stronger determinant of weight loss efforts than actual obesity in Lebanese adolescents: a national study

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Funding source: The study was funded by the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET in the US), the World Health Organization (WHO)-Lebanon, and the Lebanese National Council for Scientific Research through its support of the Associated Research Unit on Under-nutrition and Obesity in Lebanon.

Keywords: adolescent, BMI, obese, overweight, weight perception, weight loss

Descriptive Statement: The prevalence of overweight and obesity has increased in recent years. Previous studies have revealed the significance of self-perception of weight in relation to weight loss practices. This study brings recent, nationally representative findings on misperception of weight among adolescents in Lebanon to assist clinicians in their medical nutrition therapy for overweight and obese adolescents, and to provide evidence-based actions to orient policies at the national level.

Introduction: background and aims The decision to lose weight among adolescents is complex and is guided by actual and self-perceived weight, the latter of which is context-specific. This study examined the relationship between objective measure of body mass index (BMI) and self-perceived body weight and their relative importance in weight loss behaviors among Lebanese adolescents.

Methods: Participants aged 13-17 years (N=278) from the nation-wide cross-sectional WHO-based non-communicable disease STEPwise survey were included. Objectively measured weight and height yielded BMI percentiles, classified as normal, overweight and obese. Weight perception and weight management behavior were self-reported.

Results: Close to 40% inaccurately perceived their body weight (Kappa-statistics =0.318). Overall, misperceivers were more likely to overestimate (25.2%) than underestimate their body weight (14.0%), and around 36 % attempted weight loss behavior. Close to one third of the sample reported skipping breakfast and dinner on a daily basis (32.4% and 36.7%, respectively). In the multivariate analysis, self-perception but not actual body maintained its significance with weight loss effort, even after controlling for all potential confounders (OR=12.74, 95% CI [5.99, 27.06] and OR=8.02, 95% CI [2.52, 25.52] for overweight and obese individuals, respectively).

Conclusion: Compared to BMI, perception of body weight is a better predictor for weight loss among adolescents in the Lebanese context. Clinicians and public health professionals are encouraged to consider self-perception of weight along with BMI scores to guide weight loss efforts and curb obesity in this age group.

Abstract # 38

One Hundred and Seventy Pancreaticoduodenectomy with no Intensive Care Unit Admission

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Keywords: Pancreaticoduodenectomy, Intensive care unit, postoperative.

Funding: None

Descriptive Statement: Introduction to a series of Whipple procedures performed where there was no need for ICU admission due to advancement of operative procedure.

Introduction: Pancreaticoduodenectomy has been increasingly performed as the best modality for the treatment of pancreatic cancer. The developments that occurred in the surgical technique have undoubtedly been a major factor in the increased survival of patients.

Background and Aims: We have performed over 350 pancreaticoduodenectomies over the past 20 years. Before 1998, all general surgeons were performing that procedure with a mediocre outcome. However, in 1998, it was almost performed by a single specialized hepatobiliary surgeon, which led to significant improvements in outcomes. Moreover, in 2009, another specialized surgeon joined, and a standardized peri, intra and postoperative approach was implemented, causing significant decreases in operative times, length of hospital stay, and over-all complications. We are reviewing the last 170 pancreaticoduodenectomies performed at our institution with no intensive care unit (ICU) admission.

Methods: A retrospective data analysis review was performed for all pancreaticoduodenectomies performed at AUBMC from 1994 to 2014 to evaluate surgical complications and morbidity rates, comparing the outcomes between past and present.

Results: Before 1998, the median operative time was 370 mins. After 1998, it became 355 mins. After 2009, it became 313 mins, showing a significant decrease (p-value 0.0039). With this improvement came a decrease in the onset of post-operative complications with a lesser need for blood transfusions and, subsequently, better recovery of patients without the need for ICU. Before 1998, the median length of hospital stay was 25 days. After 1998, it improved to 18 days and in 2009 it became 9 days reflecting the great improvement in the surgical outcome.

Conclusion: Comparative analysis to the different parameters between different periods has showed significant improvements for the performance of the procedure by a specialized surgeon, and even more when 2 specialists worked together.

Abstract # 39

Surgical Management of Locally Invasive Gallbladder Cancer: A Single Center Experience

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Keywords: Gallbladder cancer, Cholecystectomy, Hepatectomy

Hussein Nassar: Medical Student year IV

Funding: None

Descriptive statement: Gallbladder cancer is a rare malignancy that occurs mainly in the elderly population. It is an aggressive tumor with poor prognosis unless incidentally diagnosed at an early stage, for instance after a cholecystectomy for cholelithiasis.

Background: Gallbladder cancer can present either as an incidental finding, or symptomatically with abdominal pain or jaundice. An aggressive surgical approach to gallbladder cancer has been suggested to decrease morbidity and improve prognosis. We reviewed all gallbladder cancer cases managed at our institution from 2000-2014.

Methods: Data regarding the study was extracted from the medical records after approval from IRB committee. All patients with gallbladder cancer encountered at AUBMC were gathered using an approved worksheet designed for this study.

Results: 58 cases of gallbladder cancer were encountered at AUBMC during the period 2000 - 2014. The most common presenting symptom was abdominal pain (59%). Patients were classified in 2 groups: the first group was diagnosed preoperatively with gallbladder cancer (89%). These patients either had a locally invasive or a metastatic disease upon presentation. The second groups of patient were diagnosed incidentally upon tissue examination after cholecystectomy for cholithiasis (11%). 65% of all patients received a cholecystectomy. Out of these, 36% had also partial hepatectomy due to local invasion. The remaining patients were not amenable to surgery. The most common pathology was infiltrating adenocarcinoma of the gallbladder (53%).

Conclusion: A complete R0 resection is the standard of care in patients with GBC and the only potentially curative therapy. In patients with locally advanced gallbladder cancer, major hepatectomy with extrahepatic bile duct resection can be considered, however mortality rate is still high. To date there is no evidence based consensus on the best approach to locally advanced gallbladder cancer.

Abstract # 40

The Role of Phosphorous in Diet Induced Thermogenesis of Lean Male Subjects

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Funding source: URB

Keywords: Diet Induced Thermogenesis (DIT); Protein; Phosphorous; Adenosine Triphosphate (ATP)

Descriptive Statement: Diet induced thermogenesis (DIT) of protein is known to be high. At the same time, phosphorus content of protein is high. However, it's not clear whether phosphorous is involved DIT of protein.

Introduction: Diet Induced Thermogenesis is the increase that takes place in energy expenditure after the ingestion of food, noting that this increase is above the resting (basal) metabolic rate (RMR) and accounts for 5 % to 15 % of total energy expenditure. This increase can be largely related to the increase production of ATP that is affected by phosphorus availability. Macronutrients have varied levels of DIT (fat 0-3%, carbohydrate 5-10%, and protein 20-30%). The high DIT of proteins may be partially related to their high content of phosphorous. Thus, the aim of this study was to explore the impact of role phosphorous on DIT of protein using a low phosphorus containing protein, egg white.

Methods: A cross-over design study was conducted which 9 healthy lean male subjects undertook 2 sessions separated by a minimum of one week. Subjects were asked to consume a 554 Kcal high protein-low phosphorus (using egg white) meal (E% from protein 50%) with phosphorous (500mg) or placebo tables in a random order. Energy expenditure, fat and carbohydrate oxidation were measured at baseline and for the next 4 hours in a period of 15 minutes interval with 15 minutes break using a ventilated hood and canopy system (COSMED QUARK CPET UNIT) for indirect calorimetry measurement.

Results: Increased phosphorus content of the high protein meal was associated with a significant increase in postprandial energy expenditure ($p=0.012$) and a significant decrease in carbohydrate oxidation ($p=0.038$); however, there was an increase in fat oxidation but it did not reach statistical significance ($p=0.070$).

Conclusion: Phosphorous is involved in the high thermic effect of proteins and therefore, may have a promising role in controlling obesity.

Abstract # 41

The efficacy of thymoquinone and 5-FU combination therapy against colorectal cancer stem cells

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We thank Dr. Nadine Darwiche for providing the HCT116 5-FU resistant cell line.

Keywords: Colon cancer stem cells, 5-FU/TQ combination therapy, 5-FU Resistance

Hala Oweini: Masters Student

Funding source: This work is funded by MPP grant

Background: Despite the resistance to 5-fluorouracil (5-FU) and its unpredictable cardiotoxicity, this drug remains the standard chemotherapy for metastatic colorectal cancer (CRC). The high tumor recurrence rates (as high as 50–60%) in colorectal cancer patients and the common drug resistance is thought to be due to the presence of cancer stem cells (CSCs). Therefore, it is essential to develop novel therapeutic approaches to overcome resistance by effective targeting of CSCs. The plant derived molecule Thymoquinone (TQ), with its efficacy and selectivity against colon cancer, has a potential to target colon CSCs as our studies demonstrated that TQ negatively regulates self-renewal capacity of HCT116 human colon cancer cells.

Methods and Aims: Here, we investigated the efficacy of TQ alone, 5-FU alone and a combination treatment of TQ+5-FU against parental sensitive HCT116 as well as 5-FU resistant HCT116 cell lines in 2D cultures. Moreover, we studied the effect of chemoresistance on stemness properties of these cell lines grown in 3D cultures. Sphere-formation and propagation assays were used to assess the effect of drugs on targeting self-renewal capacity of colon CSCs enriched up to 5 generations from the parental and resistant cell lines in 3D cultures.

Results: Colonospheres derived from the 5-FU resistant cell line and which survived TQ treatment at 1 and 3μM TQ and that were propagated from generation 1 (G1) to 5 (G5), showed at every generation similar decrease in sphere-forming unit (SFU) upon TQ treatment but were resistant to 5-FU treatment. Colonospheres treated with 3μM TQ showed a consistent decrease in SFU over serial passages from G1 to G5, while those treated with 1μM TQ developed resistance at G5. On the other hand, consistent with a CSC phenotype, the resistant cell line exhibited a decrease in

cellular proliferation and an increase in the doubling time compared with the sensitive cell line in 2D cultures. Chemoresistant HCT116 cells also demonstrated an increased ability to form spheres as they had higher SFU in G1 compared with the sensitive cell line. Moreover, G1 colonospheres derived from the chemoresistant cells were less responsive to5-FU+TQ combination and TQ treatments than the G1 colonospheres of the sensitive cell line. Interestingly, the combination treatment induced a 10 fold decrease in SFU in the sensitive cell line.

Conclusion: Collectively, our results provide evidence for the potential efficacy of a novel therapy against colon cancer by integrating TQ with mainstream 5-FU, thereby lowering 5-FU doses, decreasing its cardiotoxicity, maintaining its efficacy, and ultimately eradicating its associated chemoresistance.

Abstract # 42

Toxoplasma gondii Pru*ΔKU80* and its parental Pru strains display different brain cyst capacity formation due to a difference in the host immune response

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Funding source: Medical Practice Plan/CEDRE

Keywords: *Toxoplasma gondii*; chronic infection; Immune response; Pru; Pru*ΔKU80*

Descriptive Statement: Pru and its derivative Pru*ΔKU80* strain are two widely used *Toxoplasma* models to answer keys biological questions related to chronic toxoplasmosis. We and others have noticed that these strains grow differently in culture and investigated their similarities and differences. We noticed that they display a different capacity of forming cysts in the brain of different mouse strains, due a difference in the host immune response.

Introduction: *Toxoplasma gondii* is an obligate intracellular parasite causing toxoplasmosis, a disease whose outcome can be fatal in immunocompromised patients. This parasite mainly highjacks macrophages to travel to different sites within the host avoiding complete clearance by the host immune system and hence establishing a lifelong infection. Pru*ΔKU80* was generated from Pru strain to facilitate efficient knock-out of genes and study their function. We have investigated the capacity of cyst formation in different mouse strains, the host immune response against these two *Toxoplasma* strains and presumably the organ where these parasites are cleared in response to host immunity.

Methods: Mice were injected with the same number of parasites, and verification of acute infection was performed by western blotting. 28 days later, the brains of infected sacrificed mice were harvested and cysts were quantified by RT-PCR. Then the host immune response was also evaluated by RT-PCR.

Results: Swiss mice are the best murine model for studying chronic Toxoplasmosis. The two type II *Toxoplasma* strains display a different cysts production capacity due to an IFN-γ driven immune response where Pru*ΔKU80* parasites were cleared more efficiently in the peritoneum and the spleen of mice, hence producing less cysts in the brains, as compared to the parental Pru strain.

Conclusion: Since the generation of the knock-out Pru*ΔKU80* strain in 2009, we present the first to report major *in vivo* differences between the two strains hence alarming researchers on the use of either Pru or Pru*ΔKU80* according to the addressed research question.

Abstract # 43

Mutant *NPM-1*: a therapeutic target in Acute Myeloid Leukemia

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Funding source: Internal Academic Grant

Keywords: Acute Myeloid Leukemia (AML), NPM-1, Retinoic Acid/Arsenic, PML, $p14^{Arf}$, P53.

Descriptive Statement: Nucleophosmin (NPM-1) is a nucleocytoplasmic shuttling protein mainly localized in the nucleolus, where it plays a role in rRNA synthesis following a balanced tight regulation of its post translational modification *via* SUMOylation by $p14^{Arf}$/de-SUMoylation by SENP-3. *NPM-1* is the most frequently mutated gene in AML. However, little is known on the molecular mechanisms of leukemogenesis following *NPM-1* mutation and the potential targeting of mutated NPM-1 (NPM-1c) in AML.

Introduction: Addition of retinoic acid (RA) to chemotherapy improved survival of some *NPM-1c* AML patients. We recently showed that RA or arsenic trioxide (AS) synergistically induce proteasomal degradation of the mutated NPM-1c, leading to restoration of nucleolar localization of wild type (wt) NPM-1 and reformation of PML nuclear bodies (NB), resulting in cell differentiation and apoptosis. Our aim is to decipher the biochemical and cellular effects of NPM-1c mutation and to investigate the molecular basis of RA/AS induced NPM-1c degradation.

Methods: We used two AML cell lines, THP-1 and OCI-AML3 expressing wt and NPM1c respectively. Expression levels of NPM1, $p14^{Arf}$, SENP-3, p53 and SUMOyalted proteins were analyzed by immunoblotting. Co-immunoprecipitaion assay was performed to study protein-protein interaction. Localization experiments were carried out using confocal microscopy. NPM-1 SUMOylation was investigated using *in situ* proximity ligation assays (PLA) and confocal microscopy.

Results: In *NPM-1* mutated AML cells (OCI-AML3), basal $p14^{Arf}$ levels are very low whereas levels of the nucleolar de-SUMOylating enzyme, SENP-3, are very high. Accordingly, global cellular SUMOylation and particularly NPM-1 SUMOylation are very low, and PML NB are disorganized. Interestingly, AS/RA restored normal expression levels of ARF as well as NPM1-ARF interaction and lowered the expression of SENP-3. This was associated with restoration of global SUMoylation, NPM1 conjugation with SUMO2/3 and, to a lesser extent, with SUMO1. Furthermore, a normal PML NB architecture was restored and PLA experiments revealed interaction in PML NBs between endogenous NPM1 and PML. Finally AS/RA induced p53 activation. PML silencing delayed AS/RA triggered NPM1c degradation demonstrating that NPM1c degradation is PML-dependent.

Conclusion: This study provides a molecular characterization of the biology of *NPM-1c* AML and a rationale for the therapeutic use of RA/AS in this class of leukemia, highlighting the potential efficacy of therapy-induced oncoprotein degradation.

Abstract # 44

Seroprevalence of *Toxoplasma gondii* among pregnant women in Lebanon

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Funding source: None.

Keywords: Toxoplasmosis, Seroprevalence, Pregnancy, *Toxoplasma gondii*, Lebanon

Descriptive Statement: To our knowledge, there is no recent study performed in Lebanon addressing the percentage of seropositive pregnant women for toxoplasmosis, and the rate of seroconversion and its related abortion. We addressed this issue by extracting medical records of 2456 pregnant women who sought antenatal care at a private Obstetrics and Gynecology clinic located in Achrafieh.

Introduction: *Toxoplasma gondii,* the causative agent of toxoplasmosis, is a zoonotic obligate intracellular protozoan parasite responsible for the infection of almost one-third of the world's population. *T.gondii* is particularly threatening for primo-infected pregnant women and may lead, following vertical transplacental transmission, to spontaneous abortion, miscarriage or severe manifestations in the newborn.

Methods: The results of IgG and IgM anti-*Toxoplasma* antibodies serological tests were extracted from the medical records of 2456 pregnant women who sought antenatal care at a private Obstetrics and Gynecology clinic located in Achrafieh, Beirut, Lebanon. The results of seropositivity were analyzed and distributed based on collected demographic data over 3 governorates of Lebanon (i.e. Beirut, North and Mount Lebanon) and among three different age groups of 10 years interval.

Results: The overall anti-*T.gondii* IgG and IgM seropositivity among Lebanese pregnant women was determined as 82.6% (2029 out of 2456) and 1.8% (46 out of 2456) respectively. The highest IgG seropositivity was found among pregnant women aged between 35-44 years (87.81%) and in the governorate of Mount Lebanon (82.95%). The rate of abortion among pregnant women who underwent seroconversion during their pregnancies was found to be 12.5%.

Conclusion: The seroprevalence of anti-*T.gondii* IgG among pregnant women in Lebanon is the highest in the Arab region and the rate of abortion from toxoplasmosis among the pregnant women who underwent seroconversion during their pregnancies is relatively alarming. The association between toxoplasmosis and its risk factors including age, region of residency, dietary habits and other behavioral risk factors should be investigated in future studies in order to identify the population at risk and target it with effective control and preventive measures.

Abstract # 45

Radiation dose measurements: Validation of an analytical model for out-of-field dose estimates.

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Funding source: MPP Research Fund, American University of Beirut, and Grant Research Program, Lebanon National Council for Scientific Research

Keywords: Out-of-field dose, Analytical models, Radiation therapy, Peridose, Anthropomorphic phantom.

Descriptive Statement: Validate an analytical model whose purpose is to estimate radiation dose outside the irradiated region.

Introduction: Analytical models can be used to estimate out-of-field dose in radiation therapy based on out-of-field dose measurements. However, these models have not been yet validated for the newest clinical linear accelerators. The purpose of this study was to validate the estimations of out-of-field dose made by freely available Peridose software and to determine the factors that contribute to an increase in the dose deposited out-of-field.

Methods: Reference fields of various sizes were delivered and dose was measured in a water phantom tank at 18 locations comprising different depths and distances from the isocenter. These fields were of energy type of pediatric radiation therapy treatments. Hence, in addition, we also compared our measurements to measurements made in an anthropomorphic phantom for fields designed to treat pediatric localized brain tumor.

Results: Peridose values agreed well with our water phantom measurements; the average difference was equal to 0.12 ± 0.06 cGy/Gy. More specifically, when distance from field edge was smaller than 30 cm, Peridose accurately estimated the out-of-field dose with a maximum difference of 8%. However, Peridose estimates diverged largely from the more realistic, in-anthropomorphic-phantom measurements mainly when the distance from field edge was less than 15 cm. Additionally, our findings showed that out-of-field dose is a function of distance from field edge and is also affected by other factors related to the geometry and anatomy of the patient such as the size of the radiation field and the depth of our measuring point.

Conclusion: In conclusion, we found that although Peridose estimates accurately out-of-field dose in water tank phantoms, it does not for clinically realistic anthropomorphic phantom measurements. Our results also showed that out-of-field dose is mainly affected by the distance from the field edge but also the material composition and geometry of the phantom or patient.

Abstract # 46

Prevalence of Astrovirus in Children Less than 5 Years of Age in Lebanon

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Funding source: URB IRB

Keywords: Astrovirus, pediatrics, children, gastroenteritis, Lebanon

Descriptive Statement: Astrovirus causes diarrhea in pediatric patients and this study aims to assess the burden and prevalence of pediatric astrovirus infections in Lebanon.

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

Methods: Stool samples were collected from pediatric patients less than 5 years of age who clinically presented with gastroenteritis at six medical centers across Lebanon between 2011 and 2013. Ribonucleic acid (RNA) was extracted from the stool samples using a commercially available kit. RNA was screened by real-time PCR using a set of primers and probes capable of detecting classical 1-8, MLB1, and VA2 HAstV genotypes. Clinical and demographic data was analyzed.

Results: In total 739 samples were eligible for inclusion in the study. Astrovirus prevalence was found to be 5% (37/739). Astrovirus infections were mainly detected during the summer and winter seasons. The age group 0-12 months was the most susceptible to astrovirus infections. The majority of astrovirus cases were found in Northern Lebanon.

Conclusion: Our results showed that astrovirus is circulating in Lebanon. Currently, there are no treatments or vaccines available for astrovirus. Knowledge of the global prevalence of HAstV, circulating genotypes and the genetic changes is critical to developing diagnostic tools and vaccines to prevent infections. We plan to further analyze the genetic diversity and characterize prevalent astrovirus genotypes in Lebanon.

Abstract # 47

The Epidemiology of ADHD in a Beirut Community Sample: Results of the BEI-PSY Study

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Funding source: none

Keywords: Attention-Deficit Hyperactive Disorder; Epidemiology; Beirut

Descriptive Statement: Attention-Deficit Hyperactivity Disorder (ADHD) is a highly-prevalent childhood illness, presenting with inattention, hyperactivity and impulsivity. The present study provides much needed information about ADHD in the Lebanese community. It is based on the BEI-PSY study which recruited a sample of Arabic speaking adolescents living in Beirut between March 2012 and December 2012. The adolescents and their parents/legal guardians were administered a diagnostic assessment and other questionnaires. The prevalence of ADHD was found to be 10.20%. Adolescents with ADHD were found more likely to have difficulties at school (academic performance, bullying), to drink alcohol and smoke, and to additionally have emotional disorders and conduct disorders. Adolescents with ADHD and their parents reported a higher negative impact of the illness on their lives and were thus more likely to consider seeing a mental health professional. However, only 5.77% of adolescents in the ADHD subgroup had ever received any treatment for their condition. This study is the first to investigate the epidemiology of ADHD in adolescents in Lebanon. It highlights the need to further develop public awareness about ADHD and to increase treatment resources to serve the needs of the community.

Introduction: background and aims Attention-Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by symptoms of inattention, hyperactivity and impulsivity [1], [2]. Its worldwide pooled prevalence has been estimated to be 7.2% [3] but studies in the Arab region are scarce and most of them surveyed schoolchildren and relied on teachers' ratings for diagnosis [4], [5]. The Beirut Epidemiological Investigation of the Psychiatric Status of Youth (BEI-PSY) is the first general population-based survey study to investigate the epidemiology of psychiatric disorders among adolescents in Beirut. We report in the present study the prevalence, correlates and treatment seeking behavior related to ADHD in the BEI-PSY cohort.

Methods: BEI-PSY recruited Arabic speaking adolescents living in Beirut between March 2012 and December 2012. Recruitment was carried out using a multistage cluster sampling technique. Each adolescent and his/her parent/legal guardian were separately interviewed using the *Development And Well-Being Assessment* (DAWBA) [6], from which clinical diagnoses were generated. All

adolescents completed the *Peer-Relations Questionnaire* (PRQ) [7] and the *Strengths and Difficulties Questionnaire* (SDQ) [8]; the parent/legal guardian also filled out the SDQ and provided basic demographic information, including attitudes towards seeking mental health services.

Results: Among the total sample of 510, 52 (10.20%) were diagnosed with ADHD. Compared to the healthy subgroup, they were more likely to have repeated grades (44.68% vs 27.74%; p=0.002), to use special educational services (36.17% vs 13.50%; p<0.001) and to bully or be bullied. Compared to those not diagnosed with ADHD, adolescents with ADHD were at higher risk to drink alcohol and smoke, and to have comorbid emotional and conduct disorders. Adolescents and parents in the ADHD subgroup reported a higher burden of illness and were thus more likely to consider seeing a mental health professional compared to those In the healthy subgroup [11.54% vs 1.06% (p<0.001) and 42.31% vs 4.77% (p<0.001), respectively]. However, only 3 adolescents (5.77%) with ADHD had ever received any treatment for their condition.

Conclusion: This study is the first to investigate the epidemiology of ADHD in adolescents in Lebanon. It remains to be seen whether these findings will be replicated on the national scale. However, it does highlight the need to further develop public awareness about ADHD and to increase treatment resources to serve the needs of the community.

Abstract # 48

Ocular Tuberculosis at AUBMC, a Tertiary Care Center in Lebanon

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Funding source: none

Keywords: Ocular Tuberculosis, Tuberculosis Uveitis Outcome, and Steroids

Descriptive Statement: The study describes the different clinical manifestations of tuberculosis uveitis in patients who presented to AUBMC. It further evaluates their response to treatment and aims to determine possible factors affecting their prognosis.

Introduction: Ocular tuberculosis is re-emerging as a major challenge and is being increasingly recognized in nonendemic regions. Contradictory evidence exists as to whether the use of steroids ultimately affects the disease outcome. Our aim was to study the characteristics of patients with presumed ocular TB uveitis in Lebanon, a nonendemic area, and assess their outcomes and complications after receiving anti-TB drug therapy. Our goal was to also determine possible factors impacting prognosis including the effect of steroid use.

Methods: This was a retrospective analysis done on 21 patients (35 eyes) diagnosed with presumed tuberculosis uveitis at AUBMC between 2009 and 2015. Pertinent information collected included visual acuity, intraocular pressure, slit lamp examination including the anatomic location and degree of intraocular inflammation on presentation and at follow-up appointments.

Results: 57.1% had panuveitis, 40% had posterior uveitis and only 1 eye had anterior uveitis. The treatment for all patients included anti-tuberculous therapy and 18 patients received steroid after initiation of anti-TB therapy. Gain of two or more lines occurred in 25% per eye-year, while loss of two or more lines occurred in 5.8% per eye-year. All eyes showed improvement of the inflammation after treatment and supplemental use of steroids did not significantly affect final visual acuity compared to anti TB alone.

