Name	Surname	Abstract (copy your Abstract here)
Felix	**Kaplan**	Impact of formal caregivers' ethno-cultural background on maintaining the dignity and autonomy of patients with dementia Felix Kaplan1, Miriam Ethel Bentwich1 The Azrieli Faculty of Medicine, Bar-Ilan University, Safed Campus, Safed, Israel1. Aim & Background: As life expectancy increases in Western societies, a key challenge faced by these societies is addressing elderly care, and particularly ensuring a high quality of care for patients with dementia (PWD). Pivotal concepts in bioethics that are directly related to ensuring high quality of care for PWD, especially in nursing homes, are autonomy and dignity. Although in the West, most formal caregivers are multicultural, there's still insufficient knowledge and understanding of how culture may influence caregivers' handling of the autonomy and dignity of PWD under their care. Methods: An empirical ethics study, utilizing a qualitative research method comprised of 58 non-participatory field observations and 20 semi-structured interviews with formal caregivers from three ethno-cultural groups (Sabras, Arabs and Russians) who work in three nursing homes in Israel. Additionally, 10 interviews were conducted with senior staff members to gain further insights and deeper comprehension of the data. The data was analyzed via a combination of microanalysis and thematic content analysis, informed by two theoretical frameworks for the conceptualization of dignity and autonomy. Results & Conclusion: Russian caregivers were the most prominent in maintaining PWD's dignity and autonomy in their daily care compared to Sabras and Arabs, whereas Sabras and Arabs were more prominent in articulated perceptions of preserving PWD's dignity and autonomy. Ethno-cultural explanations and clarifications were given to the findings by the rich informants. Moreover, 11 new subthemes emerged in content analysis, thus enriching the existent conceptualizations of dignity and autonomy. This study is the first of its kind to focus on the real-time behaviors of multicultural formal caregivers in the care of PWD, and is therefore, able to offer a more precise depiction of the actual application of dignity and autonomy regarding PWD, as well as the differences between behaviors and perceptions in the different cultural groups.
Gon	**Carmi**	Viruses adopt non-optimal codon usage to infect multiple hosts Gon Carmi*, Alessandro Gorohovski*, Somnath Tagore*, Milana Frenkel-Morgenstern** The Azrieli Faculty of Medicine, Bar-Ilan University, Henrietta Szold 8, Safed *equal contribution ** corresponding author Introduction: The genetic code has redundancies. Many viruses introduce their tRNAs inside the host cells. We proposed that viruses introduce their own tRNAs preferentially for non-optimal codons in order to infect multiple hosts. The rational is that viruses with codon usage matched a particular host reduce their ability to infect multiple hosts efficiently. Methods: For 115 viruses with tRNA genes and corresponding 55 hosts, the codon usage preferences were estimated by our unique non-optimality score. Moreover, the codon usage tables were calculated for each virus/host. The mathematical model has been proposed to explain the non-optimal codon usage preferences for viruses during the host cell-cycle. The differential expression analysis by means of our experimental RNA-seq data (of herpes viruses) has been used to evaluate the viral genes expression during the host cell-cycle. Finally, the latent and lytic states of viruses were compared to identify unique features. Results: We found a high correlation between the non-optimal codon usage preferences of viruses and a number of multiple hosts that they affect (the Person correlation coefficient of 0.7). We found that hosts prefer optimal codons, but viruses prefer non-optimal codons in order to adapt to the host codon usage by introducing viral tRNAs into the host cells. Moreover, we found that viruses use non-optimal codons to affect their expression level during the host cell-cycle phases. We proposed a novel mathematical model to explain the non-optimal codon usage effects as well as experimental RNAseq data that demonstrate the changes in the viral genes expression during the host cell-cycle. Discussion: Our results indicate that for infection of multiple hosts, the non-optimal codon usage in viruses is unique evolutionary strategy of adoption. This strategy is an efficient to spread viruses to different niches and hosts. מספר טלפון נייד 0523664639 gon.carmi@biu.ac.il סטודנט מחקר תואר שלישי מעניין להציג את העבודה בעדיפות ראשונה כהרצאה ובעדיפות שניה כפוסטר
Elias	**Saad**	Complete blood count parameters can pedict severity of chronic obstructive pulmonary disease (COPD) exacerbation? Saad Elias1,2, Barhoum Masad1,2, Asleh Mostafa1,2, Servadio Ella1,2, Assy Nimer1,2 Department of Medicine, Galilee Medical Center1 , Azrieli Faculty of Medicine, Bar-Ilan University2 Aim & Background: Increased (Red Blood Cell Distribution) RDW values have been reported to be related with underlying chronic inflammation. Increased inflammation in the lungs, as well as a systemic inflammatory response, is now a well-established factor in COPD. Our aim is to investigate the relationship of different complete blood count (CBC) parameters such as hemoglobin, mean corpuscular volume (MCV), Mean platelet volume (MPV) or RDW with COPD exacerbation severity. Methods: In the present retrospective analysis, consecutive patients admitted with the diagnosis of "COPD Exacerbation" between 1/1/2012 and 31/12/2015 were evaluated. Results: Patients with MCV >100fL have significantly a higher Paco2 than patients with normal or low MCV (P< 0.001). Patients with a high RDW significantly a higher Paco2 than patients with normal RDW (P=0.017) , and patients with MPV< 7fL have significantly a higher Paco2 than patients with normal or high MPV (P=0.001). Patients with anemia had significantly longer hospitalization duration than patients with normal or high hemoglobin level (P< 0.001). Patients with MCV >100fL had significantly longer hospitalization duration than patients with normal or low (P< 0.001). Patients with a high RDW had significantly longer hospitalization duration than patients with normal RDW (P<0.001). Elevated CRP level also predicted longer hospitalization duration (P<0.001) and higher Paco2 during hopitalization, and patients with higher RDW had higher CRP level (P < 0.001) Conclusion: Our study demonstrated that different parameters of the CBC such as hemoglobin, MCV and the RDW can predict the severity of acute exacerbation of COPD reflected by the PCo2 level and the duration of hospitalization. Furthermore, our finding of a positive correlation between RDW and CRP levels supports the hypothesis that RDW and MCV are a markers of inflammation
Rajesh	**Detroja**	The comprehensive pedigree analysis to uncover biomarkers in complex diseases using liquid biopsy Rajesh Detroja (1), Vikrant Palande (1), Dorith Raviv Shay (1), Milana Frenkel-Morgenstern (1)* (1) The Azrieli Faculty of Medicine, Bar-Ilan University, Henrietta Szold, 8, Safed, Israel. *milana.morgenstern@biu.ac.il Health care professionals have known for the substantial amount of time that complex and chronic diseases run in families. 'Complex Diseases' can be defined as a medical condition such as heart diseases, cancers, asthma, arthritis, and diabetes that do not have a single genetic cause–they are likely associated with the effects of multiple genes and conditions (polygenic). Although complex diseases often cluster in families but they do not have a clear-cut pattern of inheritance. This makes it difficult to determine a probability of complex diseases to be reoccurring in certain families. Therefore, the identification of personalized molecular biomarkers through the genetic analysis of every individual in the families that affected by complex diseases could provide an opportunity to improve quality of life through early detection and timely treatment. "Liquid biopsy" is a new and recently developed non-invasive technique uses circulating cell-free DNA (cfDNA) fragments that are released into the blood stream. Our goal is to perform next-generation sequencing (NGS) of white blood cells (WBC) and cfDNA of the families with complex disease to make in-silico pedigree analysis that includes discovery of germline single–nucleotide polymorphism (SNPs), identification of structural variants (SV), chimeric genes and to detect microbiomes associated with the family to reveal novel biomarkers, which could be applied for the future personalized diagnostics and treatment using liquid biopsy technique.