Conclusion: According to our findings the supplemental use of steroids after initiation of antimycobacterial therapy was not associated with significant improvement or worsening with regard to visual acuity.

Abstract # 49

Automated Detection and Measurement of Corneal Haze using Optical Coherence Tomography in Keratoconus Patients after Crosslinking

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Descriptive Statement: Corneal haze describes a cloudy or opaque appearance of the cornea (i.e., the anterior clear part of the eye). The cornea is normally clear; thus, corneal haze can greatly impair vision, which occurs during laser vision correction procedures (i.e., LASIK), or during crosslinking treatment for keratoconus. We developed a novel software application to automatically detect and classify corneal haze. This offers objective view of the haze and may improve clinical decision-making after corneal surgeries.

Funding source: No funding source.

Keywords: corneal haze, cross-linking, novel software, haze detection, haze classification.

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Introduction: To evaluate a proposed technology for offering objective, and fast detection and measurement of corneal haze using spectral domain optical coherence tomography (SD-OCT) images.

Methods: Clinical pre- and post-operative SD-OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Dublin, CA, USA) images of 44 keratoconus eyes of 40 patients that underwent keratoconus crosslinking were collected at baseline pre-operatively, and at 2 weeks, 3 months, 6 months and 12 months post-operatively. The SD-OCT images were analyzed using novel software at baseline and all follow-up periods. The new image processing software is able to provide absolute measurements of corneal signal intensities and contrast using tools to detect regions of bright intensity so as to detect and classify haze. It achieves so via the following four steps: 1) detect the boundaries of the cornea; 2) compute the average brightness of the cornea and corneal thickness; 3) locate regions of interest; 4) classify location as anterior, middle, or posterior relative to the cornea.

Results: Total average brightness of the cornea in the pre-operative period for all treated eyes was 43.3±6.2%; it then increased to 50.2±4.5% at 2 weeks, and gradually decreased to 47.9±4.5%, 46.4±5.8%, and 44.9±5.4% at 3 months, 6 months and 12 months, respectively. The change compared to baseline was significant at 2 weeks and 3 months, with p values of <0.001 and 0.006 respectively. Brightness at the anterior stroma was 46.54±5.05% at baseline, 54.79±4.04% at 2 weeks ($p<0.001$ compared to baseline), 52.95±4.37% at 1 month ($p<0.001$), 52.45±5.35% at 3 months ($p=0.001$), 49.74±7.08% at 6 months ($p=0.316$) and 48.43±6.52% at 12 months ($p=1$). Less brightness was noticed at the mid stroma with values of 43.22±6.77% at baseline, 50.14±5.14% at 2 weeks, 47.43±8.93% at 1 month, 45.16±4.83% at 3 months, 45.01±6.71% at 6 months, and 44.31±5.91% at 12 months. Significant difference compared to baseline was detected at 2 weeks ($p<0.001$) only. At the posterior region, the brightness of haze was less compared to the anterior and middle third with no significant differences detected over time compared to baseline value.

Conclusion: Our novel software can provide objective, quantitative and fast measurement of corneal haze in SD-OCT images. It can detect subtle changes in corneal haze density and location over a given follow-up period, which may impact clinical decision-making after corneal surgeries. The new software has the promise to be adopted as a standardized tool for corneal stromal haze measurement of individual patients or in aggregate data for the purpose of longitudinal studies.

Abstract # 50

SYSTEMIC ASSOCIATIONS IN CENTRAL SEROUS RETINOPATHY
The MultiCenter Controlled Personality Analysis in CSR

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Keywords: Central Serous Retinopathy, Patient characteristics, Personality Analysis

Funding: None

Abstract Summary: Central Serous Retinopathy is a relatively common retinal problem that affects vision mostly in younger men; historically, it has been associated with high stress conditions. The study aims at profiling the personality characteristics of patients with CSR, and establishing systemic associations that could be helpful in controlling the disease in patients with CSR, and in referring patients to the appropriate specialist.

Purpose: Central serous retinopathy (CSR) is characterized by macular detachment due to hyperpermeable retinal pigment epithelium and choroid mostly affecting young men under perceived stress. While most previous studies have been retrospective and have focused on a single facet of the patient's personality, we conducted a prospective multicenter/multinational controlled study to dissect the multifaceted personality profile in CSR.

Methods: The authors themselves interviewed CSR patients and control patients without retinal disease from November 2014 to October 2015 using a long questionnaire in clinic setting. Controls were matched for age, gender and race across 3 continents. Statistical analyses were done using bivariate analysis (Chi-square at the 95% confidence interval) on SPSS Software (v. 22).

Results: 68 consecutive CSR patients (mean age 46; male 76.5%) and 68 controls (mean age 45.8; male 76.5%) were analyzed for 59 variables. The results were divided into 3 categories according to strength of the association. Very strong associations included type A personality ($p<0.001$), obsessive-compulsive personality disorder ($p<0.001$); aggressive behavior ($p<0.001$); presence of continuous stressful conditions ($p<0.001$); working compulsively ($p=0.004$); presence of emotional strain ($p<0.001$); history of premature ejaculation ($p<0.001$); use of drugs for erectile dysfunction ($p=0.007$); irritable bowel syndrome ($p= 0.001$) and history of sinusitis ($p=0.008$). Strong associations were found with penile erection disorder (0.016); sleep disturbance ($p=0.012$); history of panic attacks ($p=0.035$); tendonitis ($p=0.034$). Borderline associations were found with phobia (0.083); migraine ($p= 0.057$); gastro-esophageal reflux disease (0.078); history of kidney disease (0.095) and history of hypertension (0.088).

Conclusions: This prospective controlled multicenter study carried by the treating ophthalmologists sheds a new light on the unique personality of CSR patients: obsessive compulsive, aggressive, under continuous stress, prone to panic attacks and with various sexual disturbances. Ophthalmologists treating these patients should be aware of the other characteristics of this syndrome in order to be able to refer the patients with CSR to appropriate specialists when need arises. CSR should raise the attention for other systemic issues.

Abstract # 51

Perforated Duodenal Diverticulum Treated Conservatively: Another Two Successful Cases

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Funding Resources: Not Applicable

Keywords: diverticulum(a); perforation; resection; conservative management; Taylor's approach

Descriptive Statement: Diverticula, or abnormal pouches, arising from the duodenum are rare anatomical findings. Their perforation, despite multi-factorial, is associated with high morbidity, especially if approached surgically. Given that, more cases are being presented, with successful treatment using conservative bowel-rest approach.

Introduction: Diverticulum of the duodenum is a rare entity ranging from 15 to 23%, with 90% being asymptomatic. Surgery has always been the mainstay approach for symptomatic diverticula, but with the advent of medical treatments, physicians are now trending toward more conservative approaches, like Taylor's approach for upper gastrointestinal tract perforation, which is mainly employed in cases of duodenal ulcer perforation. This includes bowel rest with or without nasogastric tube insertion, intraveneous hydration and antibiotics, total parenteral nutrition, and when needed, percutaneous catheter drainage of retroperitoneal collections.

Methods: We are presenting two cases of perforated duodenal diverticuli with review of literature.
Review of the pertinent literature was conducted by searching the PubMed and Cochrane Library, for all relevant articles. A total of 171 cases of perforated duodenal diverticula were identified; 21 of which were treated conservatively using the conservative/Taylor approach.

Results: The first patient was a 53-year-old lady, with chronic history of epigastric pain. Eophagogastroduodenoscopy revealed a 3.0*3.0cm D2 duodenal diverticulum, CT scan revealed a large retroperitoneal collection which was drained percutanously .The second case was an 81-year-old male patient who presented with sudden onset of severe epigastric pain. CT scan revealed a 4.5*3.0cm duodenal diverticulum with extensive surrounding fat streaking and multiple pockets of free air, suggestive of perforation. A Percutanous drain was also inserted. In both scenarios, conservative measurements were approached, with follow up showing no evidence of contrast extravasation from within the diverticula. No surgical measures were attempted in both.

Conclusion: Two successful cases of perforated duodenal diverticula, treated conservatively, have been presented. With further success in conservatively managing such cases, physicians must adopt a less invasive approach, thus circumventing drastic surgical post-op complications.

Abstract # 52

Mesh-wrapping for the treatment of complicated liver injury

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Keywords: Liver, Trauma, Complication

Descriptive statement: The Following is a case report describing the management of a complicated liver injury that occurred following emergent laparoscopic gallbladder removal (Cholecystectomy).

Position: Ghassan Chamseddine, post graduate Year 3, Surgical resident

Funding Resource: None

Introduction:
Management of liver injuries has changed over the past decades with a trend towards multidisciplinary approach[(1)]. Liver injuries can be managed conservatively[(2)]. Hemodynamically unstable patients require emergent operation[(3).] Peri-hepatic packing is a lifesaving procedure in complex liver injuries [(4)]. However, in significant liver injury, packing is not very efficient. We present a case of laparoscopic cholecystectomy complicated by a life-threatening liver fracture that was managed by staged laparotomies and liver mesh-wrapping.

Case Presentation:
73 year old female underwent Laparoscopic cholecystectomy complicated by intra-operative liver bleeding. Twenty-four hours later, the patient was hemodynamically unstable requiring blood transfusions. Exploration revealed deep fracture in the right lobe reaching the middle hepatic vein which was sutured. The patient transferred to the intensive care unit. One day later, she was re-explored for hemodynamic instability and control of bleeding. The liver was tightly wrapped with a 10x8 inch polyester mesh. The patient had a smooth post-operative course and was discharged home after two weeks in good condition.

Case discussion:
Major liver trauma is a potentially fatal injury. In hemodynamically stable patients, conservative management is considered a safe approach[(5)]. In hemodynamically unstable patients, exploratory laparotomy is warranted. Mesh wrapping is an effective approach for achieving hemostasis by a temponading effect[(6)]. An alternative to liver packing would be the resection of the affected segmented. The advantage however of liver wrapping is that there is no need for reoperation to remove the mesh. Two important technical steps that have been previously described and are re-emphasized in this case report is the need to wrap the mesh under enough tension to create a temponade effect and to secure the mesh on two anchoring points[(7)].

Conclusion:
Using an absorbable mesh on a traumatized and fragmented liver appears to be a safe and effective approach to high grade liver injury.

Abstract # 53

Effect of Endotoxin Challenge on Normal, Tumor Initiated, and Invasive Human Breast Cells

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Funding source: Kamal A. Shair CRSL Research Fund 2014, Lebanese National Center for Scientific Research (CNRS-L) and University Research Board (URB)

Keywords: mammary epithelium; breast cancer; inflammation; endotoxin; 2D and 3D models

Descriptive Statement: Endotoxin (ET) treatment of breast cells enhances their epithelial-to-mesenchymal transition (EMT).

Introduction: background and aims: Breast cancer is the most common female cancer worldwide. Among its several types, inflammatory breast cancer (IBC) is the most lethal, mainly after the association of chronic inflammation with malignant transformation in many tissues. Our study aims at investigating the effect of ET insult on two-dimensional (2D) and 3D models of several normal and cancer breast cell lines, by monitoring inflammatory mediators' response and cancer progression.

Methods: Nitric oxide (NO) and interleukin 1-β (IL1-β) levels were measured using colorimetric assays and Elisa; gelatinases activity was assayed by Zymography; proliferation assays include trypan blue cell count, wound healing and trans-well invasion. Lumen formation will be assessed by fluorescent and DAPI staining. EMT markers will be monitored through both, RNA analysis via RT-PCR and protein analysis by western blots.

Results: ET-induced inflammation upregulated MMPs' levels and enhanced cell proliferation in normal mouse mammary epithelial cells SCp2. ET also increased levels of MMPs in 2D (plastic) cultures of normal non-neoplastic HMT-3522 S1 human breast epithelial cells, and intermediate stage of tumorigenesis S1-connexin-43-knockouts (S1-Cx43KO). Assays investigating ET effect on lumen and polarity disruption events in 3D (matrigel) cultures are still in progress. Long term ET exposure accelerated the proliferation rate of moderately invasive MCF-7 and highly invasive MDA-MB-231 breast cancer cells. Levels of inflammatory mediators NO, IL1-β, and MMPs increased in ET-treated MDA-MB-231 cells.

Conclusion: Endotoxin-induced inflammation enhanced inflammatory mediators' response and tumor progression events in normal, tumor-initiated and cancer breast cell lines.

Abstract # 54

Uptake, Delivery and Anticancer Activity of Thymoquinone Nanoparticles in Breast Cancer Cells

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Funding source: This work was funded by the Swedish Research Council and the FAS Dean's office of the American University of Beirut, Beirut, Lebanon.

Keywords: Thymoquinone, Breast Cancer, Nanoparticles, Endocytosis

Descriptive Statement: This work describes an approach for enhancing drug activity and uncovers the mechanism behind nanoparticle internalization.

Position: PhD candidate in cell and molecular biology.

Introduction: background and aims Thymoquinone (TQ) is a promising anticancer molecule but its development is hindered by its limited bioavailability. Drug nanoparticle formulation is commonly used to overcome low drug solubility, limited bioavailability, and nonspecific targeting. This project aimed at synthesizing different TQ nanoparticles (TQ-NP), characterizing them, and assessing their uptake and delivery mechanisms, as well as their anticancer potential in a panel of breast cancer cells.

Methods: TQ-NP were prepared by Flash nanoprecipitation. Dynamic light scattering and scanning electron microscopy were used for the characterization of the size, morphology and stability of the NPs. The anticancer activity was assessed by MTT. The uptake and subcellular intake mechanism of fluorescent TQ-NP were evaluated by both fluorometry and confocal microscopy.

Results: Four different TQ-NPs were formulated. The average diameter size ranged between 45-130 nm. All TQ-NPs were stable and had high entrapment efficiency (75-80%) and loading content (36-50%). *In vitro*, TQ-NP had equal or enhanced anticancer activity effects compared to TQ, in MCF-7 and aggressive MDA-MB-231 breast cancer cell lines. No significant cytotoxicity of the blank NP was noted. The uptake of fluorescent TQ-NP occurred in a time and concentration-dependent manner. Furthermore, treatment with inhibitors of endocytosis revealed the involvement of caveolin mediated endocytic pathway in TQ-NP uptake. This was also confirmed by subcellular localization findings, showing the colocalization of TQ-NP with both caveolin and transferrin, as well as with the early and late markers of endocytosis, EEA-1 and lamp-1 proteins.

Conclusion: Altogether, the results describe an approach for the enhancement of TQ anticancer activity and uncover the mechanisms behind cell-TQ-NP interaction, uptake and biodistribution.

Abstract # 55

Prevalence and correlates of undiagnosed hypertension among Lebanese adults: A national study

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Funding source: The study was funded by the Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET) as the lead organization, in collaboration with the Centers for Disease Control and Prevention (CDC). Additional funds were contributed by the World Health organization (WHO-Lebanon) and the Lebanese National Council for Scientific Research (LNCSR).
Keywords: Undiagnosed hypertension, awareness, hypertension, Lebanon

Descriptive Statement: Hypertension remains the leading cause of cardiovascular disease morbidity and mortality worldwide, with the majority of hypertensive individuals living in developing countries. Considerable proportions of these individuals are unaware of their condition, are therefore undiagnosed, and hence remain untreated. This study brings recent, nationally representative findings on the prevalence and factors associated with undiagnosed hypertension among adults in Lebanon. This can serve to inform clinicians and public health professionals in their pursuit to curb this condition, and to guide public policies and programs at the national level.

Introduction: Undiagnosed hypertension has implications on cardiovascular outcomes; yet its burden and the factors associated with it remain poorly researched in the Arab region including Lebanon. This study examines the burden and correlates of undiagnosed hypertension among a nationally representative sample of the Lebanese population.

Methods: Data was collected using the WHO Stepwise approach for the surveillance of non-communicable disease (NCD) risk factors. Participants aged ≥ 25 years and who had a blood pressure measurement taken were included in the analysis (N=2215). Participants with undiagnosed hypertension were defined as those who had not been told by a health professional that they had high blood pressure (BP), yet upon measurement had a systolic BP ≥140 mmHg and/or a diastolic BP ≥ 90 mmHg. Multivariable logistic regressions were conducted to explore potential predictors of undiagnosed hypertension, namely socio-demographic characteristics, healthcare use, participants' clinical profiles, behaviors and self-perceptions of health.

Results: The overall prevalence of hypertension was 34.2%, and close to half (49%) were undiagnosed. Compared to their counterparts, the following participants were at higher odds of being undiagnosed: adults aged 25-44 years (aOR*=9.5, 95%CI=5.78-15.76), males (aOR=2.2, 95%CI=1.56-3.13), adults with lower risk profile including those with normal body mass index (aOR= 2.3, 95% CI=1.39-3.69), normal cholesterol levels (aOR=2.8, 95% CI=1.95-4.16), not suffering from cardiovascular or cerebrovascular disease (aOR=3.5, 95% CI=2.09-5.80), and not having a family history of hypertension (aOR=5.3, 95% CI=3.52-8.13). In addition, self-perceived levels of good health and of low and/or normal weight were associated with lack of diagnosis. Utilization of health care was not a significant predictor of undiagnosed hypertension.

Conclusion: Undiagnosed hypertension is a major public health problem in Lebanon, and improving awareness is central for intervention. Early screening and periodical disease surveillance targeting the often neglected low risk profile adults are warranted.

* aOR: adjusted odds ratio

Abstract # 56

A murine model to study *Toxoplasma gondii* and influenza A virus co-infection

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Keywords: Influenza A virus, *Toxoplasma gondii*, co-infection

Descriptive Statement: *Toxoplasma gondii* is an obligate intracellular protozoan parasite that can infect a wide variety of animals, including one third of the human worldwide population. Similarly, influenza A viruses (IAV) cause significant morbidity and mortality in human population worldwide. Influenza A/H1N1 virus emerging from pigs cause a pandemic in 2009 and continues to cause infections worldwide. As both *T. gondii and IAV* infections are common, it is intriguing to investigate the outcome of co-infections with both agents, especially that the risk of infection with either pathogen is very high. To the best of our knowledge, no study investigated the outcome of co-infection with *T. gondii* and IAV.

Introduction: *Toxoplasma gondii* infects most warm-blooded animals, including humans. It causes a- to mild symptomatic disease in immunocompetent patients but may become fatal in immunocompromised patients and in fetus of primo-infected pregnant women. Influenza A virus (H1N1) is a negative-sense single stranded RNA virus belonging the *Orthomyxoviridae* family. Like other flu causing viruses, H1N1 causes the typical flu symptoms including: sore throat, cough, fever, chills and some body aches. Since the risk of infection with either pathogen is extremely high, the aim of this study is to address the effect of an acute infection with *Toxoplasma gondii* followed by an IAV infection.

Methods: 6-8 week old female BALB/c mice were intraperitoneally injected with type II *T. gondii* parasites, followed by IAV injection. Mice were sacrificed at days 3 and 5 post infection and those either infected with *T. gondii* or co-infected with *T. gondii* and IAV were verified for acute toxoplasmosis by Western Blot. Parasitic and viral loads in mice organs were quantified by quantitative Real-Time PCR.

Results: We have shown that 10% of mice infected with IAV alone and 20% of those infected with *T. gondii* alone die by day 18. Interestingly, an infection with *T. gondii* followed by IAV the next day has shown 60% mortality by day 18, while an infection with *T. gondii* followed by IAV 4 days later has shown 40% mortality. At the molecular level, the parasitic load in the peritoneum on day 3 post-infection was higher in co-infected mice than those infected with the parasite alone. This may explain the higher lethality in co-infection when compared to an infection with either pathogens.

Conclusion: In our country where *T. gondii* and IAV infection rates are high, we have shown that an infection with *T. gondii* followed by IAV is more lethal than an infection with either pathogen in mice, which is very alarming to patients, especially those who are prone to co-infection with both pathogens.

Abstract # 57

High Incidence of Respiratory Virus Co-infections among Pediatric Cancer Patients in Lebanon

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Funding Source: American University of Beirut, Faculty of Medicine Bridge Funding; Children's Infectious Diseases Center (CIDC), St Jude Children's Research Hospital

Key words: Pediatric cancer patients, respiratory viral infection, co-infection, molecular-based screening, epidemiology

Descriptive statement:
Assessing the burden and distribution of respiratory virus infections among pediatric cancer patients remains a key priority for informing patient care. However, little is known about the burden and distribution of respiratory virus infections in Lebanon. We seek to expand and improve the diagnostic capacity for virus detection among pediatric cancer patients in Lebanon in order to reduce unnecessary antibiotic administration, provide evidence to inform infection control practices, and to identify threats from emerging pathogens.

Introduction:
Background and aims: Pediatric cancer patients have a higher morbidity and mortality risk due to respiratory viral infections than other patient populations because of their immunocompromised status. Regional and local data on respiratory virus infections in pediatric cancer patients are scarce. The aim of this study is to investigate causative viruses of respiratory infections and their burden among pediatric cancer patients at the Children's Cancer Center of Lebanon.
Methods: Nasopharyngeal swabs along with clinical and demographic data were collected from eligible subjects upon obtaining informed consent. Swabs were initially screened with point-of-care rapid kit for dual detection of influenza A/B and RSV. Total nucleic acid was extracted from specimens followed by real time PCR analysis targeting 16 respiratory viruses to estimate the frequency of infections.
Results: Pediatric cancer patients have been enrolled with mean age of 5.7 ± 4.8 years. RSV, influenza A, and influenza B virus were detected in 18%, 8%, and 6% of the subjects, respectively, by using the rapid kit. Real time PCR analysis confirmed virus infection in 85% of subjects with RSV being the most common virus agent (39.3%) followed by influenza B (22.5%), Human

metapneumovirus (21.3%), parainfluenza virus (19%), influenza A (18%), Rhinovirus (18%), and Corona virus (17.9%) . Co-infections were detected in 55% of patients and RSV was the most prevalent co-infecting virus. Real time PCR screening is Superior for the detection low viral titers due to its high sensitivity compared to antigen detection kits (RSV:28% , Flu A: 50% , Flu B: 30%) that are commonly used in diagnostic laboratories .

Conclusion: The study reveals a high burden of respiratory viral infections in pediatric cancer patients in Lebanon and a high prevalence of co-infections in this patient population. The study also validates the superiority of real time PCR to improve the diagnostic capacity of virus pathogens in order to advance patient care among pediatric cancer patients in Lebanon and reduce excessive use of antibiotics.

Abstract # 58

Artificial Neural Network based model can better risk stratify patients undergoing Stress Echocardiography or Nuclear Stress Test and reduce studies by >50%.

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Funding source: none

Keywords: Artificial Neural Network (ANN), Diamond-Forrester (DF), Morise

Descriptive statement: Artificial intelligence based model improves risk stratification of patients referred to non-invasive cardiac imaging and can reduce cost.

Introduction: Coronary Artery Disease (CAD) accounts for more than half of all cardiovascular events. Stress testing remains the cornerstone for noninvasive assessment of patients with possible or known coronary artery disease (CAD). Clinical utilization reviews show that most patients who present for evaluation of stable CAD by stress testing are categorized as low risk prior to the test. Attempts to better risk stratify individuals being sent for stress testing seems to be more in need today. The aim of the present study was to compare Artificial Neural Networks (ANN) based prediction models to the other risk models being used in practice (the Diamond-Forrester and the Morise models).

Methods: We prospectively recruited patients older than 19 years old, who were being evaluated for coronary artery disease through nuclear Stress Test or treadmill Stress Echocardiography. Inclusion criteria were: patients presenting with symptoms suspicious for stable angina or with features of unstable angina with normal ECG and negative cardiac biomarkers (2 sets of troponin). We excluded patients with Non-ST elevation Myocardial Infarction, ST elevation Myocardial Infarction or with Unstable Angina and ECG changes.

Results: In 486 patients included, we demonstrated higher discriminatory power of ANN (DP=1.61; good) based model compared to Morise (DP= 0.45; poor) and Diamond-Forrester (DP=0.64; poor) scores. This ANN model has a negative predictive value of 98%, Sensitivity 91% [81% - 97%], Specificity 65% [60%- 79%] and positive predictive value 26% while reducing non-invasive studies by 59% (Table 1).

	Sensitivity %	Specifiicity %	PPV %	NPV %	LR+	LR-	DP	Stress imaging Avoided
Morise	65 [48-79]	55 [51-59]	8.2	96	1.44	0.63	0.45	54%
DF	69 [53-83]	59 [55-62]	9.5	96.9	1.68	0.52	0.64	57%
ANN	91 [81-97]	65 [60-69]	26	98	2.6	0.14	1.61	59%

Table 1.Performance of DF, Morise scores and ANN models to assess for inducible ischemia by stress imaging.

Conclusion: We showed that ANN model has a higher discriminatory power than Diamond-Forrester and Morise risk models in predicting ischemia with stress echo or nuclear stress test. This ANN model can significantly decrease downstream testing by 59% if employed.

Abstract # 59

Comparative analysis of Robotic Assisted Partial Nephrectomy (RPN) versus Open Partial Nephrectomy (OPN) during the Robotic Learning Curve: Does the End Justify the Means*?*

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Keywords: Partial, Nephrectomy, Robotic Assisted, ischemia, transfusion, glomerular filtration rate.

Introduction: To compare the outcomes of RPN vs. OPN for kidney tumors, during the introduction of Robotic Urologic Oncology at our institution

Methods: A retrospective review of all consecutive partial nephrectomies, RPN and OPN, performed at the American University of Beirut Medical Center since the inception of the robotic program in July 2013 until July 2015. Preoperative variables (patient characteristics, tumor size, R.E.N.A.L. score) and perioperative renal functional/patient outcomes (% change in GFR, ischemia time, blood loss, need for blood transfusions, total operating time, & length of hospital stay) were compared using SPSS

Results: Thirty-four consecutive patients underwent partial nephrectomy, 19 OPN and 15 RPN. Preoperative variables including the size and R.E.N.A.L. score of the tumor were analyzed. The difference in the median size of the tumor between OPN & RPN was not statistically significant (4.5 ± 2.7 cm vs. 3.6 ± 1.7 cm, respectively, p=0.25). R.E.N.A.L. score was significantly higher for OPN compared to RPN (7.3 ± 2.3 vs. 4.9 ± 1.5, respectively, $p<0.05$). Mean operative time was significantly shorter for OPN vs. RPN (178 ± 52 min vs. 296 ± 86 min, respectively, $p<0.05$). Cold ischemia time was 24 min in OPN, warm ischemia time was 17.5 min for RPN; 10 out of the total 15 robotic cases were performed with a warm ischemia time < 20 min. Intraoperative blood loss was comparable for both approaches (225 ± 132 ml in OPN vs. 243 ± 192 ml in RPN), and there was no need for blood transfusions in either group. Hospital stay was significantly longer for OPN vs. RPN (6 ± 1.6 days vs. 4 ± 0.9 days, respectively, p= 0.01). The percentage change in GFR was comparable among both procedures (OPN = -9% vs. RPN = -7%); pathological margin status was also comparable among both procedures, with 1/19 (5%) positive focal margins in OPN, vs. 0/14 in RPN. None of the robotic procedures required conversion to the laparoscopic or open approach.

Conclusion: RPN seems to be a promising approach for the treatment of kidney tumors with the advantages of decreased crude ischemia time and a shorter hospital stay, with comparable intraoperative blood loss and risk of GFR reduction. Tumor characteristics were not equivalent, with higher RENAL scores noted in patients allocated to OPN vs. RPN, thus limiting a fair comparison of outcomes. However, the data confirm that with proper selection of patients for RPN, outcomes were equivalent to OPN and were not jeopardized during the robotic learning curve. Larger prospective studies are needed to validate our results.

Abstract # 60

The Photoprotective Effects of 2-Benzoyl-3-phenylquinoxaline 1,4-Dioxide (BPQ) against UVB-Induced Damage in HaCaT Cells

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Funding source: Undergraduate Research Experience Grant Award from the Faculty of Arts and Sciences at AUB.

Keywords: UVB Radiation, HaCaT cells, photocarcinogenesis, photoprotection, BPQ, quinoxaline 1,4-dioxide, oxidative stress, sunscreen.

Descriptive Statement: A quinoxaline derivative, BPQ, was tested for its photoprotective efficacy against UVB-Induced damage in a human keratinocyte cell line, HaCaT, in culture.

Introduction: background and aims: With the increasing levels of ozone depletion in our atmosphere, much concern has been rising pertaining to the effect of the augmenting amounts of ultraviolet radiation reaching the Earth's surface in inducing skin carcinogenesis. This has led to a growing interest in the search for new active ingredients to be used in commercial sunscreens. In our study, the chemical compound 2-Benzoyl-3-phenylquinoxaline 1,4-Dioxide (BPQ) prepared by the Beirut Reaction, was tested for its ability to protect a human keratinocyte cell line (HaCaT), in-vitro, against ultraviolet B radiation (280-315 nm).

Methods: Multiple approaches were employed, including MTT cell proliferation assay for cell viability analysis, microscope image processing, measurements of absorption spectra via UV/VIS Spectrophotometry, and measurements of oxidative stress levels via DCFH assays using flow cytometry.

Results: We show that BPQ exhibited strong absorbance in the UVB range, with an overall absorption spectrum very similar to that of Padimate-O, a well-known active ingredient used in commercial sunscreens. HaCaT cells which were irradiated with UVB in the presence of multiple dosages of BPQ exhibited, in a dosage dependent fashion, a significantly higher viability and lower oxidative stress levels than those irradiated without the drug.

Conclusion: Our data show that BPQ is a potential photoprotective drug against ultraviolet B radiation. BPQ holds great promise in its potential use as an active ingredient in commercial sunscreens, aiding in the prevention of skin tumor promotion by UVB.

Abstract # 61

Discharge against medical advice from the Emergency Department. Results from a tertiary care hospital in Beirut, Lebanon

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Funding source: Research not funded
Keywords: Against Medical Advice, AMA, reasons, predictors, emergency department, Lebanon.
Descriptive statement: this study assessed the characteristics of patients who leave AMA in a payment prior to service ED model and to identify predictors for return visits to ED after leaving AMA.

Background: Patients who leave the emergency department against medical advice are at high risk for complications. AMA discharges are also considered high-risk events potentially leading to malpractice litigation.

Objectives: Our aim was to characterize patients who leave AMA in a payment prior to service ED model and to identify predictors for return visits to ED after leaving AMA.

Methods: We conducted a retrospective review study of charts of ED patients who were discharged AMA between 1/1/2012 and 1/1/2013 at a tertiary care center in Beirut Lebanon. We carried out a descriptive analysis and a bivariate analysis comparing the first visit and the return visit within 72 hours. This was followed by a Logistic regression to identify predictors of return visits after leaving AMA.

Results: A total of 1213 ED patients were discharged AMA during the study period. Mean age was 46.9 years (± 20.9). There were 654 males (53.9%), 737 married (60.8%). The majority (1059 patients (87.3 %)) had an emergency severity index of 3 or less (1 or 2). ED average length of stay was 3.8 hours (±6.8). Self-payers accounted for 53.9%. Reasons for leaving AMA were: no reason mentioned (44.1%), incomplete workup (30.5%), refusing admission (12.4%), financial reasons (7.9%), long wait times (2.9%) and others (2.2%). Discharge diagnoses were mainly cardiac (23.4%), gastrointestinal (16.4%), infectious (10.1%) and trauma (9.8%).

One hundred nineteen returned to ED within 72 hours (9.8%). Predictors of returning to ED after leaving AMA were: older age (OR 1.02 95% CI (1.01-1.03)), private insurance status (OR 4.64 95% (CI 2.89-7.47) within network insurance status (OR 7.20 95% CI (3.86-13.44), longer ED LOS during the first visit (OR 1.03 95%CI (1.01-1.05).

Conclusion: In our setting, the rate of return visit to ED after leaving AMA was 9.8%. Reasons for leaving AMA, high-risk discharge diagnoses and predictors of return visit were identified. Financial status was a strong predictor of return to ED after leaving AMA.

Abstract # 62

Description of Blast Injuries and Predictors of Admission to Hospital in Blast Victims in an Urban Civilian Setting

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Funding source: Research not funded

Keywords: Blast injuries, facial injuries, emergency department, Lebanon.

Descriptive statement: this study described blast injuries characteristics and identified predictors of hospital admission after sustaining a blast injury.

Introduction: Blast injuries characteristics and outcomes are not well described in urban civilian settings.

Objectives: we sought to describe blast injuries characteristics and identify predictors of hospital admission after sustaining a blast injury.

Methods: Retrospective chart review study of blast victims who presented to the ED of a tertiary care center in Beirut Lebanon over 8 years. We conducted a descriptive analysis, followed by a multivariate analysis to identify predictors.

Results: A total of 59 patients were included. They were mostly males (81.4%) with a mean age of 35.4 (±15) years with high rate of admission to the hospital (71.2%). Surface injury (mainly open wounds) was most common (91.5%). Injuries involved mainly the face (45.8%) and thigh/knee (33.9%). Significant associations were identified between different injury locations. Significant predictors of hospital admission in blast victims were internal injury (OR =11.6, 95%CI [1.7, 79.9]), orthopedic injury (OR= 41.1, 95%CI [3.4, 496.2]), and undergoing a chest xray in the ED (OR=14.3, 95%CI [2.2, 93.3]).

Conclusion: Blasts in a civilian setting result in a wide range of injuries. Facial injuries were most common in our setting with close associations between injuries of different organ systems. Identified predictors of hospital admission can help guide disposition decision for blast victims in the ED.

Abstract # 63

Pediatric ED visit study abstract

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Funding source: Research not funded
Keywords: common diagnoses, pediatric ED visits, emergency department, Lebanon.

Descriptive statement: This study identified the most common diagnoses for child emergency department visits AUBMC in Lebanon.

Introduction: There were over 25.5 million Emergency Department (ED) visits for children < 18 years in the US in 2010, according to HCUP (Healthcare Cost and Utilization Project). Accurate reporting in developing countries is often lacking. This project aimed to identify the most common diagnoses for child emergency department visits at AUBMC.

Methods: A retrospective chart review of pediatric patients (Age ≤18) presenting to AUBMC ED during the study period (May 2010-April 2011) was completed. Investigators looked at the most common diagnoses among 5 age groups (<1 year, 1-4 years, 5-9 years, 10-14 years, 15-18 years) in 3 categories (all pediatric ED visits, treat-and-release and admitted visits). Data included Socio-demographic variables, clinical characteristics, guarantor, Emergency Severity index, and diagnosis. Diagnoses were classified according to CCS (Clinical classification software). Descriptive statistics were performed. The Pearson chi- square test was used to stratify the most common diagnoses by age groups.

Results: A total of 12637 pediatric ED visits were included. The majority (90.2%) were among the treat-and-release group. The mean age for all 3 groups was 7.2 years with 57.1% of male gender. A high proportion (53.5%) of patients had an ESI of 3. Infants < 1year accounted for 4.1% of pediatric treat and release visits and 15.8% of those hospitalized. The age distributions of children >1 year among the three groups were comparable. The top 5 most common reasons for all ED visits included: fever of unknown origin (21.5%), injuries and conditions due to external causes (17.6%), other upper respiratory infections (8.2%), open wounds of head (7.3%), neck and truck (7.2%). Intestinal infection and noninfectious gastroenteritis were frequent across all age groups for admitted patients; whereas fever of unknown origin was common among all ED visits& outpatient in most age groups.

Conclusion: This study is the first to assess pediatric ED visits at AUBMC in Lebanon. The top most common reason for all ED visits was fever of unknown origin, contrary to North America where injury and poisoning is the most common. Assessing the burden of acute conditions in developing countries is crucial for ensuring proper resource allocation in emergency departments.

Abstract # 64

Characteristics and outcomes of snake bites at a tertiary care hospital in Lebanon

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Presenter: Dr. Reem El Assaad (postdoctoral fellow)

Funding source: Research not funded

Keywords: Snake bites, Antivenin, emergency department, Lebanon.

Descriptive statement: This study describes demographic and clinical characteristics, treatment modalities and outcomes of confirmed cases of snakebite victims treated at a tertiary care hospital in Beirut, Lebanon.

Background: It is estimated that 5.5 million people are victims of snakebites yearly worldwide resulting in about 125,000 deaths. Few reports of snakebites in the Eastern Mediterranean region exist in the literature. This study describes demographic and clinical characteristics, treatment modalities and outcomes of confirmed cases of snakebite victims treated at a tertiary care hospital in Beirut, Lebanon.

Methods: We performed a retrospective chart review of patients who presented to the Emergency Department (ED) during the study period (1/1/2000 to 9/30/2014) with a chief complaint of snakebite. Investigators extracted the following data: date of bite, patient's age and gender, geographical area where the bite occurred, time elapsed from bite until ED presentation, body location of injury, systemic and local manifestations, laboratory findings, severity of envenomation, complications and antivenin administration. Descriptive statistics and frequencies were performed.

Results: A total of 24 patients were included in the study. The mean age was 34.6 (± 16.4) years with 58.3 % of male gender. Local manifestations were documented in 15 (62.5%) patients, systemic effects in 10 (41.7%), hematologic abnormalities in 10 (41.7%) and neurologic effects in 4 (16.7%) patients (Table). Nine patients (37.5%) received antivenin (Polyvalent Antivenom-2). The median amount of antivenin administered was 40 ml or 4 vials (1–8 vials).

Twelve patients (50%) were admitted to the hospital with 9 (75%) to an intensive care unit and 3 (25%) to a regular bed. All were discharged home with a mean length of stay in hospital of 10.2 (± 14.4) days.

Among those admitted, seven patients (58.3%) had at least one documented complication during their inpatient stay, including: compartment syndrome (33.3%), fasciotomy (25%), airway compromise requiring intubation (16.6%), deep vein thrombosis (16.6%), disseminated intravascular coagulopathy (16.6%), acute respiratory distress syndrome (8.3%), sepsis (8.3%), congestive heart failure (8.3%), cellulitis (8.3%), upper gastrointestinal bleed (8.3%) and vaginal bleed (8.3%).

Conclusion: In this study, victims of snakebites developed local, systemic, hematological or neurological manifestations. Antivenin was administered Complications from the snakebite were frequent. Larger studies are needed to establish better guidelines for the treatment of snakebites in Lebanon.

Abstract # 65

Complications from the Administration of Vasopressors through Peripheral Venous Catheters: An Observational Study

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Funding source: Research not funded

Keywords: Vasopressor, Vasoactive agent, Peripheral, Complication, Extravasation, shock.

Descriptive statement: this study assessed the safety as well as the efficacy of vaso-active therapy administration through a peripheral venous catheter.

Background: Circulatory shock is a life threatening condition that is frequently encountered in the Emergency department. The early recognition and treatment of shock is essential. The introduction of vasopressors therapy along with early fluid resuscitation has shifted the paradigm of care and survival outcomes. Surviving sepsis campaign guidelines put an emphasis on vasopressors administration through a central line; however the placement of central lines is associated with life threatening complications as well as delays in vasopressors administration. Some medical institutions begin vasopressors therapy through a peripheral line until a central line is inserted in order to avoid delays in therapy. Data concerning the safety and efficacy of the peripheral administration of vasopressors is still lacking. Most of the complications of peripheral therapy in the literature have been in the form of case reports. The objective of this study is to assess the safety as well as the efficacy of vaso-active therapy administration through a peripheral venous catheter.

Methods: In this case series, 55 patients were enrolled and followed by research fellows who physically examined the intravenous access site twice daily during the period of peripheral vasopressor administration, then daily, up to 48 hours after treatment discontinuation or until the patient died. The research fellows were educated to identify the complications of interest including drug extravasation, thrombophlebitis, localized cellulitis, tissue necrosis, and limb ischemia. The duration of peripheral vasopressor treatment, type of vasopressor used, dilution, maximal infusion rate, and PVC location was recorded.

Results: Of the 55 patients that were recruited, 3 (5.45% overall, 6% of patients receiving noradrenaline) developed one of the pre-specified complications. Two developed local extravasation and one developed local thrombophlebitis. None of these complications required any medical or surgical intervention. Two of the three complications occurred in the hand, and all occurred in patients receiving norepinephrine and with 20 Gauge catheters.

Conclusion: The incidence of complications from the administration of vasopressors through a PVC is small and didn't result in significant morbidity. Larger prospective studies are needed to better determine the factors that are associated with these complications, and identify patients in which this practice is safe.

Abstract # 66

Towards a Safer Design of Helmets – Finite Element and Experimental Assessment

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Keywords: bio-inspired helmet design, Drop testing, acceleration, sensing, brain trauma, liner foam, Von Mises Stress

Descriptive Statement: As the human head is greatly vulnerable to sudden impacts, it is of importance to assess the energy absorbing capacities of motorcycle helmets, particularly foam liners in existing market helmet designs; this involves both experimental and finite element assessment to recommend a safer-design. The objective of the liner foam design is to maximize absorbance of energy, and we have used a bio-inspired design from animal hooves and horns to suggest a shock-absorbing design.

Funding source: Principal: Department of Mechanical Eng'g – AUB, Minor: Self-funded

Introduction: Head trauma requires specialized medical care and continuous rehabilitation, thus well-designed helmets can substantially reduce the costs behind such preventable crashes. Our main aim is to assess and enhance the performance of liner foam material in existing market helmets.

Methods: Experimental (Drop Test Apparatus) and Finite Element Model Simulations (ANSYS)

Results: In progress, we are currently building the drop testing apparatus, and beginning with finite element modeling.

Conclusion: Also in progress, we aim to test our design against the standardized ece22.05 acceleration limit of 275 g upon impact to see if our design meets this motorcycle helmet standard, and test it against common helmets in the market place.

Abstract # 67

Cytokine profiling in chronic neurotoxoplasmosis caused by the Knock-Out parasite for the bradyzoite marker *p18* in the C57BL/6J mouse model

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Funding source: Cèdre, MPP, CNRS-L
Keywords: *Toxoplasma gondii*, Pru*ΔKu80Δp18*, bradyzoite, C57BL/6J, chronic toxoplasmosis, immune profile

Descriptive Statement: *Toxoplasma gondii* is an obligate intracellular parasite that infects humans where it establishes a life-long chronic disease, by forming bradyzoite cysts in their brain. We generated the Pru*ΔKu80Δp18* strain in which the bradyzoite encoding marker *p18* is deleted and found a difference in cyst forming capacity with the wild type strain Pru*ΔKu80.* We have tested the immune response in C57BL/6J susceptible mice to better understand p18 function.

Introduction: *T. gondii* is capable of establishing an acute and/or latent chronic infection in a wide variety of hosts. Switching from acute to chronic phases is strongly mediated by the host immune response. IFN-γ is key driver of this process tightly controling the chronic cerebral infection, and activating microglia cells to produce nitric oxide (NO). NO, along with pro- and anti-inflammatory cytokines, triggers the conversion to bradyzoite forms and is critically important to control infection in C57BL/6 mice. We showed in prior studies that Pru*ΔKu80Δp18* displays a different capacity of forming cysts in murine neurotoxoplasmosis. We investigated the difference of immune response upon infection with Pru*ΔKu80Δp18* and Pru*ΔKu80* strains in the brains of the susceptible C57BL/6J mice.

Methods: C57BL/6J were infected with Pru*ΔKu80Δp18* and Pru*ΔKu80* strains and were treated with sulfadiazine to overcome the acute phase of toxoplasmosis. Blood was collected on day 7 post infection (p.i.) to verify the acute infection by the western blotting. Mice were sacrificed on weekly basis from week 2 until week 5. Total mRNA was extracted from the brains, and different immunomodulatory cytokines and chemokines (MCP-1, IFN-γ, iNOS, IL-12 and IL-10) were measured using Real Time PCR.

Results: We have seen a clear difference of cytokine levels in brains of mice infected with Pru*ΔKu80Δp18* and Pru*ΔKu80.* Pru*ΔKu80Δp18* stimulates higher levels of IFN-γ reaching a maximum at week 2 presumably leading to the recruitment of more macrophages as the MCP-1 levels were also higher and reached a maximum on week 3 p.i. Since Nitric Oxide (NO) plays a vital role in controlling toxoplasmosis progression, and since inducible NOS (iNOS) levels are upregulated in brains of infected mice with type II *T.gondii*, we have shown that Pru*ΔKu80Δp18* leads to higher levels of iNOS at all time points reaching a maximum at day 35, presumably controlling the infection and leading to different capacity of cyst formation as IL-12 levels decrease at day 35 while IL-10 increase to alleviate the disease burden.

Conclusion: The current study highlights the role of the bradyzoite marker *p18* in shaping the brain immune response, allowing the understanding of key molecular mechanisms related to the neurotoxoplasmosis.

Abstract # 68

Sources, dispersion and toxicity of PAHs and Dioxins at AUB, Zouk and Dora

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Funding source: [insert here]

Keywords: Pollution, Cancer, Air and chemicals

Descriptive Statement: Assessment of the air quality of Beirut

Introduction: There are two families of toxic air pollutants; polycyclic aromatic hydrocarbons (PAHs) and polychlorinated dibenzo-p-dioxins and dibenzofurans PCDD/Fs, for which assessment and characterization in the atmosphere need to be considered. Polycyclic aromatic hydrocarbons (PAHs) in the atmosphere originate from biogenic sources, such as forest fires and volcanic eruption. However, their presence in populated urban areas is influenced by anthropogenic emissions, such as domestic and industrial activities as well as gasoline and diesel combustion. Persistent organic pollutants (POPs) are semivolatile compounds associated to particulate matter and include polychlorinated dibenzo-p-dioxins and dibenzofurans PCDD/Fs, so called "Dioxins". PCDD/Fs have been reported to be carcinogenic and mutagenic possessing toxicities towards human health. They are released from the incomplete combustion of chlorinated species and incinerators.

Methods: The chaotic unregulated emission from the aforementioned sources has led us to conduct a systematic measurement and assessment of PAHs and PCDD/Fs in three representative sites (AUB, Zouk and Dora) of Beirut and its suburbans. Particulate and gaseous phase PAHs and Dioxins were collected using a high volume sampler (HVS) equipped with both quartz fiber filter and polyurethane foam (PUF). Following, thorough and careful extraction and quantification approaches were followed according to international and locally developed standard operation procedures (SOPs).

Results: Results showed spatial variations in the levels of PAHs and dioxins at AUB, Zouk and Dora. The lowest concentrations of these chemicals were registered at AUB. Higher amounts were found in Zouk, but the most toxic levels were in Dora. Strong seasonal variations were observed among PAH levels. Light PAH concentrations were always higher during the winter, whereas heavy congeners amounts were relatively higher in the summer. These sources were apportioned using PMF.

Conclusion: Collected data helped in assessing the incremental lifetime cancer risks (ILCRs) based on a scenario evaluation and suggesting policy recommendations.

Abstract # 69

Antitumor Effect and Nanoparticle Drug Development of the Adamantyl Retinoid ST1926 in Acute Myeloid Leukemia

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Background and Aims: Acute myeloid leukemia (AML) is a clinically and genetically heterogeneous disorder of hematopoietic progenitor cells, which have lost their normal ability to differentiate. AML represents one of the most complex types of leukemia. Until today, there is no standard regimen to treat AML patients. Retinoids regulate a wide range of biological processes, including development, and cell differentiation, proliferation, and death. The natural retinoid all-*trans* retinoic acid (ATRA) became the paradigm for the treatment of acute promyelocytic leukemia (APL), an AML subtype. However, in non-APL AML patients, ATRA is only effective on one subtype characterized with *nucleophosmin* mutations. Therefore, synthetic retinoids, specifically the adamantyl ST1926, emerged as potent anticancer agent. However, ST1926 development in clinic was limited due to its rapid glucuroconjugation resulting in low plasma concentrations. Nanomedicine has recently gained widespread attention, where it enables more efficient drug delivery and bioavailability. Therefore, we aimed at investigating the antitumor effect of ST1926 using human non-APL AML *in vitro* models, developing nanoparticle formulations of the drug, and reproducing an AML xenograft mouse models for preclinical drug assessment.

Methods and Results: We used representative human non-APL AML cell lines harboring different genetic mutations and representing several AML karyotypes. We showed that sub-micromolar concentrations of ST1926 inhibited the proliferation of all tested AML cell lines and primary AML patient cells in an irreversible manner. ST1926 induced apoptosis as evidenced by the accumulation of treated cells in the preG_1 region of the cell cycle, Annexin V positivity, PARP cleavage, and mitochondrial membrane dissipation. Furthermore, ST1926 increased the protein expression levels of p53 and γH2AX. Interestingly, the ST1926 antitumor effect was shown to be p53 and RAR-independent but was reversed upon the addition of DNA damage inhibitors. Polymer-stabilized ST1926 nanoparticles were developed using Flash NanoPrecipitation, and were shown to have comparable anti-growth activities to the naked drug in vitro. Finally, we have successfully reproduced and optimized an AML xenograft mouse model using immunocompromised NOD/SCID mice.

Conclusion: Our studies highlight the use of ST1926 and its nanoparticle development as promising anticancer drugs for further preclinical investigation in AML therapy.

Keywords: Acute myeloid leukemia; Retinoids; Apoptosis; Nanoparticles; Drug delivery; Cancer therapy, Xenograft mouse models

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Abstract # 70

Neo-adjuvant FOLFIRINOX in borderline-resectable/locally advanced pancreatic adenocarcinoma

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Funding source: AUBMC

Keywords: FOLFIRINOX; neoadjuvant therapy; pancreatic cancer

Descriptive Statement: Our study aims at assessing the benefits of using the FOLFIRINOX chemotherapy regimen in a preoperative setting to patients with locally advanced/borderline resectable pancreatic cancer.

Introduction: Neo-adjuvant therapy with FOLFIRINOX in patients with locally advanced/borderline resectable pancreatic cancer has the potential to down-stage tumors enabling surgical resection. The aim of this study was to evaluate the effect of neo-adjuvant FOLFIRINOX and determine the proportion of patients who proceeded to surgery (resulting in R0 or R1 resection) following FOLFIRINOX induction therapy. Secondary objectives included response rate to FOLFIRINOX therapy (Complete Response (CR) / Partial Response (PR) / stable disease (SD)), assessing the toxicity and calculating Progression Free Survival (PFS) and Overall Survival (OS).

Methods: This was a prospective cohort study. After IRB approval, patients with locally advanced/ borderline resectable pancreatic cancer gave written consent for data collection and follow-up Patients were treated with FOLFIRINOX chemotherapy every 2 weeks until surgery, progression of disease or toxicity necessitating discontinuation of treatment.

Results: Twenty patients were included in the study with a median follow-up of 12 months. 12 of the included patients (60%) were unresectable at baseline due to vascular invasion. After neoadjuvant chemotherapy 11 patients (52.4%) had a significant partial response, only 2 (10%) were amenable to resection. At 12 months, PFS was44.2% 12m survival was54.9%, the median PFS was 12 months and the median OS was 17 months. The median number of FOLFIRINOX cycles administered was 12 with good tolerability.

Conclusion: FOLFIRINOX therapy in locally advanced/borderline pancreatic cancer in this cohort was well tolerated with a significant partial response rate (52,4%). Although, the down staging capacity was limited (10%). The median PFS and OS are promising, this is to highlight the role of neoadjuvant chemotherapy, and emphasize the necessity of further prospective studies in this category of patients with pancreatic cancer.