Baruh	**Polis**	Norvaline, a novel Alzheimer's disease-modifying agent. Alzheimer's disease (AD) is an irredeemable chronic neurodegenerative disorder and the predominant cause of dementia. The disease progression is associated with amyloid plaques' deposition and neurofibrillary tangles' formation in the brain, yet clinical dementia is the end and culminating stage of the enduring pathology. Recent empirical evidence points to severe characteristic metabolic dysfunction as a leading cause and hallmark of AD that is apparent decades prior to the disease manifestation. State-of-the-art metabolomics studies prove that complex arginine and branched-chain amino acids (BCAAs) metabolism disturbances accompany AD. Lower plasma valine levels are associated with accelerated cognitive decline, and, conversely, an increase in valine concentration is associated with a significantly reduced risk of AD. We administered an arginase inhibitor norvaline, which is an uncommon non-proteinogenic BCAA and a valine's isoform, chronically to a mouse model of AD. A set of immunohistochemistry, proteomics, and transcriptomics assays was applied to evaluate the neuroprotective effect of the substance and identify the biological pathways activated by the treatment. The results verify that norvaline reverses the cognitive decline in the AD mice. The neuroprotective effect is associated with significantly reduced hippocampal arginase levels and diminished amyloidosis. Moreover, the treatment moderates the rate of Tau protein phosphorylation, alleviates microgliosis and apoptosis. Additionally, we disclose the treatment-associated increase in the hippocampal expression levels of synaptic plasticity-related proteins, expression levels of cytosolic branched-chain amino acid aminotransferase, and an activation of several, involved in cell survival and neuroplasticity, biological pathways. The data suggest that norvaline is a potent arginase inhibitor and modulator of glutamate metabolism. The substance possesses various modes of action, which improve the symptoms of AD and even interfere with its pathogenesis. Therefore, norvaline presents a promising neuroprotective molecule with manifold biological potentials that might be tailored for the treatment of a range of neurodegenerative disorders.
Noa	**Abrahami**	Do Young Women with Unexplained Infertility Demonstrate Manifestations of Decreased Ovarian Reserve? Noa Abrahami1, 2, Ido Izhaki3, Johnny S. Younis1, 2 1The Azrieli Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel. 2Reproductive Medicine Unit, Department of Obstetrics and Gynecology, Baruch-Padeh Medical Center, Poriya, Israel. 3Department of Evolutionary and Environmental Biology, University of Haifa, Haifa, Israel. Aim & Background: Poor ovarian response (POR) amid fertility treatments is considered an early sign of ovarian aging, a crucial factor affecting pregnancy achievement and maintenance. Nevertheless, POR was properly explicated only in 2011 with the publication of the Bologna criteria. Although designed to devise a uniform definition, they did not, however, outlined risk factors for POR, rendering its use precarious in some populations, especially younger infertile women This study aims to evaluate whether unexplained infertility at a young age demonstrates manifestations of decreased ovarian reserve. Methods: A case-control study carried out between April 2015 and November 2016. Power analysis was a priori conducted to determine statistical significance. The study group comprised women age ≤37 years diagnosed with unexplained infertility, and the control group included age-matched women with either mechanical factor or severe male factor infertility. Results: Groups were comparable in basic characteristics. Overall, women with unexplained infertility had inferior ovarian reserve results set against controls. The number of ≥14mm follicles on the day of hCG administration was significantly lower in the study compared with the control group (7.0±4.5 vs. 10.4±4.1 follicles, P<0.001). Basal serum FSH was higher in the study compared with controls (8.4±5.5 vs. 6.4±1.7 IU/L, P=0.015), while antral follicle count (AFC) was lower (10.9±6.6 vs. 16.2±6.6 follicles, P<0.001). Women with unexplained infertility required a higher total dose of FSH for ovarian stimulation but exhibited a lower number of retrieved oocytes, alongside a lower number of embryos achieved. Interestingly, the cumulative clinical pregnancy rate was not significantly different between the groups (44% vs. 58%, P=0.163). Conclusions: Young women aged ≤37 years with unexplained infertility have clear manifestations of decreased ovarian reserve set against controls. Our findings support the notion of unexplained infertility as a risk factor for poor ovarian response, specifically as a quantitative, rather than a qualitative, risk factor.