Abstract # 71

BRCA1 and *BRCA2* mutation spectrum in Lebanese women undergoing testing for hereditary breast/ovarian cancer

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Funding source: MRP

Keywords: *BRCA* mutations, Breast cancer, ovarian cancer, Familial, Lebanon

Descriptive Statement: This study represents an updated evaluation of the deleterious genetic variants and the unclassified ones in the *BRCA1*/*BRCA2* genes among a group of Lebanese women with high risk for breast/ovarian familial cancer.

Introduction: background and aims In Lebanon, breast cancer is considered the most common malignancy among women, with 50% diagnosed before the age of 50 years. Up to 10% of breast cancers are considered directly related to the inherited germline mutations in *BRCA1* or *BRCA2* genes. In this retrospective study, we aimed at reporting the prevalence of *BRCA1* and *BRCA2* mutations in a Lebanese cohort of individuals with personal or strong family history of breast/ovarian cancer, in order to determine the role of *BRCA* testing in risk assessment for inherited breast/ovarian cancer in our population.

Methods: All Lebanese patients who underwent clinical full-sequence DNA testing for mutations in *BRCA1/2* at AUBMC between 2011 and 2015 with a reported self and/or family history of breast/ovarian cancer were considered for the study. This cohort consisted of 200 patients (197 women and 3 men) from 188 unrelated Lebanese families of different demographic groups. Demographic and personal/family cancer history data were collected and the archived genetic results were reviewed. Variants were analysed according to ENIGMA consortium, Bic database and the bioinformatic tools: SIFT, Polyphen, Align-GVGD.

Results: Deleterious mutations were identified in 10.6% of the families (20/188), sixteen in *BRCA1* gene and four in *BRCA2* gene. In total, twelve deleterious mutations were recognized, four of them were novel. In 30% (6/20) of the carrier families the *BRCA1* C44F mutation was identified, this is reportedly the most common breast cancer causing mutation in our population, suggesting a possible founder effect. Two other mutations IVS24-1G>A and E720X accounted for respectively 15% and 10% of the familial mutations. Twenty five variants were considered of unknown clinical significance (10 *BRCA1*, 15 *BRCA2*).

Conclusion: Prevalence of *BRCA1* and *BRCA2* mutations was found to be high among tested women. Three mutations accounted for more than 55% of the total detected mutations. Two mutations previously reported in Europe and one reported solely in our population. This study stresses on the importance of *BRCA* testing in Lebanese women at high risk for breast/ovarian cancer. It also highlights interesting data in terms of prevalence and spectrum of BRCA mutations in our population.

Abstract # 72

Impact of Vitamin D Replacement in the Middle East and North Africa: A systematic Review and Meta-analysis of Randomized Controlled Trials

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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 Reseach Program (SHARP).

Keywords: Vitamin D replacement, Middle East and North Africa, meta-analysis.

Descriptive Statement: Hypovitaminosis D is prevalent in the Middle East and North Africa (MENA) region. This meta-analysis pools the data of vitamin D randomized controlled trials conducted in adults in the MENA countries. The aim is to assess the effect of various vitamin D replacement doses on vitamin D status and other outcomes. The results show that doses that are 2-3 folds higher than those recommended for Western populations may be required to allow to the majority of individuals from our region to reach desirable vitamin D levels.

Introduction: Hypovitaminosis D is prevalent worldwide, more so in the MENA region. Our aim is to compare, in subjects from the MENA region, the effects of vitamin D on the mean difference in 25-hydroxyvitamin D [25(OH)D] level reached, on skeletal and extra-skeletal outcomes, and to characterize the vitamin D dose response.

Methods: A comprehensive search based on 7 search engines was conducted until July 2015. We considered relevant randomized trials in adults comparing the effect of low (< 800 IU), intermediate (800 - 2,000 IU) or high (> 2,000 IU) daily dose of vitamin D or placebo. We selected articles and abstracted data independently in duplicate. We calculated the mean difference (MD) and 95% Confidence Interval (CI) of 25(OH)D level reached for eligible comparisons, and pooled data using RevMan version 5.3. We conducted a multivariate meta-regression using STATA version 12.

Results: We identified 17 studies in adults. Comparing a high vitamin D dose (weighted mean (WM) dose of 4,856 IU/d) to placebo, the MD in 25(OH)D level achieved was 18.3 (14.12;22.49) ng/ml; comparing an intermediate dose (WM dose of 1,750 IU/d) to placebo, the MD in 25(OH)D level achieved was 14.7 (4.57;24.89) ng/ml. Accordingly, 89% and 71% of participants, in the high and intermediate dose groups, respectively, reached the desirable 25(OH)D level of 20 ng/ml. Data on other outcomes was scarce. In the meta-regression, the average increase in 25(OH)D level was 0.4 ng/ml per 100 IU/d increment of vitamin D dose.

Conclusion: In the MENA region, a vitamin D dose ≥ 2,000 IU/d may be needed to allow to the majority of adults to reach a conservative desirable 25(OH)D level ≥ 20 ng/ml, the target level defined by the Institute of Medicine. Long term data is needed to confirm the safety and the efficacy of such doses on various outcomes.

Abstract # 73

Frequencies and Distribution Patterns of Y-chromosome Micro-deletions in a Sub-population of Lebanese Men with Severe Male Infertility

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Funding source: Johnny Awwad unrestricted fund

Keywords: Male infertility, Microdeletion, Genetics, Y-chromosome.

Descriptive Statement: Deficient sperm production accounts for more than half of couples with inability to conceive after one year of unprotected intercourse. Structural gene defects are believed to account for 10 to 50% of severe male infertility, and have significant prognostic implications on lasting sperm production. Our findings suggest a very low occurrence of these defects (2.5%) in the Lebanese infertile men population. Different mechanisms of disease processes are entertained. More appropriate methodologies of screening in uncharacterized populations are revisited.

Introduction:

Background. Deficient spermatogenesis accounts for more than half of infertile couples presenting for counseling. Intriguingly, infertility of male etiology remains poorly investigated and for that matter highly misunderstood.

It is believed that micro-deletions occurring in the AZF sub-regions of the P arm of the Y chromosome constitute the most common structural genetic abnormalities associated with severe spermatogenetic defects. In men with severe oligospermia (sperm count ≤ 5 M/mL) and/or azoospermia (absence of sperm in the ejaculate), the occurrence of micro-deletions has been reported in about 10 to 50% of cases depending on the population under investigation.

Specific microdeletions may indicate complete spermatogenetic arrest. Others are believed to predict an imminent failure of ongoing spermatogenesis. They are also believed to carry a significant risk of vertical transmission.

Aim. In Lebanon, the incidence of Y-chromosome micro-deletions is not known. We planned to investigate the frequency and distribution patterns of Y-chromosome micro-deletions in a sub-population of Lebanese infertile men presenting with severe oligo- and azoospermia.

Methods: One hundred and twenty men with severe male infertility underwent genetic studies at the Human Genetics Laboratories at AUBMC between January 2007 and December 2014.

Multiplex PCR technique was performed on peripheral blood leucocytes to check for the presence or absence of defined Y chromosome loci using the sequence tagged sites (STS

markers) recommended by the European Society of Human Genetics (ESHG) Consortium. Blood samples from confirmed affected subjects were used as positive controls, and from women as negative controls.

Results: Three of 120 men investigated for severe oligo- and/or azoospermia were identified to harbor a Y-chromosome microdeletion, for a calculated incidence of 2.5%. Detected microdeletions were mapped to the AZFc sub-region in all three cases. Fourteen per cent of men showed chromosomal abnormalities on karyotype analysis; one fourth of which were 47, XXY Klinefelter.

Conclusions: The findings of this study suggest a much lower frequency of Y-chromosome micro-deletions in the Lebanese infertile men, than reported elsewhere.

The likelihood of other pathophysiological mechanisms affecting spermatogenesis in this population of infertile men, should be entertained and further explored.

Alternatively, it may also be possible that the panel of STS markers proposed by the ESHG Consortium does not cover adequately gene defects relevant to the Lebanese infertile male population. The investigators propose the use of gene sequencing as the initial methodology of choice for yet uncharacterized populations to define community-specific micro-deletion patterns and develop appropriately-tailored STS markers.

Abstract # 74

Adiponectin Exerts a Protective Role against Vascular Remodeling During Hypertension

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Funding source: Medical Practice Plan (MPP)
Keywords: Adiponectin, mechanical stretch, hypertension, vascular, hypertrophy

Descriptive Statement: Leptin is a hormone whose circulating levels are higher in obesity and hypertension, exerting detrimental effects on the heart and vasculature. Adiponectin is a hormone whose plasma levels are reduced in obesity and hypertension. It has been shown to be protective on the heart in cardiovascular disease, but whether adiponectin plays a protective role on the vascular wall during hypertension has not been studied.

Introduction: Hypertension is associated with increased leptin production and reactive oxygen species (ROS) formation in vascular smooth muscle cells (VSMC) and contributes to the development of vascular remodeling. Adiponectin (APN) exerts a cardioprotective role on the heart, but the protective role of APN on VSMC during hypertension has not been fully elucidated yet. The aim of this research is to study the potential protective effect of APN on hypertension-induced VSMC hypertrophy.

Methods: To mimic hypertension, the rat portal vein was cultured either mechanically stretched with 1.2 gram weights or left unstretched. APN, leptin, and p-ERK1/2 expressions in VSMC were evaluated by Western blot. Real-Time PCR analysis was done to study the effect of stretch on the mRNA expression of APN and its receptors. The protective effect of APN (5-10 µg/ml) was investigated on ROS formation by DHE staining and on hypertrophy by protein synthesis via [^{3}H]-leucine incorporation rate.

Results: Mechanical stretch for 24 hr reduced the expression of APN in VSMC (0.49 ± 0.08 fold, n=6, $p<0.05$) and increased leptin (2.51 ± 0.39 fold, n=6, $p<0.05$) compared to controls. Stretch (24 hr) decreased APN mRNA expression by 0.31 ± 0.11 fold (n=7, $p<0.05$) but had no effect on APN receptor R1 or R2 expression (n=8). This effect of stretch was associated with increased protein synthesis by 1.39 ± 0.06 fold (n=6, $p<0.05$), while APN significantly inhibited stretch-induced hypertrophy (n=6, $p<0.05$).

Mechanical stretch (15 min) increased ERK1/2 phosphorylation by 2.10 ± 0.25 (n=5, $p<0.05$), while APN reduced p-ERK1/2 by 0.82 ± 0.26 fold (n=4, $p<0.05$) in stretched vessels.

Stretch for 1 hr increased ROS by 5.69 ± 0.13 fold (n=5, $p<0.05$), whereas APN significantly inhibited ROS formation in stretched vessels (1.71 ± 0.22 fold, n=3).

Conclusion: Mechanical stretch reduces the APN/leptin ratio in VSMC. APN plays a protective role against vascular remodeling during hypertension by affecting ERK1/2 phosphorylation, ROS formation, and VSMC hypertrophy.

Abstract # 75

Deciphering the miRNA cargo of rhabdomyosarcoma-derived exosomes and their implication in tumor cell biology

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Funding source: MPP grant, AUBMC

Keywords: Rhabdomyosarcoma; Exosomes; miRNA; cell behavior; Biomarkers.

Descriptive Statement: Rhabdomyosarcoma-derived exosomes carry biologic cargo and induce proliferation, migration, and invasion of recipient cells.

Introduction: Rhabdomyosarcoma (RMS) is an aggressive childhood soft tissue tumor, with two distinct subtypes, embryonal (ERMS) and alveolar (ARMS) histologies. Exosomes are small membranous vesicles secreted into body fluids by multiple cell types, including tumor cells. Tumor exosomes contain intact and functional protein, mRNA and miRNA that may alter the cellular environment to favor tumor growth. To date, no studies have been performed to investigate the miRNA cargo and the role of exosomes in paracrine signaling in RMS in general and ARMS in particular.

Methods: We isolated and characterized exosomes from a panel of 5 RMS cell lines. We then performed functional assays to investigate the effect of exosomes on migration, invasion, proliferation and angiogenesis *in vitro* and *in vivo*. Moreover, we characterized the miRNA cargo of ERMS- and ARMS-derived exosomes using array profiling.

Results: Functional assays revealed that RMS-derived exosomes exert a positive effect on cellular proliferation of both fibroblasts and human RMS cells. They also significantly increased the cellular migration and invasion of normal human fibroblasts and the *in vitro* angiogenesis of human endothelial cells. Matrigel plug in assay showed a positive effect on the migration of stromal cells within the plug compared to control.

Expression array analysis showed that exosomal miRNA clustered together well, and to a higher extent than cellular miRNA, in both ARMS and ERMS cell lines. There were only 2 miRNA in common among both ERMS and ARMS cell lines. These putative targets were found to be implicated in cancer and inflammation. We were able to identify pathways and networks that may contribute to the paracrine signaling in tumor progression.

Conclusion: Taken together, our results suggest that RMS exosomal cargo results in specific effects on cell biology, enhancing invasive potential of recipient cells. Commonly-enriched miRNA in exosomes of ERMS and ARMS cells may define potential biomarkers for RMS.

Abstract # 76

Deciphering Neuroproteomic Alterations in Experimental TBI: Comparative Analysis of Aspirin and Clopidogrel Treatment

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Funding: MPP and CNRS-Lebanon

Keywords: Anti-platelets, Traumatic-Brain-Injury (TBI), Neuroproteomics

Descriptive Statement: Neuroproteomic effect of Aspirin and Clopidogrel in Experimental TBI

Introduction: Patients sustaining TBI and concomitantly receiving Aspirin (ASA) and/or Clopidogrel (CLOP) have been linked with an increased risk of morbidity and mortality; however, the exact molecular mechanisms altered by ASA and CLOP contributing to these unfavorable outcomes are still unknown. In this novel work, we aimed to identify and compare the altered proteome expression imposed by these drugs when administered alone or together, following the experimental controlled cortical impact model of TBI.

Methods: Cortical brain tissues were harvested from TBI, ASA, CLOP and ASA+CLOP groups 48 hours post-injury and analyzed using an advanced neuroproteomics Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) platform to assess glycoproteomic alterations. Additionally, advanced bioinformatics/systems biology and clustering analyses were performed to evaluate molecular pathways and protein-protein interactions involved.

Results: The identified upregulated proteins in the TBI+ASA and TBI+CLOP groups were found to be involved in neuroprotective cellular pathways. However, in the group where ASA and CLOP were concomitantly administered, enrichment in biological pathways relevant to inflammation and pro-injury mechanisms was revealed.

Conclusion: This work provides promising explanations pertaining to the underlying mechanisms following TBI and may offer better insights to the actual role of ASA and/or CLOP in this context.

Abstract # 77

Neural Stem Cells as a new cell-based therapy for Traumatic Brain Injury

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Funding sources: Medical Practical Plan (MPP), CNRS
Keywords: TBI, CCI, NSC, Neurospheres, astrocytes, neurons

Introduction: Traumatic brain injury (TBI) is a major cause of death worldwide. It is characterized by neuronal injury via apoptosis or necrosis. In this study, we aim to transplant Neural Stem Cells (NSCs) into a TBI mouse model.

Methods: NSCs were isolated from E14 mouse embryos and cultured to produce neurospheres. After NSC differentiation, different types of cells were injected into the cortex of a previously injured TBI mouse model (C57BL6).

Results: NSC differentiation was induced *in vitro* and different cell populations of astrocytes and neurons were obtained and validated. The NSCs transplantation was assessed using Immunohistochemistry and immunofluorescence analysis. Results showed that the majority of the transplanted cells were positive for neuronal, astrocytic, and microglial markers such as NeuN, Dcx, GFAP, and Iba-1. Our findings demonstrated that both differentiated and NSCs migrated to the site of injury, enhanced neurogenesis and recovery. Neurogenesis was significantly increased post-injection of NSCs, along with the induction of neuroprotective cells.

Conclusion: Exogenous stem cells may play a role in enhancing neurogenesis along with cognitive and motor recovery following TBI.

Abstract # 78

The rhabdomyosarcoma-specific Pax3-FOXO1 fusion oncoprotein modulates exosome content and function in myoblasts

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Funding source: MPP grant, AUBMC
Keywords: Rhabdomyosarcoma, Pax3-FOXO1, exosomes, myoblasts, miRNA

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

Introduction: Exosomes are small secreted microvesicles shown to mediate paracrine signaling by delivering protein and miRNA to recipient cells. Rhabdomyosarcoma (RMS) is an aggressive childhood soft tissue tumor, with two distinct histologic subtypes: alveolar (ARMS) and embryonal (ERMS). In pediatric cancers, few studies have investigated the role of exosomes in tumor biology. ARMS is characterized, in the majority of cases, by the genetic translocation PAX3-FOXO1 (P3F), which results in a fusion oncogenic protein. This protein is thought to contribute to its aggressive and metastatic behavior. We hypothesize that the P3F fusion protein results in specific effects on exosome cargo and biology, enhancing invasive and metastatic potential of ARMS cells through paracrine signaling.

Methods: Myoblasts are thought to be the cell-of origin of rhabdomyosarcoma. We transduced mouse myoblasts (C2C12 cells) with vector containing the P3F fusion oncoprotein, versus empty vector. We then isolated secreted exosomes, and evaluated their differential effects on recipient cell proliferation, invasion, migration, and angiogenesis. We also 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 (mouse fibroblasts and myoblasts) proliferation, invasion, migration and angiogenesis. Array analysis revealed unique miRNA enrichment signatures in exosomes derived from P3F-transduced C2C12 cells compared to those transduced with empty vector, identifying pathways that may contribute to P3F-specific paracrine signaling in tumor progression.

Conclusion: We have identified specific effects of the P3F oncogenic fusion protein on paracrine signaling in myoblasts. The identified pathways are currently being verified in rhabdomyosarcoma samples, and specific miRNA are being evaluated for their role in P3F-mediated tumor invasion. Findings will help devise targeted therapeutic interventions in ARMS, which are urgently needed.

Abstract # 79

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

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Funding source: Kamal Shair (KS) grant

Keywords: p53, Rb, adult neurogenesis, neural stem cells, neurosphere, proliferation, differentiation.

Descriptive Statement: This study investigates the combined roles of two tumor suppressor genes, p53 and Rb, on the regenerative capacity and fate of adult neural stem cells (aNSCs) in culture. aNSCs are restricted in number and generate specific types of neurons at a relatively low rate. Identifying the mechanisms that control their development and expansion will help improve the regenerative capacity of the brain in case of injury or neurodegenerative diseases.

Introduction: Adult neurogenesis is 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 and cell 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*. Moreover, we have recently demonstrated that Rb specifically regulates progenitor proliferation and is needed for the long-term survival of adult-born OB interneurons. Given the above findings, we have examined here how both genes function together to control the developmental properties of aNSCs and progenitors *in vitro*.

Methods: We induced a temporal deletion of Rb (conditional Knock-out, cKO) in aNSCs/progenitors in p53 null mice (2 months old) carrying the Nestin-CreERT2-YFP cassette and performed primary cultures of dissected SVZ tissues from p53-null and RbcKO;p53null mice. We then sorted by FACS the green neurospheres at the second passage and conducted neurosphere and differentiation assays.

Results: Compared with p53-null cultures, aNSCs/progenitors derived from Rb-cKO; p53null cultures showed a 2.8-3 fold increase in their self-renewal capacity and amplification rate. Thus, they generated more primary and secondary neurospheres and seem to have retained a strong differentiation potential without excessive cell death.

Conclusion: The population of aNSCs/progenitors can be expanded *in vitro* by manipulation of the p53/Rb pathways without affecting aNSCs differentiation potential. However, we are presently testing this *in vivo* and whether long-term survival of adult-born neurons is affected by the dual loss of these genes.

Abstract # 80

Investigating the role of Rb in induction and maintenance of senescence

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Funding source: QNRF grant NPRP 4 - 096 - 3 - 037

Keywords: Retinoblastoma, Senescence, Cancer therapy

Descriptive Statement: Our studies show that the retinoblastoma tumor suppressor gene (RB) is necessary for induction and maintenance of cellular senescence, a tumor suppressor response that inhibits progression of premalignant lesions. Findings have direct implications on novel therapeutic strategies to activate RB as a cancer prevention strategy.

Introduction: Cellular senescence is defined as irreversible cell cycle exit induced by tumor-promoting insults. The irreversibility of senescence *in vivo* has been questioned, since premalignant lesions-where senescent cells have been found- do progress to invasive tumors even after long periods of time. The role of the retinoblastoma gene (Rb) in induction and maintenance of senescence has not been fully investigated. We assessed the role Rb in induction and maintenance of senescence, to evaluate RB-activation as possible strategy for tumor prevention and therapy.

Methods: We used *in vitro* models of RasV12-induced senescence in fibroblasts, and *in vivo* model of Cyclin-D1 induced senescence in pineal cells. A CRE-recombinase system was used to inactivate Rb, and a constitutively active Rb-construct was used for RB activation. To decipher the role of RB independent of p53 pathway activation, a conditional system for p53 inactivation was used, where P53 is inactive unless cells are treated with 4-OH tamoxifen (p53ER(TAM) system).

Results: Inactivation of Rb prior to onset of senescence led to failure of senescence induction, with impaired cell cycle exit (shown by persistent Brdu incorporation) and failure to upregulate senescence markers such as Dec1 and p15Ink4b. In addition, cells which entered senescence were able to reverse some features of the senescence phenotype upon Rb loss, including increased BrdU incorporation and decreased Dec1 and p15Ink4b expression. Interestingly, in the absence of p53, constitutively active Rb was sufficient for the cells to undergo RasV12-induced cell cycle exit, shown by a decrease in BrdU incorporation and overexpression of Dec1, p15Ink4b and p21Cip1, which are markers of senescence.

Conclusion: Rb is necessary for both the induction and maintenance of senescence *in vitro*, and therefore may contribute to tumor suppression in both settings. Importantly, Rb activation is sufficient for senescence induction both in the presence and absence of p53, which has implications for activating Rb as a therapeutic strategy in tumors with dysfunctional p53 pathway. *In vivo* studies are in progress to confirm these findings within a cancer progression model.

Abstract # 81

Pediatric Tumor Tissue Banking for Scientific Research

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Funding source: Operational Lab Funds

Keywords: Pediatric Tissue Bank, Translational research, biomarker

Descriptive Statement:
A pediatric tumor biorepository will serve as a critical resource to facilitate translational research in pediatric malignancies.

Background and Aims
Tissue biorepositories provide a resource that can be utilized to investigate cancer pathology, genetics, and biomarkers. We therefore aimed to establish a pediatric tumor biospecimen repository, to collect tumor tissue, with paired somatic DNA, serum, and plasma.

Methods: The IRB-approved research biorepository includes frozen and paraffin-embedded tissue, somatic DNA, and serially collected serum and plasma. All newly diagnosed patients and families are approached for consent. The surgical pathologist determines whether leftover tissue is available for submission to the tissue bank. Tissues are snap-frozen, then stored at ultra-low temperature. Paraffin-embedded tissue is also collected, whenever possible. Histologic analysis is performed to assess extent and viability of tumor cells in the collected tissue. In parallel, peripheral blood is collected and processed to separate serum, plasma, and extract somatic DNA. Data is recorded including basic patient and tumor characteristics, date and type of specimen collected, and histologic analysis of collected sample. Linked outcome data is collected prospectively.

Results: To date, 491 patients have consented, and 42 have refused enrollment. As of January 2016, a total of 266 frozen and 141 paraffin embedded tumor tissues have been collected. All tumor types are included, including hematologic, solid, and brain tumors. Somatic DNA from 475 participants has been banked, as well as 266 serum and 268 plasma samples. Recently, the protocol was amended to include serial collection of serum/plasma during treatment and follow-up, for use in future biomarker studies.

Conclusion: The pediatric tumor/tissue biorepository will serve as a valuable resource for collaborative studies aiming to understand links between tumor biology and clinical behavior and response to therapy. These specimens can also be used to evaluate prognostic biologic markers in relation to serial clinical interventions.

Abstract # 82

The Dual Neurotherapeutic Effects of Docosahexaenoic Acid and Neural Stem Cell Transplantation on Neurogenesis and Motor Recovery Post-TBI

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Funding: MPP and CNRS-Lebanon

Keywords: Neural Stem Cells, Docosahexaenoic acid, Traumatic-Brain-Injury

Descriptive Statement: Effects of docosahexaenoic acid and neural stem cell transplantation on neurogenesis and motor recovery post-TBI

Introduction: Traumatic-Brain-Injury (TBI) is a leading cause of mortality and disability worldwide, with 1.5 million persons inflicted yearly. TBI causes considerable neuropathological as well as behavioral and motor deficits. Recently, the use of neural stem cell (NSC) transplantation along with neurotherapeutic drug intervention has been proposed as potential neurotherapeutic approaches to attenuate post-injury complications. Among these therapeutic drugs, Docosahexaenoic acid (DHA) has been proposed as therapy drug due to its neuroprotective and neurogenesis capabilities.

Methods: The effect of NSC transplantation was assessed in combination with DHA administration in an experimental controlled cortical impact mouse model of TBI utilizing 4 cohorts (DMSO, DHA, NSC+DMSO and NSC+DHA groups). NSCs derived from neonatal pup's sub-ventricular-zone (SVZ) were cultured into neurospheres, and then dissociated into cells that were transplanted one week post TBI at the ipsilateral cortex region in adult C57BL/6 mice.

Results: Our Immunofluorescence and immunohistochemical results have revealed migration of NSCs to the SVZ and hippocampus; this was coupled with activation of gliogenesis and neurogenesis as well. Similarly, the behavioral testing revealed differential improvements in motor skills using Rotarod and pole climbing skills.

Conclusion: DHA in combination with NSC enhances neurogenesis capabilities along with motor activities post-TBI.

Abstract # 83

Pancreatic Neuroendocrine Tumors in an AUBMC Cohort

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Funding source: AUBMC

Keywords: Pancreatic Neuroendocrine tumors (PNET), ki67, surgery, stage IV

Descriptive Statement: descriptive analysis of 27 patients with PNET at AUBMC.

Introduction: Pancreatic neuroendocrine tumors (PNET) are rare functionally and biologically heterogeneous tumors accounting for less than 5% of pancreatic cancer.
The aim of this study was to describe the characteristics and outcomes of patients with PNET at AUBMC.

Methods: The study was a retrospective chart review of 27 patients diagnosed with PNET between 2005 and 2015 at AUBMC.

Results: Of the included patients**,** 17 were male and 10 were female. Median age at diagnosis was 52 years. The most common presentations were abdominal pain (59%) and weight loss (48%) while 11% were asymptomatic. 4 patients had MEN1 syndrome. The tumor was multifocal in 59% of cases. 11 (40%), 14 (50%), and 3 (10%) patients had G1, G2, and G3 respectively. 26% of patients had lymph nodes involvement. 15 out of 27 had upfront metastates (stage IV), 14 to the liver and 1 to the bones. Of these 15 patients, 8 received chemotherapy and/or Somatostatin analogues (SSA), without surgical resection; 2/8 (25%) responded with tumor regression, 4/8 (50%) with stable disease, and 2/8 (25%) progressed. In 5 patients, the primary was surgically resected followed by chemotherapy and SSA; 2/5 had complete remission and 1/5 had a stable disease. The most frequently used regimen was Capecitabine and Temozolomide. One and two-year survival rates of stage IV were 93% and 74% respectively. The mean survival of stage IV was 61 months. Stage, grade and Ki-67 were independent predictors of poor outcomes.

Conclusion: Prognosis improved in patients with PNET who underwent surgical resection including those with stage IV disease.

Abstract # 84

Characterization of the molecular and physiological role of TET proteins in Glioblastoma

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Funding source: MPP

Keywords: GBM; *Drosophila melanogaster;* Tet

Descriptive Statement: The role of TET proteins in *Drosophila melanogaster*

Introduction: Ten-eleven translocation 1-3 (TET 1-3) proteins have recently been discovered in mammalian cells as members of a family of DNA hydroxylases, a well-characterized epigenetic modification which plays an important role in regulation of gene expression and maintaining cellular identity with an enzymatic activity towards the methyl mark on the 5-position of cytosine (5-methylcytosine 5mC). Acquired point mutations and deletions in Tet proteins have been frequently observed in human cancers implicating a key role for cytosine demethylation in controlling cellular differentiation and transformation. We have identified missense Tet mutations for the first time in glioblastoma multiforme (GBM) patients in a set of exome sequenced samples and interestingly, some of these mutations have never been described before. We aim to investigate TET function in *Drosophila* by generating Tet loss-of-function mutants and identifying its potential role *in vivo*.

Methods: We have identified dTET Loss of function mutant flies. RT-PCR and quantitative PCR for dTET was performed to indicate the absence of transcripts. We validated the phenotypes observed with dTET mutants by further targeted inhibition of dTET using RNAi methodology specifically in the body wall muscles. Furthermore, we analyzed the phenotypes by dissecting third instar larvae body wall muscles and examined the overall anatomical morphology by immunostaining. Climbing and crawling assays for dTET loss of function adults and larvae were performed to analyze locomotor activity.

Results: dTET (MI03920)/Deficiency adult flies have striking phenotypes, they are unable to survive and die as soon as they hatch. Furthermore, adult flies display abnormalities in the wing shape. At larval stages, these mutants are characterized by abnormal muscle morphology and have defective locomotor activity.

Conclusion: We believe our discoveries of TET and its function in *Drosophila* will help understand and identify a yet undiscovered role of TET in humans which might explain its involvement in brain tumor development.

Abstract # 85

Inducible Rb-Knockout mice display enhanced but transient neurogenesis in the adult olfactory bulb with diverse functional outcomes depending on the type of olfactory task

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Funding source: University Research Board (URB), Lebanese National Council for Scientific Research (LNCSR)
Keywords: neurogenesis, Rb, olfactory bulb, knock-out mice, survival, olfaction, plasticity

Descriptive Statement: This study investigates the fate and functional impact of an increased supply of adult-born olfactory bulb neurons following the loss of the Retinoblastoma protein (Rb) in the brain.

Introduction: Newborn neurons are continuously generated in the adult mammalian brain from neural stem cells (NSCs) residing in the subventrivular zone (SVZ) lining the lateral ventricles and the subgranular zone (SGZ) in the hippocampus. SVZ-aNSCs generate fast-dividing progenitors which in turn give rise to neuroblasts that migrate to the olfactory bulb (OB) where they differentiate into GABAergic interneurons. We have shown recently that Rb controls progenitor proliferation in the SVZ and the rate of adult neurogenesis whereby loss of Rb triggered enhanced neurogenesis in the OB at 28 days post-Rb deletion. Despite this, the number of Rb-null newborn neurons gradually declined to match control levels 3 months later. We have investigated here whether Rb plays a role in the long-term survival of adult-born neurons and the functional outcomes associated with enhanced neurogenesis in the OB.

Methods: We induced a temporal deletion of Rb in aNSCs/progenitors using NestinCreER^{T2}; Rosa26^{YFP}; Rb$^{flox/flox}$ mice, and, retroviral-mediated Cre delivery in the lateral ventricles. We assessed cell death and neuronal birthdating by immunohistochemistry against active-caspase 3 and Bromodeoxyuridine (BrdU), respectively. We also performed odor-reward associative learning tasks and habituation/dishabituation tests following dichlobenil-induced damage to the olfactory system.

Results: Compared with heterozygous controls, we detected a significant increase in cell death inside the OB in the absence of Rb in both our transgenic model and the viral-inducible KO model with a peak at 60 days post-deletion in the former model. Moreover, the number of newborn neurons (YFP+;BrdU+) was severely reduced after loss of Rb. In parallel, the integration of excess newborn neurons was dependent on the difficulty of olfactory associative task: conditional Rb-null mice thus performed worse compared to controls when the task involved discrimination between dissimilar odors but were slightly better discriminating between similar odors.

Conclusion: Rb is required for the long-term neuronal survival of adult-born OB neurons. The transient increase in OB neurogenesis observed in the absence of Rb seems to be functionally significant in difficult olfactory discrimination tasks and sensory recovery after damage which holds a promising therapeutic potential for neurodegeneration.

Abstract # 86

Combustible and electronic cigarette smoke extracts impair tissue repair

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Funding source: MPP/URB

Keywords: smoke, electronic cigarette, stem cells, differentiation

Descriptive Statement: Smokers develop chronic diseases, suggesting that their repair mechanisms are compromised. In this study we address cellular damage, in the context of cigarette smoking as compared to electronic cigarette. This study shows that smoke alters potential tissue regeneration and that e-cigarettes are not as inoffensive as they are claimed to be.

Introduction: Smoking creates a state of systemic inflammation and loss of local healing potential. Stem cells are mobilized upon tissue injury to regenerate and repair organs back to functionality. However, smokers develop chronic diseases with no known cure. The impairment of tissue repair and remodeling has been attributed to defects in the stem cell pool. Electronic cigarettes (e-cigarettes) are advertised as smoking cessation tools; however, they contain toxicants inhaled by 'vapers' and released in the environment. More research is needed before reliable and definite data on the long-term safety of e-cigarettes become available. The aims of this study were to further investigate how smoke compromises tissue repair and to explore the impact of the e-cigarette on the growth and differentiation potential of adult stem cells.

Methods: For 25 days, adult bone marrow-derived mesenchymal stem cells (MSCs) were repeatedly exposed to either smoke extracts alone or simultaneously with osteogenic inducers. Cell viability and morphology were assessed. Osteogenic differentiation was evaluated in terms of mineralization and calcium deposition (Alizarin Red staining), expression of osteogenic genes (quantitative real-time PCR) and enzymatic activity. The integrity of cell-cell communication, a key player in cell survival and differentiation, was tested by looking at the levels and functionality of connexin 43 (Cx43), the main connexin found in MSCs.

Results: Both cigarette and e-cigarette extracts had detrimental effects on MSC growth and morphology. The differentiation of MSCs into osteoblast-like cells was hindered in both conditions, though to a lesser extent for the e-cigarette, as shown by decreased alkaline phosphatase activity, calcification and mineralization. This was paralleled by a major downregulation of Cx43, in cells exposed to cigarette or e-cigarette smoke, leading to the loss of gap junction-mediated cell communication.

Conclusion: This study offers a plausible scenario for the occurrence of chronic diseases in long-term smokers. Indeed, cell death and failure of smoke-challenged stem cells to differentiate explain the compromised tissue repair, where e-cigarette did not come out as a harmless alternative to combustible cigarette smoking.

Abstract # 87

ATL-derived Exosomes Modulate Mesenchymal Stem Cells Properties by Tax Activity

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Funding source: MPP/URB

Keywords: Exosomes, Tax, Leukemia, miRNA, MSCs, NF-κB

Descriptive Statement: The significance of exosomes is attributed to their role in cell-cell communication. They deliver signaling cues to target cells, contributing to many pathological conditions including cancer. We investigated whether exosomes derived from Adult T-cell leukemia/Lymphoma (ATL) cells deliver leukemia-related genes to human mesenchymal stem cells (MSCs), which modulate their properties in favor of leukemia progression.

Introduction: Exosomes are membranous nano-vesicles that harbor biological constituents such as proteins, mRNA and miRNA. Exosomes can potentially transfer their cargo to other cells, implicating them in many patho-physiological processes. We assessed whether exosomes from ATL cells act as intercellular messengers delivering leukemia-associated genes to MSCs, residents of the bone marrow and metastatic niches, resulting in leukemia support.

Methods: Leukemia-derived exosomes were isolated by ultracentrifugation and characterized by scanning electron microscopy and exosome-specific markers by western blot. Quantitative PCR and western blot were performed to identify their cargo and to assess the regulation of gene expression in MSCs exposed to leukemic exosomes. Proliferation of MSCs was assessed by Trypan blue exclusion assay. Confocal microscopy was performed to document the uptake of exosomes by MSCs and the expression of Nuclear Factor-kappa B (NF-κB) phospho-p65 in MSCs by immunofluorescence microscopy.

Results: Tax is detected in the exosomes of Adult ATL cell lines and patient-derived cells. Additionally, the exosome cargo of HuT-102, an ATL cell line, contained miR-21, miR-155 (both implicated in…) and vascular endothelial growth factor (VEGF). We demonstrated that HuT-102-derived exosomes not only deliver Tax to recipient MSCs, but also induce NF-κB activation leading to a change in cellular morphology, enhanced proliferation and the induction of gene expression of migration and angiogenesis markers.

Conclusion: These findings demonstrate that HTLV-I cells-derived exosomes deliver Tax and other leukemia-associated genes to MSCs and modify their properties to further support leukemic cells in the bone marrow and metastatic sites.

Abstract # 88

Induced expression of the human solute carrier SLC35b4 upon glucose stimulation; implication on glucose homeostasis

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Funding source: CNRS and URB

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

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 expression of SLC35b4 upon glucose stimulation.

Introduction: Type II diabetes (T2D) is one of the most common endocrine disorder worldwide. The cumulative action of the identified genetic variants accounts for only 10 percent of heritability. SLC35b4 is a solute receptor that has been recently associated with obesity, insulin resistance and gluconeogenesis. It exhibits a dual activity in transporting UDP-N-acetylglucosamine and UDP-Xylose. However, the correlation between SLC35b4 expression and functionality in liver human cells has not been fully elucidated. This study aimed to investigate the *in vitro* regulation of SLC35b4 expression and localization in order to decode its implication in macromolecules glycosylation.

Methods: SLC35b4 responsiveness was assayed using western blot analysis and immunostaining post to glucose stimulation in HepG2 cells. To better identify the cytoplasmic compartment harboring SLC35b4, double immunofluorescence (SLC35b4-Golgi apparatus and –endoplasmic reticulum) studies were performed. The subcellular localization was next confirmed using an adaptation of the PLA technique (duo-link).

Results: Results revealed that the SLC35b4 protein is markedly increased up to 60% upon glucose stimulation when compared to the control. SLC35b4 localized with Golgi apparatus and to a lesser extent with the endoplasmic reticulum, suggesting a widespread distribution of this solute receptor in these two compartments. This pattern of localization was also observed in human liver tissue from normal donor.

Conclusion: Our data suggest that, in response to glucose stimulation, SLC35b4 activation alters the glycosylation pattern inside the cells causing an improvement of the insulin ability to inhibit endogenous glucose production. Furthermore, the presence of SLC35b4 in the Golgi apparatus favors its involvement in the biosynthesis of glycoconjugates proteins. The further elucidation of the mechanisms of transport and distribution of nucleotide sugar by SLC35b4 may reveal much about the underlying metabolic control of T2D.

Abstract # 89

Reciprocal Communication between Hematopoietic and Mesenchymal Stem Cells: Role of Junctional Complexes in Hematopoiesis.

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Funding source: MPP/URB

Keywords: Hematopoietic stem cells, mesenchymal stem cells, niche, hematopoiesis, connexins.

Descriptive Statement: A specialized microenvironment in the bone, the niche, composed of stromal cells including (MSCs), support hematopoietic stem cells' (HSCs) self-renewal and differentiation. This study will enhance our understanding of the mechanisms by which the bone marrow niche, and more specifically MSCs, affects hematopoiesis and influences leukemic progression.

Introduction: The interaction between MSCs and HSCs is mainly mediated through two mechanisms to regulate hematopoiesis in the bone marrow niche. The role of paracrine interaction has been extensively explored; however, the direct intercellular communication is yet to be elucidated. This study was developed to investigate the role of MSCs in modulating HSCs' differentiation through direct interaction *via* connexins and N-cadherin.

Methods: HSCs were isolated from blood of diseased patients by cell sorting using magnetic beads against CD34. Flow cytometry analysis was done to evaluate the percentage of HSCs CD34 marker and differentiation markers (CD45 and CD38). Direct co-cultures were assessed at 1:1 ratio and cells were then separated by cell sorting using CD73 as a specific MSCs marker or by cell washes. Following 24h of co-culture, gene expression of stemness and adhesion markers was examined by Real-time PCR and western blotting. HSCs' differentiation was evaluated using Colony Forming Unit (CFU) assay. To assess the direct interaction between HSCs and MSCs, co-immunoprecipitation and duo-link experiments were performed.

Results: A reciprocal interaction exists between MSCs and HSCs whereby the expression of adhesion and communication markers (N-cadherin and Cx43) were induced following direct co-culture. We also demonstrated that after 24h of co-culture, MSCs increase the clonogenic potential of HSCs comparing to freshly sorted HSCs.

Conclusion: These findings demonstrate a direct role for the interaction between MSCs and HSCs and a potential role of gap junctions in regulating hematopoiesis and in controlling HSCs fate. Over-expression and down-regulation experiments are ongoing to further decipher this role.

Abstract # 90

Effect of Vitamin D Replacement on Cognition in Multiple Sclerosis Patients

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Keywords: Vitamin D, Multiple Sclerosis, Cognitive function

Descriptive Statement: The MS patients cognitive performance improved on most cognitive tests after 3 months of vitamin D supplementation and vitamin D level was a predictor of a better cognitive performance on the Brief Visuospatial memory test – delayed recall after adjusting for all the variables (*Disease duration, EDSS, Age, Education, Physical Activity, Smoking, Alcohol, Score Leisure Activities, Anxiety score, and Depression score)*

Background: Multiple Sclerosis (MS) is a chronic inflammatory disease of the central nervous system that is linked to genetic and environmental such as vitamin D status. Vitamin D is associated with cognitive performance. This is a prospective study to evaluate the effect of vitamin D supplementation in MS patients with Vitamin D deficiency (serum level <25µg/ml) to those with normal Vitamin D (serum level >35 µg/ml) on cognitive function.

Methods: Eighty-eight patients diagnosed 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. Demographic and health behavior information was collected, patients 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 –Revised (BVMT-R). Vitamin D, and calcium levels were measured. Subjects were evaluated at baseline and 3 months after vitamin D supplementation (10,000 IU daily for 3 months or 50,000 IU weekly for 3 months).

Results: 46.5 % of the patients had vitamin D deficiency. There was a significant difference between the vitamin D groups on BVMT-DR at baseline and at 3 months ($p<0.04$). SDMT differed between the groups at baseline ($p=0.07$). Age was a predictor of cognitive performance on all tests at baseline and at 3 months. More years of education predicted better cognitive performance on the Stroop (beta12.1, $p<0.001$) and BVMT-T1 (beta 2.02, $p<0.004$) at baseline, and the SDMT (beta 14.54, $p<0.001$) and MoCA (beta 3.90, $p<0.0001$) at 3 months.

Conclusion: A significant proportion of MS patients had vitamin D deficiency and cognitive impairment. The significant correlation between the cognitive tests and vitamin D level provides early positive association between vitamin D level and cognitive performance in MS.

Abstract # 91

Gonadotropin Releasing Hormone Agonist to Trigger Final Follicle Maturation in Women at Risk for Ovarian Hyperstimulation Syndrome: A Novel Multi-Dose Protocol

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Funding source: Johnny Awwad unrestricted fund

Keywords: Gonadotropin releasing hormone agonist, Ovarian hyperstimulation syndrome, High-responders, Human chorionic gonadotropins, Ovarian stimulation.

Descriptive Statement: During clinical practice, induction of ovulation in infertile women is achieved by administration of human chorionic gonadotropin (hCG), or pregnancy hormone. Despite its proven efficacy, hCG has been associated with excessive ovarian stimulation leading to significant morbidity and mortality in women. Gonadotropin releasing hormone (GnRH) agonists have been used as safer alternatives, but suffered inferior pregnancy outcome. Our experience with a novel modification of the standard GnRHa protocol has shown superior pregnancy rates and significantly lower complications.

Introduction:

Background. Follicle maturation is the final differentiation of an immature egg before fertilization, and is triggered in the natural cycle by the LH surge. During fertility treatment, this step is accomplished by the administration of human chorionic gonadotropin (hCG), which mimics LH activity. Its prolonged half-life, however, has been associated with excessive and prolonged follicle stimulation leading in some occasions to severe ovarian hyperstimulation syndrome (OHSS). OHSS is a major cause of morbidity and rarely mortality in women. One strategy to prevent it is to substitute hCG with a single-dose of gonadotropin releasing hormone (GnRH) agonist.

Despite a high safety profile, single-dose GnRH agonist triggered cycles were associated with a decreased probability of clinical/ongoing pregnancy rates and high miscarriage rates. A profoundly deficient luteal phase is believed to be the cause of compromised reproductive outcome.

Our personal clinical experience at the AUBMC Fertility Center with a modification of the commonly used GnRHa trigger protocol, by using a novel multi-dose approach appears to favor an improved reproductive outcome.

Aim. We aim to evaluate the reproductive performance (ongoing pregnancy rates) and safety (severe OHSS) of the proposed multi-dose GnRHa protocol compared with standard hCG cycles in women with excessive ovarian response.

Methods: This is a retrospective cohort study of 215 women high-responders who underwent ovarian stimulation for ICSI at AUBMC Fertility Center, between May 2013 and July 2015.

Women were identified as being at high risk for OHSS based on their follicular response. They were divided into two groups according to the follicle maturation triggering method. Group A (n=120) received three doses of GnRHa at 12-hour intervals, with estradiol and progesterone luteal supplementation. Group B (n=95) received standard hCG trigger and luteal support.

Results: Women characteristics in both groups were comparable for age, BMI, duration of infertility and number of failed attempts. The total number of oocytes collected (14.98±5.60 vs. 15.35±5.56; P = 0.63) and total number of embryos available for transfer (7.08±3.39 vs. 7.86±3.91; P = 0.119) were comparable between both groups. The GnRHa group had significantly less fresh embryos transferred per cycle (2.62±0.74 vs 3.18±0.85; P = 0.000); yet, it had significantly higher ongoing pregnancy rates per cycle started (beyond 20 weeks of gestation) (44.1% vs. 28.0%; P = 0.021). Miscarriage rates were similar in both groups (17.1% vs. 25.6%; P = 0.289). There were no cases of severe OHSS in the GnRH agonist group and three in the hCG group (0% vs. 3.2%; P = 0.085).

Conclusions: During ovarian stimulation, women with excessive ovarian response when given multi-dose GnRHa trigger and estradiol/progesterone luteal supplementation can be offered fresh embryo transfer with high ongoing pregnancy rates, and no apparent increase in severe OHSS.

Abstract # 92

Oxaliplatin-Induced Increase in Spleen Volume; Accurate Detection and Correlation with Other Oxaliplatin Adverse Events.

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Funding source: AUBMC.

Keywords: oxaliplatin, spleen volume, peripheral neuropathy, liver function.

Descriptive Statement: Oxaliplatin chemotherapy is known to cause liver sinusoidal injury and portal hypertension with an increase in spleen size. The aim of this study was to investigate the correlation between early splenic enlargement and other adverse events associated with oxaliplatin such as peripheral neuropathy.

Introduction: Oxaliplatin is a non-conventional third generation platinum compound. It is an important chemotherapeutic agent in regimens used in gastrointestinal carcinomas as well as other malignancies. Oxaliplatin toxicity profile includes neurotoxicity, gastrointestinal side effects and hepatotoxicity. The primary aim of this study is to measure the spleen volume of patients on oxaliplatin therapy before and during chemotherapy to detect any increase in splenic size as a biomarker for early oxaliplatin toxicity.

Methods: This was a prospective pilot study conducted at AUBMC. 50 patients newly started on oxaliplatin were included. The spleen volume was measured from the patients' baseline CT scan using the ISP upgraded system (using RECIST) and again for each follow up CT scan. Side effects were evaluated with each patient visit and graded according to severity.

Results: 64% of sampled patients developed peripheral neuropathy at 3 months and 68% developed splenomegaly. 77.8 % of those who did not develop peripheral neuropathy and 62.5% of those who developed peripheral neuropathy were found to have an increase in their spleen volume, with a p-value of 0.661.

Conclusion: There was no significant correlation between spleen size increase and the development of peripheral neuropathy in this cohort of patients treated with oxaliplatin. Further analysis is ongoing to assess other non-invasive markers of liver toxicity.

Abstract # 93

p53 and Rb are indispensable for normal kidney development in mice

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Funding source: Kamal Shair (KS) 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 the dual loss of these genes leads to several morphological 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 also demonstrated that p53 is required for early renal development particularly during nephrogenesis, and, metanephroi differentiation at later stages. p53 knockout mice hence exhibit abnormal metanephric and uterine development, however, this effect is strain-specific and not embryonic lethal. In contrast, the role of Rb in kidney development has not been addressed to date. We have recently generated an inducible deletion of Rb in p53-null mice during development that resulted in perinatal lethality with almost complete penetrance due to severe kidney failure.

Methods: We have used an inducible Nestin-CreERT2-YFP system to conditionally delete Rb in p53-null (-/-); Rb flox/flox mice. 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. Few animals only survived the dual loss of Rb and p53 at E18.5 but not earlier, and survived till P40. To characterize the morphological and developmental defects in these animals, we have performed: 1) histological analysis using Hematoxylin and Eosin 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.

Results: We compared the kidney phenotypes in p53-/-; Rbflox/flox mice treated with tamoxifen or vehicle only (p53-/- as controls). Our results revealed the presence of severe renal developmental defects manifested by the presence of 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.

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

Abstract # 94

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

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Running Title: Clopidogrel in TBI.

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Background: Traumatic Brain Injury (TBI) is one of the leading causes of death and disabilities worldwide. It involves approximately 1.5 million people each year and is associated with severe symptoms such as sensory and motor deficits. Antiplatelet agents such as clopidogrel (CLOP) and aspirin (ASA) inhibit the formation of blood clots by inhibiting platelet aggregation and activation and are used as essential adjuncts to the medical care of patients with cardiovascular diseases. Clinical studies showed that patients taking anti platelets before head trauma are at an increased risk to develop serious intra cranial hemorrhage when compared to untreated patients.

Aims: Following TBI in a rat model, the effects of CLOP and ASA were studied on systemic changes such as bleeding, platelets activation and thromboxane levels as well as bio-markers of brain injury.

Methods: Rats were divided into five groups (Control, TBI, TBI+ASA, TBI+CLOP, TBI+ASA+CLOP) and treatments given for 48 hours post injury, and before sacrifice. Changes in the levels of different proteins was assessed using either western blot (Spectrin, GFAP and transferrin), or Immunofluorescence (NeuN). Serum proteins associated to brain injury and inflammation (IL6, IL10, TNFα and thromboxane, TXB2) were examined by ELISA or EIA.

Results: ASA and CLOP inhibited platelet aggregation alone and in combination. In addition, TXB2, whose level is indicative of activated platelets, increased after TBI, in comparison to controls, but its level remained similar to control in all treated samples. Spectrin cleavage, an early marker of necrotic and apoptotic cell death following TBI, was confirmed to be increased in TBI, in comparison to controls, and showed highest expression in rats treated with combination treatment.

Keywords: Controlled cortical impact, Traumatic brain injury, Clopidogrel, Aspirin

Abstract # 95

Ceramide Regulation by *E4orf4* gene during adenoviral infection

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Cancer is a leading cause of death worldwide. Current therapies are of limited value because most agents depend on the tumor suppressor p53 for their cell killing. *E4orf4*, one of the early adenoviral genes, seems to overcome this obstacle as it can induce cell death in a wide range of cancer cells independent of p53 status. This raises the possibility of using *E4orf4* in cancer gene therapy in order to overcome resistance to treatment and prevent cancer recurrence. Understanding the mechanisms of its action is critical for its development as a therapeutic agent.

Keywords: Cancer, Adenovirus, E4orf4, Ceramide, Cell survival.

Funding source: None

Background: *E4orf4*, one of the adenoviral genes, represents a major potential tool in cancer therapy. It is able to trigger p53 and caspase-independent apoptosis selectively in cancer cells. The aim of this study is to investigate the mechanism of action of *E4orf4* by examining its regulation of ceramide accumulation, one of the major pathways of p53-independent apoptosis.

Methods: a T-Rex tetracycline inducible system has been used. The E4orf4 gene was introduced into a vector pcDNA4/T0, where its expression is repressed by another vector pcDNA6/TR. This system controls the expression of E4orf4 in A549 cell lines stably transfected. Real-time PCR and western blot analysis were used to confirm the expression of *E4orf4* in these clones. Analyses of viability by Trypan Blue, cell cycle distribution, expression levels of apoptotic-related proteins and ceramide levels were measured.

Results: We have demonstrated that the expression of E4orf4 in A549 cells did not have any effect on the cell growth as compared to the wild type cells as well as to A549-Ø cells. Moreover, it increases the number of cells in the S phase along with an elevation of cyclin A levels in A549-E4orf4 cells. Our results showed that the presence of E4orf4 in A549 cells modulates the balance between antiapoptotic and proapoptotic proteins of the BCL2 family by increasing BCL2 and decreasing BAK and $BCLX_{S/L}$ expression levels. Furthermore, E4orf4 transiently transfected in A549 cells enhanced the accumulation of ceramide significantly at 6 h and 24h.

Conclusion: These findings indicate that A549 cell line can survive E4orf4 expression. Therefore, this is a cell-specific response and could be explained by the molecular mediators in A549 cell line that makes it respond to E4orf4 differently than other cell lines. An improved understanding of the mechanisms in which E4orf4 is involved may help in design novel-E4orf4-based cancer therapeutics.

Abstract # 96

Semen Human Papilloma Virus (HPV) shedding in men undergoing assisted reproductive technologies: Prevalence and clinical outcome

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Funding source: National Council for Scientific Research CNRS

Keywords: Human papilloma virus, semen, fertilization.

Descriptive Statement: HPV, a common sexually transmitted virus, has been reported in about 40% of men and women worldwide. Silent asymptomatic shedding of the virus in semen has been observed, and has been associated with poor fertility and high miscarriages. Our study showed a very low prevalence of the virus (1.3%) in the male population studied, suggesting that routine universal screening for HPV in males suffering from infertility in our community is not warranted at this point of time.

Introduction:

Background. Human papilloma virus (HPV) infection is the most common sexually transmitted infection worldwide with a prevalence reaching 40% in some communities. HPV DNA has been recovered lately in seminal fluid and sperm cells.

Limited information is available on the effects of HPV infection in men on sperm parameters and reproductive outcome, despite some reports linking it to male infertility. Recently, a negative influence on sperm mobility and an increased risk of pregnancy loss have also been suggested.

In Lebanon, the prevalence of HPV infection amongst men is unknown, and data on the subject are lacking. We anticipated that data collected from this study could serve as a platform to evaluate: (a) patterns of risk behavior in Lebanese men; (b) the need for 'Pre-IVF semen HPV screening' to reduce early miscarriage rates and potential vertical transmission; and (c) the need for 'HPV screening prior to sperm cryopreservation' as a pre-requisite for artificial donor insemination programs; and (d) the usefulness of 'universal prophylactic HPV vaccination for Lebanese men' as a means of primary viral prevention of horizontal transmission.

Aim. We planned to investigate the prevalence of semen HPV shedding in a sample of Lebanese men and evaluate the effects on reproductive efficiency during assisted reproductive technology cycles.

Methods: This was a prospective observational clinical study of male partners within infertile couple undergoing intracytoplasmic sperm injection (ICSI) cycles. Semen obtained on the day of oocyte collection from 78 men were analyzed for HPV shedding by polymerase chain reaction (PCR) and subsequent reverse dot blot hybridization with sequence-specific oligonucleotide probes (SSOP).

Results: Thirty-nine men (50.0%) had abnormal semen parameters according to WHO criteria. One of 78 men participants expressed evidence of HPV semen shedding (low risk subtype in this particular case), a prevalence of 1.3%.

Conclusions: The prevalence of HPV infection in sperm of couples seeking fertility treatment in the Lebanese population was very low. These findings suggest that routine universal screening for HPV in males suffering from infertility in our community is not warranted at this point of time.

Abstract # 97

Effect of Vitamin D on Th17 Cell Survival

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Keywords: Vitamin D, Th17, Cell survival

Funding: MPP grant

Background & Aims: CD4+ Th17 cells are implicated in the pathogenesis of Multiple Sclerosis (MS). Vitamin D was shown to reduce Th17 cells and exert an anti-inflammatory effect. We sought to examine the effect of Vitamin D on the differentiation and survival of Th17 cells in healthy controls in vitro, and whether the active form of vitamin D ($1,25(OH)_2D3$) and its precursor metabolite (25(OH)D3) exerted comparable effects on Th17 cells.

Methods: We sorted CD4+CD45RO+ memory and CD4+CD45RO- naïve T cells and activated them with beads coated with antibodies to CD3, CD28 and CD2. Some cells were polarized into a Th17 phenotype by activation in the presence of polarizing cytokines in the presence or absence of vitamin D metabolites for 5 days. We then gated on CD45RA+ CCR7+ CD95+ cells that exhibit enhanced survival, self-renewal, and multipotency.

Results: Our findings show that vitamin D decreased CD45RA and CCR7 expression on Th17 polarized naïve CD45RO- CD4+ T cells, as well as CCR6 expression (Th17 specific) within both naïve and memory subsets. Further, the frequency of CD95+ cells within CD45RA+CCR7+ subset was reduced with a decrease in CD95 mean fluorescence intensity (MFI) in vitamin D treated T cells compared to untreated cells in naïve Th17 cells and not memory Th17 cells. In order to ascertain whether the effect of vitamin D is due to enhanced cell survival or increased proliferation, we performed proliferation assays using CFSE labeling of cells as well as viability assays using a live/dead cell stain. Both vitamin D metabolites enhanced cell viability in naïve and memory CD4+ T cells cultured in Th17 polarizing conditions. Preliminary results show that vitamin D induced the expression of the anti-apoptotic molecule (bcl-2) as shown by flow cytometry in both naïve and memory Th17 pol CD4+ T cells, and reduced the frequency of apoptotic cells.

Conclusion: Vitamin D enhances the survival of CD4+ T cells cultured in Th17 polarizing conditions, and this is particularly observed in naïve T cells. Further experiments are underway to examine the mechanism underlying this effect.

Abstract # 98

Awareness and Attitudes of the Lebanese Population with regards to Physician - Pharmaceutical Company Interaction: a survey Study

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Funding Source: none

Keywords: Physician-Pharmaceutical company interaction; Awareness, Attitudes.

Descriptive Statement: In our research, we studied the awareness and attitudes of the Lebanese population regarding physician-pharmaceutical company interaction. Several studies about this interaction have been conducted in the United States of America and Europe, but none was done in the East Mediterranean Region.

Background: Interactions of physicians with pharmaceutical companies may negatively affect their prescribing behavior. A number of studies have assessed the attitudes and views of physicians concerning this topic, yet few have assessed the views of the general public and none have been conducted in Lebanon.

Objective: To assess the awareness of the general public in Lebanon, and their attitudes towards these interactions.

Methods: We conducted a self-administered survey using a validated questionnaire. We recruited individuals in the waiting rooms of five primary health care clinics and in four shopping malls in the greater Beirut area. Eligible participants were Arabic- or English-speaking adults (age ≥ 18 years) residing in Lebanon for at least five years. We conducted descriptive and regression analyses.

Results: 263 out of 295 invited individuals (89% response rate) completed the questionnaire. While the majority of participants were aware of pharmaceutical company presence (or absence) in physicians' offices (range of 71% to 76% across questions), smaller percentages were aware of gift-related practices of physicians (range of 26% to 69% across questions). Forty percent thought that accepting small gifts or meals by physicians is wrong/unethical. The percentage of participants reporting lower trust in physicians due to their participation in various pharmaceutical company-related activities ranged from 12% to 45% (the highest percentage being for large gifts). Participants who reported receiving free medication samples were significantly more likely to consider physicians' acceptance of small gifts as "not a problem" than "unethical" (OR=1.53; p=0.044).

Conclusion: Participants in our survey were generally more aware of pharmaceutical company presence (or absence) in physicians' offices than of gift-related practices of physicians. While the level of trust was not affected for the majority of participants for various types of interactions, it was affected the most for accepting large gifts.

Abstract # 99

Addressing Medical Errors in the Lebanese Healthcare System

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Funding source: International Development Research Center (IDRC)

Keywords: medical error, patient safety, healthcare

Descriptive Statement: This study examines the process of improving patient safety practices in Lebanon by conducting a comprehensive synthesis of evidence supplemented by key informant interviews to develop a policy brief which defined the problem and presented four elements of a policy approach to address it.

Introduction: background and aims While there has been an increase in the incidence and reporting of medical errors in Lebanon, the associated implications and debates about causes, responsibilities and accountabilities are ill-informed and in many cases not leading to real improvement of patient safety practices. Using an "integrated" knowledge framework to link research to action, this study examines the process of improving patient safety practices in Lebanon through the application of Knowledge Translation (KT) tools and the use of the Knowledge to Policy (K2P) Center as an intermediary KT platform between researchers and policymakers.

Methods: This study employed the following KT tools: 1) development of a policy brief to address medical errors in the Lebanese healthcare system, 2) semi-structured interviews with 10 policymakers and key informants, and 3) convening of a national policy dialogue

Results: Findings from the key informant interviews and a comprehensive synthesis of evidence were used to develop a policy brief which defined the problem and presented four elements of a policy approach to address it. These included 1) enhancing clinical governance through the integration of evidence-based clinical guidelines, education and training of providers and conducting audits and performance appraisals; 2)developing and implementing policies that promote anonymous incident reporting at the organizational and national level; 3) revising and updating current accreditation systems to ensure patient safety goals, indicators, and training requirements are explicit in the standards and integrated in the contractual arrangements; and 4) empowering patients to enhance quality of care and patient safety. This policy brief was circulated to 24 participants prior to the dialogue to inform the discussion and action.

Conclusion: Problems at the system, organizational and professional levels are contributing to the incidence of medical errors and the associated suboptimal responses. This case study showed that the use of KT tools, including the engagement of stakeholders throughout the process to help generate evidence-informed interventions is promising in Lebanon.

Abstract # 100

Impact of Fatigue on Patients with Multiple Sclerosis at AUBMC

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Funding source: Nehme and Therese Tohme MS center

Keywords: Multiple Sclerosis, Fatigue

Descriptive Statement: A cross-sectional study at the AUBMC Nehme and Therese Tohme Multiple Sclerosis Center

Introduction: Fatigue is one of the most common symptoms of Multiple Sclerosis (MS). More than 80% of MS patients experience fatigue on a regular basis and this affects their lives in multiple ways. There are several options for dealing with fatigue (pharmacological and non-pharmacological) therefore it is of crucial importance for health care professionals to measure fatigue during routine clinical visits. Since causes of fatigue remain unknown, and assessment of its severity during routine neurological examination is difficult, it is necessary to have a more comprehensive understanding of this problem. The aim of this study is to identify the functional aspects (cognitive, physical, or psychosocial) that are mostly affected by fatigue in MS. In addition, the relationship between (1) cognitive impairment measured by the symbol digit modalities test (SDMT), (2) Quality of Life measured by the Multiple Sclerosis International Quality of Life questionnaire (MusiQoL), (3) serum Vitamin D levels, with fatigue as measured by the Modified Fatigue Impact Scale (MFIS) were assessed.

Methods: This study plans to enroll a convenient sample of 100 clinically definite MS patients and 100 age-matched healthy control subjects. During their routine clinical visits, patients participating in the "Comprehensive Multiple Sclerosis Database" study are being asked to answer MFIS and QoL questionnaires. SDMT scores, EDSS scores, Vitamin D levels, as well as information about age and education were obtained from the patients' medical charts. Control subjects, mostly volunteer AUBMC visitors and social contacts, are being asked to fill the MFIS and a basic health and demographics questionnaire.

Results: To date, 126 subjects were selected (96 patients; 30 controls). The patient sample was divided into: 76 with Relapsing Remitting MS (RRMS), 16 with Progressive MS (PMS), 3 with Clinically Isolated Syndrome (CIS) and 1 with Radiologically Isolated Syndrome (RIS). The mean MFIS score is 29.7 among MS subjects. A total score cutoff point of 38/84 was chosen to identify individuals with clinically significant fatigue. We found clinically significant fatigue in 32.3**%** of patient (62.5 % RRMS and 37.5 % PMS), 42.7**%** in the physical subscale, 37.5 **%** in the cognitive subscale, and 10.4**%** in the psychosocial subscale.

Conclusion: The available data shows that fatigue is a highly prevalent symptom among MS patients mainly affecting physical and cognitive aspects. The influence of fatigue however did not extend as much to the psychosocial aspect in this sample.

Abstract # 101

Retinal Optical Coherence Tomography Measures Correlate with Cognitive and Physical Disability in Patients with Early Multiple Sclerosis

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Funding source: Supported by an unrestricted grant from Novartis pharmaceuticals

Keywords: Optical coherence tomography, multiple sclerosis, cognitive function, disability

Descriptive Statement: cross-sectional part of an ongoing 2-year prospective study to explore the relationship between retinal OCT measures and cognitive function as well as disability in patients with early MS.

Introduction: Retinal optical coherence tomography (OCT) is being explored as a biomarker of central nervous system axonal damage in patients with multiple sclerosis (MS). Thinning of the retinal nerve fiber layer (RNFL) has been associated with disability and brain atrophy which in turn has been associated with poor cognitive function in advanced MS while thinning of the ganglion cell/inner plexiform layer (GCIPL) correlates better with MS subtype, and has been associated with active MS as well. However, OCT findings are not yet incorporated as outcome measures in clinical trials until more evidence is accrued to correlate OCT measures with physical and cognitive disability, especially in patients with early MS (disease duration of 5 years or less) without history of optic neuritis. The aim of this study is to explore the relationship between retinal OCT measures and cognitive function as well as disability in patients with early MS.

Methods: This study is the cross-sectional part of an ongoing 2-year prospective study performed at the Nehme and Therese Tohme Multiple Sclerosis Center of the American University of Beirut between January 2014 and December 2015. Study participants were adult patients with RRMS and disease duration of 5 years or less, stable and on any MS treatment since at least 3 months, without history of optic neuritis in one or both eyes. Patients were evaluated clinically as per standards of care at baseline, 12 and 24 months. A battery of validated cognitive tests in MS as well as a retinal OCT scan was performed at each time point. A parallel cohort of healthy age and gender matched participants, were invited to participate as controls for the OCT measures that included GCIPL thickness, RNFL thickness, and macular volumes. Physical disability variables included expanded disability status scale (EDSS) scores, timed 25-foot walk test (T25FWT), and 9-hole peg test (9HPT). Cognitive function was determined through a battery of tests validated in MS which included the Symbol Digit Modalities Test (SDMT), The Montreal Cognitive Assessment (MoCA) tool, and The Brief Visuospatial Memory Test- Revised (BVMT-R).

Results: 47 RRMS and 18 healthy age and gender matched controls were recruited for the study. MS patients were treated with Interferon beta-1a (N=32) or Fingolimod (N=15). There were no significant differences between treatment groups regarding demographic and clinical characteristics. However, the mean RNFL thickness in controls (99.5 μm) was significantly greater than that in either Interferon (92.0 μm) or Fingolimod (87.2 μm)-treated patients (P= 0.03 and P<0.001, respectively). Similarly, GCIPL thickness was significantly higher in controls (86.8 μm)

than in Interferon (79.9 µm, P= 0.001) and Fingolimod (75.0 µm, P< 0.001)-treated patients. GCIPL thickness was significantly greater in Interferon than Fingolimod-treated patients (P= 0.03). At the bivariable level there was a negative correlation between age and SDMT score (r= -0.33, P= 0.02) as well as Total Recall score (r= -0.35, P= 0.02), and a positive correlation between level of education and MoCA score (r= 0.42, P= 0.01). The cognitive scores measured by the SDMT, Total Recall, and Delayed Recall correlated negatively with physical disability variables (EDSS, T25FWT, and 9HPT). Multivariable analyses controlling for age, gender, disease duration, level of education, and treatment group, showed that RNFL correlated negatively with EDSS (standardized Beta= -0.35, P= 0.02) and the 9HPT (standardized Beta= -0.52, P<0.001), and positively with the SDMT (standardized Beta= 0.42, P= 0.01). The GCIPL thickness correlated negatively with the 9HPT (standardized Beta= -0.34, P= 0.03).

Conclusion: In patients with early MS, without clinical or subclinical optic neuropathy, retinal thickness measures correlated with physical and cognitive disability, supporting their potential as biomarkers of axonal loss and neurodegeneration.

Abstract # 102

Assessment of preventive and curative care in assessing the determinants of dental services utilization

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Keywords: dental services, preventive care, curative care

Descriptive statement: We examine the reasons for differences in visiting the dentist by children in private and public schools. We try to answer questions such as: are they getting the needed treatment, and more importantly, are they getting curative or preventive care?

Introduction: While oral health services utilization are aggravated by social inequalities, understanding the pattern of service utilization allows more comprehension of the oral health burden, and provides a framework for strategies to address disparities. We hypothesized that public (PBS) and private (PVS) schools provide a vehicle to test the premise of utilization in presumably socially disparate groups. Aims: Assess 1-inequalities in the utilization of dental services by secondary school children attending private and public schools. 2-determinants of utilization of dental services.

Methods: Data in this cross-sectional study were collected from 948 parents, and 830 adolescents through questionnaires to both groups and adolescent clinical examination. Calibrated examiners recorded DMFT and orthodontic treatment need. Three levels of statistics were conducted; descriptive, bivariate, and multivariate analysis.

Results: DMFT scores were significantly higher in public (5.83) compared to private (4.08) schools. Nearly 11% of adolescents had never been to the dentist (5% of PVS children compared to 17% in PBS), with more than 1/3 of PBS children having not seen a dentist for over a year. Disparities in the utilization of dental services between PVS and PBS remain significant even after adjusting for other co-variates; the odds of service utilization among PVS was 1.6 times those among PBS children. School type (Adjust.OR1.5; p=0.037) and college education (Adjust.OR1.5; p=0.046) were the most significant predictors for utilization of preventive dental services; however marital status (Adjust.OR3.8; p=0.015) and presence of caries (Adjust.OR2.1; p=0.001) were significant predictor for curative dental services.

Conclusion: Children in general and those disadvantaged by poverty in particular face a twin burden of poor oral health and lack of dental care. The utilization of dental services is complex and multifaceted; therefore the present analysis of segregating dental services into preventive and curative services is crucial for more comprehensive explanation of such a process.

Abstract # 103

Comparison of palatal vault Characteristics in adult patients with various mandibular divergence patterns

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Keywords: palatal vault, divergence pattern, palatal rugae
Descriptive statement: We compare of the palatal vault characteristics (anatomy and dimensions) in the oral cavity of patients with various vertical jaw morphology.

Introduction: Different vertical facial patterns have been associated with variations in maxillary arch width, determined to be narrower in hyperdivergent phenotypes. Objective: to compare the anatomy and dimensions of the palatal vault between subjects with different vertical skeletal patterns.

Methods: Pretreatment dental casts of 87 adult patients were stratified into 4 subgroups according to mandibular plane inclination to cranial base (MP/SN): A.low (MP/SN≤27o;n=21), B.medium-low (27o<MP/SN≤32o;n=21), C.medium-high (32o<MP/SN<37o;n=20), D.high (MP/SN>37o;n=25). Maxillary arch measurements included palatal width (at level of first molars, premolars and canines) and depth (at level of first molars and premolars), palatal width/depth ratio and characteristics (orientation, shape, strength, length) of the right and left rugae. Statistics included bivariate analysis including t-test and fisher's exact test for categorical variables; regressions to predict palatal height; and Pearson product moment for associations among variables.

Results: Height/width ratio at the level of molars was higher in the hyperdivergent compared to the hypodivergent group (p=0.04). When the data were pooled in 2 groups (A,B vs C,D), the intercanine and interpremolar widths, and the second right rugae length were significantly higher in the hypodivergent group; shapes of the second left and right rugae were significantly different (p=0.033 and 0.044, respectively). The rugae contributed to predicting palatal height (PH): 11% of the variation in PH at the molar level was predicted by the combination of the 2nd left rugae length, MP/SN and PH at the premolar level (p<0.02); the lengths of both left second and third rugae, along with the intercanine distance, predicted PH at the premolar level (R2=0.19;p<0.02).

Conclusion: Similarity of maxillary vault dimensions in the various mandibular divergence patterns may imply functional adaptation of the nasopharyngeal matrix. The anatomical variation of the seconds palatal rugae, already reported to change with orthodontic treatment, suggests an adaptive nature of the rugae to environmental influences.

Abstract # 104

Palatally Impacted Maxillary Canines: A New Assessment for Application of Finite Element Analysis

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Keywords: impacted canines, palatally, maxillary

Descriptive statement: We evaluate the severity of non-erupted permanent upper canines that are usually exposed surgically and moved orthodontically into the dental arch. The movement is simulated through an engineering method (finite element analysis).

Introduction: Palatally impacted canines (PIC) have been stratified on positional components (e.g. horizontal position, angulation, height) to gauge treatment difficulty, based mostly on 2D radiographs. While more accurate 3D methods have not yielded additional prognostic information, we established a new approach to evaluate PIC position relative to their virtual alignment, relating better projection of impaction severity, potential for correction, and providing a basis for finite element analysis (FEA) of orthodontic movement of PIC. Objectives: Determine on 3D-images positional components associated with impaction severity and test individual variation in the FEA model.

Methods: Various measurements were made on 31 cone beam computed tomography (CBCT) scans of patients having PIC: PIC inclination to virtually aligned canine (VAC); PIC angulation to midline; PIC angulation to palatal plane (PP), cusp-tip to occlusal plane, and to interincisal alveolar crest; cusp-tip and apex deviation between PIC and VAC. Statistics included t-tests for subgroup comparisons based on PIC/VAC severity (cutoff at 30^{o}) and Pearson product moment for associations among variables. A model was developed for FEA processing.

Results: The average PIC/VAC angle was 32.97^{o}+/-16.35^{o} (range:9-59°) in the total sample and respectively, 14.11+/-6.88^{o} and 46.28+/-10.04^{o} in the less (n=15) and more (n=16) severe subgroups ($p<0.0001$). Differences between subgroups were statistically significant for cusp-tip ($p=0.02$) and apex ($p=0.01$) deviations, and coronal inclination to midline ($p<0.0001$). High correlations were observed between angulation to midline and both PIC/VAC ($r=0.86;p<0.0001$) and cusp-tip ($r=0.72;p<0.0001$). Moderate correlations ($0.42<r<0.60$; $0.001<p<0.028$) were noted between PIC/VAC and: cusp-tip, apex, and angulation to PP, and between cusp-tip and angulation to PP ($r=0.40;p=0.028$).

Conclusion: A novel measurement of PIC inclination to its virtual aligned position indicates that the most severe PIC is inclined to the midsagittal plane (canine tip farther away from the crest). FEA testing showed a heretofore not investigated potential for evaluating individual variation in PIC position.

Abstract # 105

Missing maxillary lateral incisors: systematic review on space management

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Keywords: missing, lateral incisors, space management
Descriptive statement: Treatment of missing maxillary incisors is limited to either space opening or space closure. Advantages and guidelines of either approach are evaluated.

Two opposite approaches can remedy missing maxillary lateral incisors (MLI): space maintenance and replacement by implant or bridge, or space closure and substitution by the canine. Both require interdisciplinary management for tooth replacement or reshaping of the canine. Aims: to conduct a systematic review on space management after orthodontic treatment in patients with missing MLI.

Methods: A computerized search involved using (up to June 1, 2015) Pubmed, Medline, Cochrane Database of Systematic Reviews, Scopus, and Embase. Terms used included ''maxillary lateral incisors'', "maxillary laterals", "agenesis of lateral incisors", "missing lateral incisors", "canine substitution", "canine lateralization", "single-tooth implants" and ''dental prosthesis/ses.'' Selection and specific use of each term with its respective truncation, if applicable, were facilitated by a librarian specialized in health sciences database searches. Reference lists of the retrieved articles were also hand-searched for additional relevant publications that may have been missed in the database searches.

Results: Higher evidence is lacking to compare space closure with space opening. One systematic review (covering articles up to December 2011) reached the same conclusion. Lower quality evidence provided suggestions and primary "guidelines" for treatment selection. Accordingly, lower level evidence, including case reports and reviews, was reviewed to determine common grounds or emerging trends regarding decision making, treatment options, and practice. While various indications and conditions were advanced for canine substitution, replacement of incisors has shifted towards the use of osseointegrated implants, except in patients with cleft palate. Randomized clinical trials are difficult to set up, as multiple variables must be controlled for: malocclusion, amount of overjet/anterior crossbite, size and shape of teeth, periodontal considerations, space requirements, functional and esthetic requirements.

Conclusion: Both replacement of incisors and canine substitution demonstrate success rates (esthetics and longevity of treatment), but also potential esthetic and functional failure. High level evidence must be generated to avoid treatment bias.

Abstract # 106

Adherence in orthodontics, the design of an instrumented orthodontic appliance to measure compliance

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Funding source: Not applicable

Keywords: Cooperation, adherence, monitoring, timer, sensing inputs

Descriptive Statement: Compliance of the orthodontic patient in wearing a headgear will be monitored and recorded via a timer integrated in the neck strap. A novel approach using different sensors with inputs on force, temperature and touch will be used.

Introduction: Background and aims: Compliance, as it relates to health care, reflects the concordance of a person's behavior with medical or health advice. In orthodontics, one of the essential aspects of adherence relates to wearing various appliances, such as a retainer or headgear, as instructed. Unfortunately, lack of cooperation prevails among many orthodontic patients, leading to reduced effectiveness and increased length of treatment, and may demand more invasive alternatives like extractions, placing mini-screws and surgery. The aim of the project is to provide the orthodontist with an objective tool for measuring patient compliance, especially that subjective measures (self-reporting) often are unreliable.

Methods: The design of the hardware will consist of three distinct sensing schemes. The first one is a temperature model able to sense body heat, the second method is a force model activated upon pulling of the headgear spring, and finally a capacitive sensing model sensitive to the dielectric difference specific to human tissue, which is activated upon touch.

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 the three methods greatly minimizes the possibility of cheating or tampering. The weakness of this approach is the increased complexity of the circuitry and possible discomfort (yet to be proven in a large population of children).

Conclusion: The designed instrumented orthodontic device employs a novel sensing technology that can be 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 and offers the basis of clinical applications to even stimulate patient compliance.

Abstract # 107

Craniofacial anatomy and inheritance associated with Class III malocclusion

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Keywords: Class III, inheritance, malocclusion, prognathism.
Descriptive statement: We will be discussing the craniofacial characteristics of Class III malocclusion with emphasis on genetic/environmental etiologies.
Position: PGY2 resident, Division of Orthodontics and Dentofacial Orthopedics.
Funding source: Not applicable.

Introduction: Background: Class III malocclusion is a dentofacial phenotype characterized by mandibular prognathism and/or maxillary retrognathism, leading to a more prominent mandible, a concave profile and an anterior cross bite.
Aims: 1. Characterize the maxillary and mandibular traits of Class III malocclusion compared to a control group of normal Class I malocclusion. 2. Expose the inheritance and segregation of mandibular prognathism in Mediterranean families.

Methods: Part 1: 168 subjects were divided into Class I (n=89) and Class III malocclusions (n=79). Cephalometric linear and angular measurements gauged sizes and positions of the jaws and their relationships to each other. Part 2: Initial findings on inheritance patterns of mandibular prognathism from a study on eight Mediterranean families.

Results: Part 1: Class III malocclusion is characterized by a retrognathic maxilla and\or prognathic mandible, small maxillary and large mandibular lengths in comparison to Class I malocclusion. Gender differences indicate a more pronounced mandibular prognatism in males than females, along with larger jaw sizes. Part 2: Pedigree patterns suggest autosomal dominant inheritance patterns of mandibular prognathism, with predominance of female affected members.

Conclusion: Class III malocclusion with maxillary retrognathism may be induced by a sustained environmental intragrowth orthopedics generated by functional forces transferred through the occlusion. However, a predominant genetic component exists in true mandibular prognathism. The candidate loci and gene(s) responsible for the development and familial transmission of mandibular prognathism in Mediterranean families will be deciphered in the next phase of our ongoing research.

Abstract # 108

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

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Funding source: Farouk Jabre Interfaculty Grant, Faculty of Medicine, AUB
Keywords: ablation, radiation therapy, Atrioventricular node
Descriptive Statement: Stereotactic Ablative Radiotherapy is feasible for ablation of Swine Atrioventricular Node.

Background & Aims: Stereotactic Ablative Radiotherapy (SABR) delivered to cardiac arrhythmogenic foci could be a promising catheter-free ablation modality. We tested the feasibility of in vivo atrioventricular node ablation in swines using SABR.

Methods: Four (4) Large White breed swine (weight 50-75kg; 3 females) were used in this study. Single-chamber pacemakers were implanted in each pig. The pigs were then placed under general anesthesia and computed tomographic scans were performed to localize the atrioventricular (AV) nodal region of the heart. Computed tomographic scans were acquired and SABR beam treatment planning for atrioventricular (AV) node ablation was conducted. Orthogonal x-rays with matching of implanted fiducials were used for positioning. Stereotactic robotic radiotherapy (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 4 pigs had disturbances of atrioventricular 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 and there was no evidence of collateral damage. The swine echocardiogram after SABR showed a normal systolic function.

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

Abstract # 109

Integrated Analysis of mRNA and microRNA Expression in Lebanese Breast Cancer Tissues

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Funding Source: Farouk Jabre, Medical Practice Plan, Kamal A. Shair CRSL and Richard and Susan Kiphart Northwestern Global Health Research Fund

Keywords: microRNA, mRNA, microarray, breast cancer, biomarkers, Lebanon, mRNA-miRNA integration

Descriptive statement: To comprehend early onset breast cancer in the Lebanese population, we integrated screening results of microRNA and mRNA expression in cancerous and normal adjacent breast tissues.

Introduction: Breast cancer (BC) is the most common type of cancers in Lebanese women with a higher percentage of young-aged patients than the West. microRNA (miRNA) are small noncoding RNA that act as master players in any stage of BC development. We have recently shown that differential expression of certain miRNA in Lebanese BC tissues could be different to what is reported in the West. This suggested the necessity of a global miRNA profile in Lebanese BC tissues and an integration with mRNA profile of the same tissues. Hence, the aim of this study is to examine the miRNA expression in Lebanese BC tissue and to predict their role through miRNA-mRNA integration analysis.

Methods: miRNA profiling was performed using Affymetrix GeneChip miRNA 3.0 array after RNA extraction of formalin fixed paraffin embedded (FFPE) 45 tumor and 17 normal adjacent tissues from Lebanese BC patients. Validation of dysregulated miRNA was done using quantitative reverse transcription real time PCR. mRNA profiling was performed using Affymetrix SensationPlus™ FFPE Amplification and Labeling Kit and GeneChip® Human Genome U133 Plus 2.0 Array on 6 tumor and 5 normal adjacent tissues from Lebanese BC patients. Ingenuity pathway analysis was used for mRNA-miRNA integration.

Results: A total of 74 miRNA were significantly dysregulated between tumor and normal adjacent breast tissues. The top differentially expressed miRNA were validated. mRNA profiling showed that our samples are mainly of luminal B subtype. Integration results gave 719 potential mRNA that could be targeted by 51 miRNA. These dysregulated mRNA are mainly involved in cellular movement, growth, and proliferation. miRNA with the highest number of targets in a negative mRNA-miRNA interaction were miR-183 and miR-182.

Conclusion: mRNA-miRNA integration analysis revealed a potential miRNA role in regulating important dysregulated tumor suppressive or oncogenic mRNA mainly involved in cellular proliferation. Further functional studies will be done on the dysregulated miRNA to comprehend BC onset especially in young patients.

Abstract # 110

Insights into the Deregulation of Rbm20 in Lamin A/C and Emerin Related Cardiomyopathies

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Funding source: Farouk Jabre Interfaculty Grant, Faculty of Medicine, AUB

Keywords: Cardiomyopathy, Lamin A/C, Emerin, RBM20

Descriptive Statement: The role of Rbm20 in the progression of the cardiac phenotype associated with the disruption of the nuclear lamina.

Background & Aims: Cardiomyopathies are among the leading causes of premature sudden death. Their etiology is genetically heterogeneous with more than 50 genes linked to them. The most substantial mutations involved in the cardiac phenotypes are those affecting the integrity and structure of the nuclear lamina; *LMNA* gene coding for Lamin A/C, and *EMD* gene coding for the inner nuclear membrane (INM) protein emerin. Additionally, recent studies identified mutations in the *RBM20* gene coding for the intracellular RNA-binding protein as highly implicated in familial cardiomyopathies. We sought to get a better understanding of how Emery-Dreifuss Muscular Dystrophy (EDMD) and Dilated Cardiomyopathy (DCM) originate from deficiency and/or mutations in the *LMNA* and *EMD* genes. Accordingly, we aimed to investigate potential deregulations in *Rbm20* transcript and protein expression in addition to intracellular localization in the context of *Lmna* and *Emd* deficiency.

Methods: For the purpose of this pilot study, we used mouse embryo fibroblast (MEF) lines that were derived from mice lacking the expression of either Lamin A/C (*Lmna*$^{-/-}$) or emerin (*Emd*$^{-/Y}$) which have an EDMD phenotype, or mice expressing the *Lmna* N195K homozygote mutation (*Lmna*$^{N195K/N195K}$) which have the DCM phenotype versus wild-type (WT) controls, under baseline conditions. We have also used *Lmna* null MEFs that were transduced by retroviral infection to re-express the *Lmna* WT or different mutant forms that result in EDMD (E358K, L530P). Real Time PCR quantification, Western Blot analysis, and immunofluorescence staining were performed on these cell lines to test for alterations in *Rbm20* transcript or protein expression and intracellular localization.

Results: *Rbm20* showed a significant reduction in the transcript levels in all the three mutant MEFs which was reversed upon re-expression of *Lmna* confirming the direct effect of lamina disruption on the expression of *Rbm20.* Likewise, the protein expression of Rbm20 was significantly reduced in the mutant cell lines compared to the wildtype, while there was no significant alteration in its intracellular localization.

Conclusion: Taken together, our findings highlight the implication of Rbm20 in lamin A/C and emerin related cardiomyopathies. Ongoing work and future directions will focus on investigating the consequential aberrations in Rbm20 – mediated splicing of a number of targets that mediate key signaling pathways altered in these diseases.

Abstract # 111

Insights into the Deregulation of Caveolin-1 in Myopathic Laminopathies

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Funding sources: AUB's University Research Board (URB) Fund, K.A. Shair CRSL Research Fund

Key words: Lamin A/C, Emerin, Caveolin-1, Liver Kinase B1

Descriptive statement: Laminopathies are a group of disorders arising from mutations or altered post translational processing of nuclear envelope/lamina proteins. Many of these disorders are manifested as pathologies affecting a wide range of tissues including skeletal and cardiac muscle. We hypothesize that mutations in the *Lmna* or the *Emd* gene alter the expression levels and functions of Caveolin-1 (Cav-1) encoded by the *Cav-1* mechanosensitive gene.

Introduction: Myopathic laminopathies are caused by mutations in the *Lmna* and the *Emd* genes, which respectively code for the nuclear lamina proteins lamin A/C, and the inner nuclear membrane protein emerin. To date, the cellular and molecular mechanisms underlying the disease pathogenesis remain in question. Our objective is to investigate if complete loss of or specific mutations in *Lmna* or *Emd* genes alter the expression and/or distribution of caveolin-1 and its upstream modulator LKB1, which may adversely influence critical signaling pathways indispensable for muscle biology.

Methods: Quantification of gene and protein expression in mouse embryo fibroblast (MEF) lines derived from $Lmna^{-/-}$ or $Emd^{-/Y}$ mice which have Emery-Dreifuss Muscular Dystrophy (EDMD) or from $Lmna^{N195K/N195K}$ mice with Dilated Cardiomyopathy (DCM) phenotype versus wild-type (WT) controls was done using Real-Time PCR and Western Blot (WB) analysis respectively. Immunofluorescence staining was utilized for the assessment of Cav-1 intra-cellular distribution in MEFs. Physiologically relevant concentrations of H_2O_2 were used for the induction of oxidative stress.

Results: *Cav-1* transcript expression (*α,* β isoforms) is reduced in $Lmna^{-/-}$ MEFs and elevated in $Lmna^{N195K/N195K}$ and $Emd^{-/Y}$ MEFs at baseline culture conditions. Intriguingly, *Cav-1* transcript levels are restored in $Lmna^{-/-}$ MEFs modified by retroviral transduction to express the *LMNA* WT or E358K mutant (EDMD). Moreover, *Cav-1* transcripts are significantly reduced in heart muscle derived from 4-weeks old $Lmna^{+/-}$ and $Lmna^{-/-}$ mice in comparison to $Lmna^{+/+}$ littermates (n=3/group). Whereas *Cav-1* transcript and protein levels are not significantly altered in $Lmna^{+/+}$ MEFs post exposure to 0.1 or 0.5μM H_2O_2 for 5, 15, 30, or 60min, we obtained a differential pattern of response in Cav-1 expression in the mutant MEFs. WB analysis revealed no significant change in Cav-1α in MEF mutant lines versus WT controls at baseline conditions. However, LKB1 protein levels were significantly elevated only in the $Lmna^{-/-}$ MEFs, and were found to colocalize with Cav-1α in the $Lmna^{+/+}$ and mutant MEFs by immunofluorescence staining.

Conclusion: Work is underway to explain the differential response pattern of Cav-1α in the mutant MEFs post H_2O_2-induced oxidative stress. Further assessment of the expression and localization of caveolin-1 and its modulator LKB1 will be performed in C_2C_{12} myoblast cells, and in striated muscle derived from the aforementioned mouse models.

Abstract # 112

Proteomic Profiling of Nuclei from Lamin A/C-Deficient Mouse Embryo Fibroblasts by Differential Phage Display Screens

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Presenter: Hind Zahr

Funding source: AUB's University Research Board (URB), Lebanese National Council for Scientific Research (CNRS), K.A. Shair CRSL Research Fund

Keywords: lamins, nucleus, phage display, muscular dystrophy

Descriptive Statement: To map nuclear-associated proteomic heterogeneity in the context of laminopathies.

Introduction: Laminopathies are a group of genetic disorders including skeletal and cardiac muscular dystrophy. They are caused by mutations in the *LMNA* gene which encodes for the nuclear lamina proteins lamin A/C that anchor other nuclear envelope (NE) proteins to the nuclear membrane. To date, the molecular mechanisms underlying the phenotypic diversity and the tissue-specific impaired function in laminopathies have not been deciphered. We rationalized that the phenotypic and mechanistic differences seen between laminopathies may result from varied expression, localization, and/or impaired function of a number of nuclear interacting proteins mediated by their interactions, or lack thereof, with wild-type or mutant lamin A/C resulting in differential deregulation in critical signaling pathways that are tissue-specific. To address this hypothesis, we performed proteomic profiling of nuclei isolated from either wild-type (WT) mouse embryo fibroblast (MEF) cells or lamin A/C-deficient MEFs.

Methods: Phage display-based technology termed Biopanning and Rapid Analysis of Selective Interactive Ligands (BRASIL), PCR of amplified plaques, sequencing of amplicons, bioinformatics tools (protein BLAST, CLUSTAL W, Statistical Programming Language R) were employed.

Results: Successive rounds of biopanning showed significant enrichment in differential phage binding to nuclei expressing WT A-type lamins as determined by a 2.4-fold change in relative phage binding units in Round III. No significant enrichment in differential phage binding to nuclei lacking A-type lamin expression was obtained. Direct phage display biopanning performed without pre-clearing the library also showed significant enrichment in phage binding to nuclei expressing WT A-type lamins and nuclei lacking A-type lamins with a 2.3- and 2-fold increase in relative phage binding respectively. Nearly 200-300 phage plaques were selected from various rounds per screen, PCR amplified, and inserts sequenced. Multiple high frequency peptides were obtained with preferential binding to either type of nuclei. Bioinformatic analysis indicates differential clustering of enriched peptides. Analysis is underway to identify the natural proteins that are mimicked by the binding peptides with matching motifs.

Conclusion: Hits identified in this project will offer new insights into the molecular mechanisms responsible for the phenotypic complexity of laminopathies including a better understanding of the causes for debilitating diseases such as dilated cardiomyopathy and Emery-Dreifuss muscular dystrophy.

Abstract # 113

Identification of Binding Partners for the Cardiomyopathy Related Protein Rbm20 by Phage Display

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Presenter: Michael Jim Bejjani, BSc candidate

Funding source: Faculty of Medicine Translational Program Research Grant

Keywords: cardiomyopathies, Rbm20, nucleus, phage display

Descriptive Statement: Phage display screens are performed on recombinant Rbm20 protein to identify a network of interacting partners.

Introduction: Cardiomyopathies are the most common type of genetic cardiac muscle disorders with a relatively high incidence rate and high risk of sudden death. These heterogeneous disorders are caused by mutations in about 50 genes. Despite the identified genetic causes of these diseases, much of the underlying molecular mechanisms remain in question. Recently, mutations in the *Rbm20* gene, which codes for the nuclear matrix splicing factor RNA binding motif protein 20 (Rbm20), have also been identified as a cause for some types of cardiomyopathies. Rbm20 has been shown to regulate splicing of over 30 genes most of which are implicated in cardiomyopathy, ion homeostasis and muscle biology, but not much is known about its interacting partners. The objective of this project is to identify binding partners for Rbm20 by phage display profiling.

Methods: Two screens of phage display biopanning were performed on the C-terminal fragment of recombinant RBM20 protein. The first screen done without acid elution aims to identify partners that bind RBM20 weakly and the second screen with an acid elution step aims to identify strong binders to RBM20. In both screens, the PhD CX_7C phage library (NEB) was used along with PCR amplification of plaques, and subsequent sequencing of amplicons. Bioinformatics tools (protein BLAST, CLUSTAL W, Statistical Programming Language R) are employed to perform data analysis and interpretation.

Results: Successive rounds of phage display biopanning resulted in significant enrichment in phage binding to RBM20 in the first screen, as determined by a 2.1- and 2.9-fold change in relative phage binding units in Rounds III and IV respectively. Significant enrichment in phage binding to RBM20 was also obtained in the second screen with a 2-fold increase in relative phage binding in Round IV. Nearly 200 phage plaques were selected from various rounds per screen, PCR amplified, and inserts sequenced. Multiple high frequency peptides were obtained from each screen. Work is underway to identify and validate the natural proteins that are mimicked by the binding peptides and to determine their bio-functional relevance in the context of cardiomyopathies.

Conclusion: This work reveals novel interacting partners of Rbm20 and provides better insights into the molecular mechanisms implicated in its role in cardiomyopathies.

Abstract # 114

Mechanisms Implicated in the Enhanced Sensitivity of MDA-MB-231 Breast Cancer Cells to Anti-neoplastic Agents Post Sub-lethal HIFU Exposure

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Funding source: Dar Al Handassah Endowment Fund, FEA, AUB; AUB's University Research Board (URB) Fund; TWAS-COMSTECH, Trieste, Italy

Keywords: HIFU, Breast Cancer, Chemotherapy, Caveolin

Descriptive Statement: Previous studies in our laboratory showed that sub-lethal HIFU exposure sensitizes MDA-MB-231 breast cancer cells to suboptimal cytotoxic doses of Paclitaxel and Doxorubicin. We rationalized that sonoporation and/or caveolin-dependent endocytosis are involved in this enhanced *in vitro* sensitivity of MDA-MB-231 cells post sub-lethal HIFU.

Introduction: High Intensity Focused Ultrasound (HIFU) is a therapeutic modality used to destroy solid tumors. At the focal point, cell death can result from cavitation and/or thermal ablation effects. However, the effects of sub-lethal HIFU exposure on cell function are not well understood. Previous work from our laboratory showed that sub-lethal HIFU exposure of MDA-MB-231 breast cancer cells *in vitro* results in significant alterations in transcript expression of a number of mechanosensitive genes, including *Cav-1* gene which encodes for caveolin-1 protein. Moreover, there was enhanced cellular sensitivity to suboptimal cytotoxic doses of Paclitaxel and Doxorubicin. Here, we aim to identify the mechanisms implicated in the enhanced *in vitro* sensitivity of MDA-MB-231 cells to anti-neoplastic agents post sub-lethal HIFU exposure.

Methods: We utilized a commercial HIFU setup that operates at the fundamental resonance of 0.5MHz. To examine if sonoporation is implicated in the enhanced drug uptake post sub-lethal HIFU, FITC-dextran uptake exposure to sub-lethal HIFU was assessed by two methods: cell fixation followed by flow cytometry or laser confocal microscopic imaging and analysis. To determine if caveolin-dependent endocytosis was implicated as a mechanism of enhanced drug uptake, we applied pre-treatment with Genistein, a specific potent inhibitor of this pathway. Cellular viability was quantified using trypan blue vital stain exclusion assay.

Results: We found no significant change in FITC-dextran uptake in MDA-MB-231 cells post sub-lethal HIFU exposure at 30hr prior to the *in vitro* addition of agents by flow cytometry and laser confocal microscopy. Likewise, no significant change in FITC-dextran uptake was noted at the 6hr time point by laser confocal microscopy. Interestingly, pre-treatment with Genistein resulted in a significant increase in cellular viability in comparison to control group.

Conclusions: Our findings indicate that sonoporation does not seem to play a significant role in enhanced drug uptake post exposure of MDA-MB-231 breast cancer cells to the sub-lethal HIFU levels that we applied, whereas caveolin-dependent endocytosis is implicated in this process. Work is underway to validate the latter results using various levels of exposure and time points.

Abstract # 115

Reporting of conflicts of interest by authors of systematic reviews: a methodological survey

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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, funding, systematic review

Descriptive Statement: 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. Non-financial COIs, such as intellectual, professional, and institutional, are being increasingly recognized.

Introduction: Systematic reviews are conducted to ensure that clinical decision-making is based on the best available empirical data. They also help in defining research gaps and directing funding. Conflicts of interest may bias the findings of systematic reviews. This in turn may bias decisions made by patients, clinicians, and policy makers. The objective of this study was to assess whether and what conflicts of interest are reported by authors of Cochrane and non-Cochrane systematic reviews.

Methods: We conducted a methodological survey using standard systematic review methodology. We searched for systematic reviews using the Cochrane Database of Systematic Reviews and Ovid MEDLINE (limited to the 119 Core Clinical Journals and the year 2015). Teams of two reviewers selected eligible studies and extracted data in duplicate and independently using piloted standardized forms. We defined a COI disclosure as the reporting of whether a COI exists or not. We classified COI into individual financial, professional and intellectual COI, and institutional financial and advocatory COI based on a framework we developed based on our review of the literature and of the International Committee of Medical Journal Editors (ICMJE) COI disclosure form. We conducted descriptive analyses of the characteristics of the systematic reviews, the reported funding, and the reported COI disclosures. We conducted a regression analysis to explore for any association between the proportion disclosing each type of COI and the following variables: number of authors, Cochrane status, whether amongst the top 5 general medical journals, number of included RCTs, and funding source.

Results: Of the 200 systematic reviews papers, 194 (97%) reported authors' COI disclosures, typically in the main document, and in few cases either online (2%) or upon request (5%). Of the

194 Cochrane and non-Cochrane reviews, 49% and 33% respectively (p=0.023) had at least one author reporting any type of COI. Institutional COI types were generally less frequently reported than individual COI types, and Cochrane reviews were more likely to report individual intellectual COI compared to non-Cochrane reviews (19% and 5% respectively, p=0.004).

Conclusion: Our study shows a highly skewed distribution of the percentage of systematic review authors reporting COI, attributed to the high number of authors that reported absence of COI. This in turn may reflect the under-reporting of COI due to systems that depend on "self-reporting". Thus, it is essential that journals and policymakers elucidate to investigators the potential biases that can result from COI, and establish strategies to mitigate these biases, mainly by enforcing standardized systems for reporting and verifying COI.

Abstract # 116

Knowledge, Beliefs, and Attitudes of Patients and the General Public towards the Interaction of Physicians with Pharmaceutical and Surgical Device Industry: A Systematic Review

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Funding source: Alliance for Health Policy and Systems Research, World Health Organization

Keywords: Knowledge, beliefs, attitudes, physicians, pharmaceutical company representatives, conflict of interest, patients, general public

Descriptive Statement: Understanding patients' and the general public's perceptions of physician-pharmaceutical industry interactions is necessary for informing policies and designing appropriate interventions. Therefore, we conducted a systematic review on the knowledge, beliefs and attitudes of patients and the general public regarding the interactions of physicians with the pharmaceutical and surgical device industry.

Introduction: The aim of this study was to systematically review the evidence on the knowledge, beliefs and attitudes of patients and the general public regarding the interactions of physicians with the pharmaceutical and surgical device industry.

Methods: We included quantitative and qualitative studies addressing any type of interactions between physicians and the industry. The outcomes of interest included knowledge, beliefs and attitudes of practicing physicians. We searched MEDLINE and EMBASE in April 2014. Two reviewers completed the study selection, data abstraction, and assessment of methodological features in duplicate and independently. We summarized the findings narratively, stratified by outcome and country

Results: Of the 11,194 identified citations, 19 studies met the eligibility criteria. In summary, higher percentages of participants reported awareness of educational and office-use gifts relative to personal gifts. Also awareness of physicians' interactions was lower for surgical device industry compared to pharmaceutical industry. Physician's interaction with the industry was believed to generally not affect prescription pattern or quality of care with mixed results obtained for cost and trust. In terms of attitudes, the acceptability was higher for free drug samples, pens and medical books, compared to trips, social dinners, and sporting events. The majority of respondents were not concerned about financial conflict of interest between their surgeons and device manufacturers. The results were mixed with regards to requiring physicians' disclosure of

their interaction with the industry. Generally, participants were in favor of regulations being imposed on physician-industry interactions.

Conclusion: There is a need for policy interventions to disclose interactions between physicians and the industry. For the latter to be effective, it needs to take into account the knowledge, beliefs and attitudes of patients. The results highlight the need to raise the awareness of patients and educate them about the potentially negative impacts of such interactions on their clinical care as a pre-requisite to patients' inferences on such deliberation.

Abstract # 117

Faculty Advancement Program in Clinical Research: A Clinical Research Institute Training Program for Junior Faculty

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Funding source: Departmental funds
Keywords: clinical research, capacity building, research education, training, mentorship

Program director: Dr. Mona Nabulsi
Program faculty: Dr Elie Akl, Dr. Marwan Refaat
Program coordinator: Ms. Rola El Rassi

Descriptive statement: This program is intended to support the Dean's vision of strengthening AUB Faculty of Medicine (FM) leadership in clinical research. It will help in building FM research capacity and create a supportive forum to discuss and collaborate on research projects.

Introduction: The vision of the FM since 2009 is to be the leading institution "in cutting edge medicine and biomedical research in the whole region". The Faculty Advancement Program in Clinical Research (FAP) targets the capacity building component to help junior faculty members at FM in conducting clinical research at AUB.
The objective of the program is to train junior faculty members in clinical research with the ultimate aims of:

- Supporting the development of FM junior faculty members into clinical researchers
- Building capacity to support CRI training activities and provision of services in clinical research
- Creating a supportive faculty forum to discuss and collaborate on research projects.

Methods: Junior faculty members at the Instructor or Assistant ranks at FM were nominated by their respective departments to attend this program. The program extends over one year and includes 17 bimonthly seminar series and 5 training workshops. The seminar series cover a wide range of topics and are coupled with an Integrated Project (IP) with the aim of having each participant submit a well-rounded research proposal at the end of the Program for funding. Each participant is allocated a peer advisor based on their research interests. The FAP joined forces with the Scholars in HeAlth Research Program (SHARP) to offer robust mentorship training for our peer advisors.

Results/Expectations: A total of 18 participants were selected based on their interest and commitment to clinical research and their basic knowledge, skills and experience in clinical research. The outcomes expected from this program are concrete research projects from participants that can be submitted for intramural or extramural funding at the end of the program.

Conclusion: This ongoing program is a major investment for participants and departments alike. It plays a major role in FM's strategy to enhance research productivity.

Abstract # 118

Second primary cancer after radical prostatectomy

Mohammed Shahait, Deborah Mukherji, Raja Khauli, Muhammad Bulbul, Mark Jabour, Thuraya Abu Merhi, Albert El-Hajj

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Funding source: None

Keywords: Prostate cancer, second malignancy, treatment

Descriptive Statement: Improved survival of prostate cancer patients has led to longer follow up and might contribute to the increased risk of occurrence of second malignancies .Our aim was to evaluate the incidence of second primary malignancies in men treated with radical prostatectomy for localized prostate adenocarcinoma.

Introduction: Prostate cancer is the most common malignancy diagnosed in men and the second most common malignancy leading to death. However, since the adoption of prostate cancer screening, along with the refinement of the treatment modalities for local disease; the mortality rate has decreased. Improved survival of prostate cancer patients has led to longer follow up and might contribute to the increased risk of occurrence of second malignancies

In recent analysis of the Surveillance, Epidemiology and End Results (SEER) data, the incidence of second primary malignancy (SPM) is 19%. Increased risk of SPM is observed after radiotherapy and chemotherapy. Nevertheless, there are other factors that can contribute to developing SPM such as genetic predisposition, exposure to carcinogens. Our aim was to evaluate the incidence of second primary malignancies in men treated with radical prostatectomy for localized prostate adenocarcinoma.

Methods: Overall, 408 patients underwent radical prostatectomy at the American university of Beirut Medical center between 1998 and 2012. The database was scrutinized to find the incidence developing second primary malignancy.

Results: 43 of 408 patients (10.5%) developed second primary malignancy. The most frequent pelvic second primary malignancy was bladder cancer (11 cases). Five of the eleven patients received adjuvant radiotherapy (45%).The most frequent extra-pelvic malignancies were lymphoma & leukemia (10 cases), and lung (7 cases). Median preoperative PSA was 4.62 ng/ml. Gleason score was ≥ 3+4 in 62% of the cases. Extra-prostatic extension & Seminal vesicle involvement was present in 32.5% and 16.2% of the cases, respectively.

Conclusion: Patients with localized prostate cancer are likely at a significant risk for second primary malignancies, future studies are needed to assess genetic susceptibility in our population and the impact of increased surveillance, and treatment effects.

Abstract # 119

Correlation between Ki-67 in Prostate Cancer and Risk of Biochemical Recurrence after Radical Prostatectomy

Mohammed Shahait, Samer Nassif, Wassim Abou Kheir, Deborah Mukherji, Ola Hadadeh, Thuraya Abu Merhi, Raja Khauli, Mohammad Bulbul, Albert El-Hajj

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Funding source: MPP fund

Keywords: Prostate cancer, KI-67

Descriptive Statement: Multiple factors affect the recurrence of prostate cancer after surgical treatment. There are well studied pathological features that can predict disease recurrence. We aim in this study to assess the value of a proliferation index (Ki-67) to predict early disease recurrence.

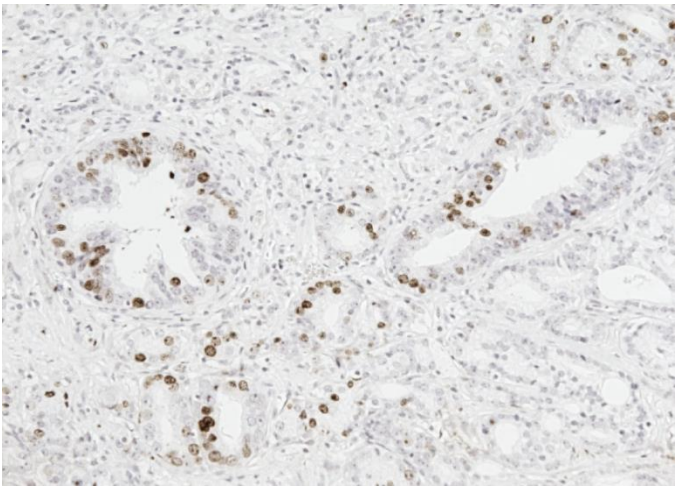
Introduction: This is a retrospective cohort study that aims to stratify patients after radical prostatectomy using Ki-67 and correlate the findings with BCR and disease progression in a sample of patients diagnosed with prostate cancer at a single large teaching hospital (American University of Beirut Medical Center AUBMC). The clinical integration of Ki67 into models that aid in improved prediction of biochemical recurrence may improve individual patient surveillance protocols. For instance, patients who underwent radical prostatectomy with positive surgical margins who have high levels of Ki67 may require a closer monitoring than patients with normal expression of Ki67. Additionally, the integration of Ki67 could have a significant impact on the role of adjuvant therapies after extirpative therapy

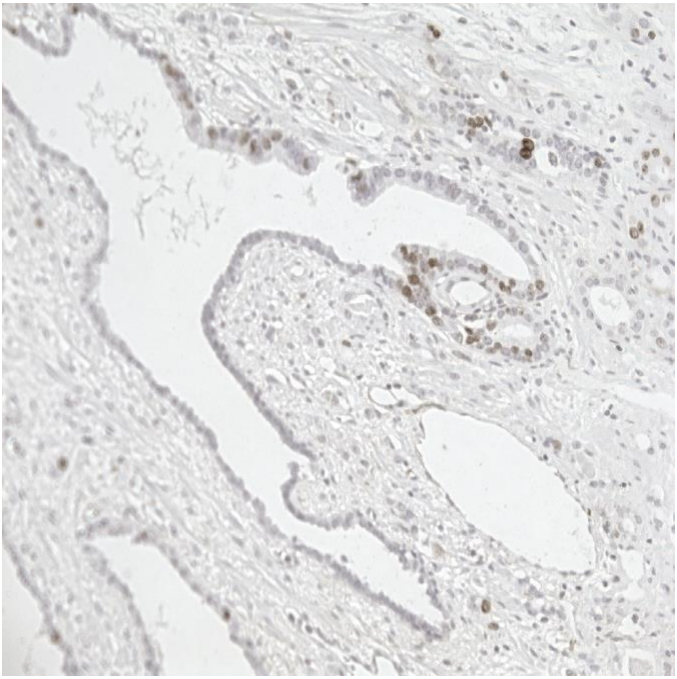
Methods: Pathology blocks of 400 patients who underwent radical prostatectomy between January/1998-Sep/2015 will be retrieved for review and for Ki-67 staining. After that we will explore the associations between Ki-67 expression in the tumor with biochemical recurrence and disease specific survival.

Results: A total of 77 pathology slides were analyzed to date. Most common Gleason score grade was 7 (3+4) in 44% and Gleason 7 (4+3) in 28% of patients. Ki67 proliferation index was negative in 58% of the patients and <or= 3% in 34% of the patients. Ki67 expression was not associated with the Gleason grade of the disease.

	Ki67 index (%)							
Gleason Grade	0%	1%	2%	3%	4%	5%	10%	Total patients
6(3+3)	4	2	2	0	0	0	0	8 (10%)
7(3+4)	18	6	5	5	0	0	0	34 (44%)
7(4+3)	14	1	1	1	2	1	1	21 (28%)
8(4+4)	6	0	0	1	1	1	0	9 (11%)
8(3+5)	1	0	1	0	0	0	0	2 (3%)
9(4+5)	2	1	0	0	0	0	0	3 (4%)
Number of patients	45 (58%)	10 (13%)	9 (12%)	7 (9%)	3 (4%)	2 (3%)	1 (1%)	77

Conclusion: Preliminary results show that there is no correlation between Ki-67 expression and pathological grade (Gleason score). Ki-67 may act as an independent prognostic factor to predict biochemical recurrence after radical prostatectomy. Further data analysis is underway to determine the impact of Ki67 expression on recurrence.





Abstract # 120

Combined Multi-Parametric MRI & Targeted Biopsies Improve Detection of Clinically Significant Prostate Cancer

Mohammed Shahait, Rami Abou Ghaida, Fadi El Merhi, Raja Khauli, Rami Nasr , Albert El-Hajj, Racha Kerek, Muhammad Bulbul

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Funding source: None

Keywords: Prostate cancer, Mp-MRI, Biopsy

Descriptive Statement: Prostate cancer diagnosis is based on random biopsy of the prostate, however, with the implementation of the Mp-MRI as an adjunct tool to guide our biopsies. We looked into the outcome between patients who underwent targeted biopsy of the indexed tumor only with patients who systematic random cores were taken.

Introduction: In attempt to optimize prostate biopsy Multiparametric MRI of the prostate allows targeted biopsies thus by overcoming of the shortcoming of the standard random systematic biopsy. The PROFUS trial showed that there is no difference in cancer detection rate between MRI-ultrasound targeted biopsy (MRF-TB) and visual (cognitive) fusion (VE-TB).Whether systematic cores should be abandoned when performing targeted biopsy remains unknown. Our aim was to compare biopsy outcome between patients who underwent targeted biopsy of the indexed tumor only with patients who systematic random cores were taken.

Methods: Between January 2014 and December 2015, prostate biopsies were performed in 95 consecutive men with suspicious regions identified on prebiopsy -3T MRI consisting of T-2weighted, diffusion-weighted, and dynamic-contrast enhanced sequences. Group A comprised of 46 patient in whom MRI guided-Visual targeted biopsy of indexed tumor was performed, systematic biopsies were not taken. Group B consisted of 49 patients in whom standard systematic random biopsies were taken.

Results: Group A comprised of 46 patient in whom MRI guided-Visual targeted biopsy of indexed tumor was performed, systematic biopsies were not taken. Group B consisted of 49 patients in whom standard systematic random biopsies were taken in addition to the targeted biopsy. In 44/95 (46%) had positive biopsy. In group A 25/46 (54%) had positive biopsies, 20/25 (80%) had clinically significant tumor (Gleason≥7) .The Median number of cores taken in group A was 6.While group B 19/49 (38.7%) had positive biopsies, 12/19(63%) had clinically significant tumor. The Median number of cores taken in group B was 13.5.

Conclusion: MP-MRI of the prostate offers unprecedented level prostate's zonal anatomy which allows targeted biopsies with less number of cores. Performing targeted biopsy of the indexed tumor alone lead to improvement in the detection rate of overall and clinically significant cancer. Our results need to be validated in larger prospective study.

Abstract # 121

Pathological Stage Disparity between Young and Elderly Men undergoing Radical Prostatectomy

Mohammed Shahait, Jad Dgheili, Muhammad Bulbul, Fady Geara, Ali Shamseddine, Deborah Mukherji, Rami Nasr, Wassim Wazzan, Raja Khauli

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Funding source: None

Keywords: Prostate cancer, Elderly, Pathological grade

Descriptive Statement: Our aim in this study was to highlight the seriousness of prostate cancer among elderly patient.

Introduction: Age discrimination is defined as "the denial of the privilege or other unfair treatment based on the age of the person who is discriminated against. Multiple studies have addressed the denial of treatment for the elderly patient diagnosed with prostate cancer and other cancers. The United States Preventive Services Task Force (USPSTF) issued a blanket recommendation against prostate cancer screening in 2012; similarly active surveillance and targeted focal treatment in elderly patients with low-grade disease has been gaining more popularity. The aim of this study is to highlight the differences in the pathological stage between young and elderly men (>70 Years) undergoing radical prostatectomy at our center. Finally, to discern the seriousness of prostate cancer in elderly and need for aggressive treatment.

Methods: Using Radical prostatectomy database of AUBMC, we analyzed pre-op PSA level, Gleason grade pathological tumor stage in men underwent radical prostatectomy from 1998 to 2012. In total, 365 patients (91%) were younger than 70 years, and 35 patients (9%) were 70 years or older.

Results: The PSA mean for the younger men and elderly was 9.3 ng/ml ±7.5and 10.9 ng/ml±8.9, respectively. Non-organ confined disease (T3) was noted in 26% vs. 37% ($P<0.05$) in younger vs. elderly patient, respectively. Pathological Gleason score ≥ 8 was noted in 14.28% vs. 12% ($P>0.05$) in elderly and younger patients, respectively.

Conclusion: This study underscores the high prevalence of clinically significant prostate cancer in the elderly. Our findings stress the importance of early diagnosis, which allows for definitive therapy in healthy elderly. We believe that elderly patients with prostate cancer should not be denied radical prostatectomy; provided they have a life expectancy more than ten years.

Abstract # 122

Engineering biomimetic sulfated substrates for enhanced growth factor binding

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Funding source: This work was supported by the American University of Beirut University Research Board (URB) grant.

Keywords: Glycosaminoglycans, biomimetic, sulfation, growth factors, nanofilms, biotin-streptavidin interactions

Descriptive Statement: In the current work, the interaction between sulfated alginate and FGF-II was assessed. The sulfated polysaccharides were immobilized to substrates using layer-by-layer films or using biotinylated sulfated GAGs. The custom-made substrates with controllable growth-factor affinities can be used to induce predefined cell responses such as proliferation, migration and differentiation.

Introduction: Glycosaminoglycans (GAGs) are key factors in various molecular and physiological processes. In particular, it has been shown that the modification of sulfation codes, or sulfation arrangements of GAGs affect developmental processes and numerous diseases in the brain. Sulfation codes have been specifically shown to be responsible for the differential binding to growth factors. However, few mechanisms that regulate the action of sulfated GAG molecules have been elucidated. Understanding the role of sulfated GAGs will enable the development of engineered biomimetic sulfated substrates that would enhance growth factor binding and ultimately be used in the treatment of neural diseases/injuries.

Methods: Alginate was prepared with different sulfation densities. Binding of the sulfated biomimetic materials was assessed with ELISA. The biotin-streptavidin system will be implemented in the preparation of custom-made sulfated substrates. Measurement of the binding of FGF to the prepared substrate will be done using quartz crystal microbalance with dissipation monitoring (QCM-D). The engineered substrates will be used to study the neural differentiation of stem cells and neural progenitors.

Results: Binding of growth factors to GAGs was found to be dependent on the degree of sulfation. In a previous study, the effect of different degrees of sulfation of synthesized alginate LbL films was studied on FGF-II binding. Using ELISA, it was found that the binding of the growth factor significantly increased by increasing the degree of sulfation. However, since LbL films of natural polymers do not possess long-term stability, implementing a biotin-streptavidin system is expected to provide more stable films and allow the preparation of custom-made sulfated substrates with predefined sulfation degrees.

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 # 123

Alginate sulfate enhances the binding of growth factors with rat aortic smooth muscle cells (RASMC)

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

Keywords: rat aortic smooth muscle cells (RASMC), insulin-like growth factor-I (IGF-I), fibroblast growth factor-II (FGF-II), alginate sulfate, sulfation, glycosaminoglycans (GAGs).

Descriptive Statement: In this study, rat aortic smooth muscle cells (RASMC) 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 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.

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 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 # 124

American University of Beirut GRADE Center
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Funding source: self-funded
Keywords: practice guidelines, adaptation, GRADE

Descriptive Statement: The American University of Beirut (AUB) GRADE Center is one of the centers for the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. The center was launched in 2015 to promote and support the use of the GRADE methodology. The services offered include development of guidelines using the GRADE methodology, adaptation of guidelines using the GRADE methodology and provision of educational sessions, graduate courses, and training workshops in guideline development and the GRADE methodology.
Introduction: The GRADE working group began in the year 2000 as an informal collaboration involving many international organizations involved in the development of systematic review and/or practice guidelines. Currently more than 80 organizations have adopted GRADE. The overall aim of the AUB GRADE center is to provide advocacy, capacity building and support for guideline development nationally, regionally and internationally and contribute to advancing the methodology of guideline development, with a major focus on the adaption of guidelines.
Description:
Collaborators of the GRADE center include: McMaster University GRADE center (MacGRADE), German GRADE Center, Weill Cornell Medical College in Qatar and WHO Eastern Mediterranean Region Office (EMRO)

Service users of the GRADE center include: The AUB GRADE center has provided (or is currently providing) methodological support to:

1. American Society of Hematology (ASH)
2. American College of Physicians (ACCP)
3. American College of Rheumatology (ACR)
4. World Health Organization (three different departments)
5. Kingdom of Saudi Arabia Ministry of Health
6. Weill Cornell Medical College in Qatar and the Middle East Rheumatoid Arthritis Consortium (MERAC)
7. RARE-Best practices, a European Seventh Framework Program project

Methodology projects include: systematic surveys of frameworks for adaptation of health guidelines, methodologies used in adaptation of health related guidelines and reported processes for national adaptation of the World Health Organization guidelines for HIV and Tuberculosis.
Conclusion: There has been growing demand on GRADE expertise to support guideline development efforts due to the increasing uptake of the methodology. The GRADE working group has responded to this demand by creating centers (based in specific institutions) and networks (organized across a number of institutions). The AUB GRADE center will help with increasing opportunities for GRADE-related services. Some of the services can generate income. It will also increase the visibility of AUB regionally and internationally and facilitate scientific collaborations that go beyond guideline development.

Abstract # 125

Using Mass Media to impact Health Policy-making: A Systematic Review

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Funding source: Alliance for Health Policy and Systems Research, World Health Organization

Keywords: mass media, health policymaking, systematic review

Descriptive Statement: Mass media is a key stone in shaping health policies. This systematic review examines the effects of media on health policymaking.

Introduction: Mass media can potentially play an important role in influencing health policies. This systematic review aims to assess the effects of planned media - including social media - interventions on the health policymaking process.

Methods: Eligible studies included randomized and non-randomized designs, process evaluations, qualitative methods and case studies. We electronically searched Medline, EMBASE, Communication and Mass Media Complete, Cochrane Central Register of Controlled Trials, and the WHO Global Health Library. We followed standard systematic review methodology for the selection, data abstraction, and risk of bias assessment.

Results: Sixteen studies met our eligibility criteria. Four used quantitative method, one used a qualitative method, three used mixed methods and seven were case studies. Out of the 16 included studies, only two case studies were about social media interventions. Three of the studies assessed the impact of media campaigns as part of multi-component interventions. All studies except for one showed that the media campaigns were effective in achieving their intended objectives of impacting the policymaking process and inducing policy change. The overall methodological quality of studies is low.

Conclusion: This systematic review can inform researchers, civil society organizations and public health advocates on the different media channels and strategies that can be used to design media interventions aiming at influencing health policymaking. Given the rise in the use of social media, more primary research is needed to examine the impact of social media on the health policymaking process.

Abstract # 126

A New Boundary Condition Methodology Coupled to a 3D CFD Model for Non-Invasively Diagnosing Ischemia in Diseased Coronary Arteries

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Funding Sources and Acknowledgment: The financial support provided by the Farouk Jabre grant (2015), FEA, and the Lebanese National Council for Scientific Research (LNCSR) are gratefully acknowledged.

Keywords: Ischemia, coronary arteries, non-invasive, finite volume method, impedance.

Abstract

Background and aims: Recently, non-invasive predictive techniques for diagnosing ischemia in diseased coronary arteries have shown to be promising, however not yet fully formulated and validated. Few studies based on coupling lumped-parameter coronary models of the downstream vascular bed with patient specific 3D CT scan data have been recently reported to evaluate coronary computed tomographic angiography-FFR (CCTA-FFR). Though these studies "claiming" to be "non-invasive", however, on the contrary are not. Such models, though comprehensive, require invasive measurements of patients' time-dependent pressure and blood flow waveforms to tune the lumped-elements of the coupled downstream coronary impedance. Hence, these approaches can't be considered as been claimed to be non-invasive tools, and thus, couldn't be translated into future clinical practices. In this research, the problem has been viewed from a different perspective, not reported on previously. A new boundary condition has been formulated and coupled to a 3D computational model to account for the myocardial blood flow demand by a downstream vascular bed. This boundary condition relates different patient dependent parameters which can be non-invasively extracted for each patient. The current formulation allows a "purely" non-invasive diagnosis of ischemia for suspected patients with coronary artery disease under steady state conditions rather than conducting full transient simulations, while preserving same level of accuracy. This further allows computing the level of ischemia with minimum time and thus translating it into future clinical practices.

Methods: The solution methodology starts by constructing the geometry of the diseased artery using image processing techniques. The physical domain is then decomposed into small elements forming the basis of the numerical platform. While previous studies have adopted allometric scaling laws to quantify total coronary flow and myocardial resistance, an effort was put in this study to develop new comprehensive physical-based approach to quantify the arterial-venous impedance at the outlet boundary of the truncated diseased vessel. This starts by quantifying the total baseline coronary hypothetical artery flow to the left myocardium following different approaches. The specific coronary artery flow for each artery is then computed based on the surface area of the target vessel to be simulated. Then, the arterial-venous impedance of the modeled vessel is computed based on the central pressure, taking into account the reduction of arterial-venous impedance during maximal hyperemia. The set of conservation equations with

the developed boundary condition formulation are then solved numerically via a collocated pressure-based finite volume method following a segregated approach.

Results: To validate the designed method, available experimental data of dog patients (taken from the study of Gould et al.) were considered. Predictions of normalized blood volume flow rates in healthy and diseased left circumflex arteries were compared with 240 experiments performed on 12, 17 to 40kg, black Labrador dogs simulated under rest and maximal hyperemic conditions. A viscosity shear dependent model was implemented to account for the shear thinning effects of blood. Similar behavior was obtained between the numerical and experimental results (computed R^2 values for a selected dog model were 0.9290 and 0.9504 and RMS values were 0.0833 and 0.3111 for rest and hyperemic conditions respectively). The normal hyperemic response became blunted when the %DS reached 30 % narrowing and decreased markedly before the resting flow was affected (changes in resting mean flow from the hypothetical value was reported when %DS became more than 70%). For all dog models, third order polynomials were initially fitted to the numerical normalized mean flow predictions for each simulated single dog, with R^2 values ranged from 0.9376 to 0.9850 and 0.9804 to 0.9847 for rest and hyperemic conditions respectively. A single average correlation was then obtained for each of the rest and hyperemic simulated cases in order to compare with those generated by the study of Gould et al. The computed R^2 values of the obtained average numerical based correlations were 0.8809 and 0.9733 for the rest and hyperemic conditions respectively. Extensive parametric studies were then done on the validated dog models and constructed idealized human single and branch arterial models by varying various physiologic parameters. A criterion was then developed to identify patients prone to higher levels of ischemia.

Conclusion: As a summary, the future significant value of the designed method lie in its potential to (1) replace the traditional experimental method which is based on intrusive process and (2) be done at low computational cost. The numerical tests performed on dog patients and idealized human arterial models have proven viability and were promising towards translating the developed method into clinical, research and educational applications.

Abstract # 127

A patient-aware n-gram based epileptic seizure prediction algorithm

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Descriptive Statement: This research aims at developing epileptic seizure prediction algorithms that forecast the occurrence of a seizure some time before its onset in order to alert the user to stop any activity (e.g., driving, handling sharp objects) that could aggravate the physiological effects of the seizure. In particular, results related to an n-gram based pattern counting approach are presented.

Funding Source: NeuroPro AG (www.neuropro.ch)

Introduction:

Background and aims: Epilepsy is a human brain disorder in which cells of the brain's nervous system start malfunctioning. As a result, it may generate the abnormal electrical signals that cause an instant defect of the human brain, leading to a change or complete loss of awareness. Statistics have shown that around 1% of the world's population is affected by this disease. This high figure in addition to the number of annual casualties from sudden unexpected death in epilepsy (SUDEP) have triggered a significant research activity into smart and efficient epilepsy prediction/detection algorithms. Electroencephalography (EEG) is a typical method for acquiring the electrical activity of the brain. It provides a measurement of the electric activity in the brain, translating the chemical currents into voltage recordings. The monitoring of EEG signals is central to the understanding of many brain disorders that may affect a human being. One major use of EEG signal is in the diagnosis of brain diseases, in particular, epilepsy. In this research, we aim at developing efficient seizure prediction algorithms that could alert seizure patients of its occurrence to reduce its detrimental effects.

Methods: This research is based on an n-gram pattern counting approach. Patterns of EEG signal amplitude variations are captured during, before and after a seizure onset. These statistics are then fed to a machine learning algorithm which creates a classification model that would eventually decide the occurrence of an imminent seizure with high accuracy. The algorithm was further optimized to select the best preictal period length for each of the patients to maximize the prediction performance

Results: The prediction algorithm was tested on a large number of EEG data records from the Freiburg database. For a total of 13 patients, an average accuracy of 91% was recorded along with a sensitivity of 92% and a false alarm rate lower than 10%.

Conclusion: This ongoing research will provide, upon its completion, a comprehensive prediction of epileptic seizures, towards safer and better convenience of the patients during regular daily activities due to the continuous monitoring and real-time processing of the brain activity though EEG recordings.