Daniel	**Baumel**	The function of iASPP in Cardiomyocytes Daniel Baumel, Yiftah Barsheshet, and Orly Avni Faculty of Medicine, Bar-Ilan University Aims & Background: Dilated cardiomyopathy (DCM) is a life-threatening disorder whose genetic basis is heterogeneous and mostly unknown. In our recent published work in collaboration with Prof. Tzipora C. Falik-Zaccai, five Arab-Christian-infants, ages 4-30 months from four families were diagnosed with DCM associated with mild skin, teeth and hair abnormalities. All passed away before age 3. A homozygous sequence variation in PPP1R13L encoding the iASPP protein, was identified in three infants, and heterozygous in the mother of the other two. The patients' fibroblasts and PPP1R13L-knocked down human fibroblasts presented higher expression levels of pro-inflammatory cytokine genes in response to Lipopolysaccharide (LPS), as well as ppp1r13l-knocked down murine cardiomyocytes and hearts of ppp1r13l-deficient mice. The hypersensitivity to LPS was NF-κB-dependent, and NF-κB-inducible binding activity to promoters of pro-inflammatory cytokine genes was elevated in patients' fibroblasts. RNA-sequencing of ppp1r13l-knocked down murine cardiomyocytes and of hearts derived from different stages of DCM development in ppp1r13l-deficient (Wa3) mice revealed the crucial role of iASPP in dampening cardiac inflammatory response. Altogether, these results demonstrated PPP1R13L as the gene underlying a novel autosomal recessive cardiocutaneous syndrome (CCS) in humans, and strongly suggest that the fatal DCM during infancy is a consequence of failure to regulate transcriptional pathways necessary for tuning cardiac threshold response to common inflammatory stressors. However, the mechanisms underlying the function of iASPP in regulating NF-κB activity and cardiac response are unknown. Methods: Heart tissues were purified, and cardiomyocytes were harvested from homozygous BALB/c wa3 mice and their littermate WT mice and were processed for confocal microscopy imaging and molecular assays. Results & Conclusion: Our preliminary results suggest that iASPP regulates cellular translocations of NF-κB. Mobile phone: 054-462-2080 Laboratory phone: 072-264-4921 Email: daniel.baumel@gmail.com Ph.D. student Presented as a poster
Dr. Chen	**Ryder**	The relations between abnormal sensory processing patterns and ADHD subtypes compared with a healthy control group Chen Hanna Ryder, Kari Ramsted-Ohana, Darian Ryder, Karin Wiegler-Beiruti, Naaem Simaan & Radi Shahien Abstract Background: Sensory Processing Disorder (SPD), an early childhood developmental disorder, is highly co-morbid with ADHD and shares similar prevalence (5%-16%), yet receives much less attention, while features difficulties in detecting, modulating, interpreting and organizing sensory stimuli to a degree interfering with daily function. Since SPD persists into adulthood yet the DSM-5 does not recognize it as such, many ADHD patients suffering from this co-occurring sensory processing symptoms in adulthood fail to undergo an SPD diagnosis and receive respective treatment. The study in question aimed to evaluate the co-occurrence of SPD's different modalities among the different subtypes of ADHD in the adult population and to compare it with a healthy control group. Methods: A total of 60 individuals (n=60) between 18 and 45 years of age, divided into two different groups: the study group (ADHD group) n=30 adults with valid ADHD diagnosis and control group n=30 adults (Healthy control group) with no ADHD or other Neurological or Psychiatric diagnosis. The participants completed questionnaires regarding ADHD in adulthood and SPD symptoms and subtypes. The results of sensory profile in different subtypes of ADHD were statistically analyzed and compared with control group. Results: individuals suffering from combined type ADHD exhibited more frequent and extreme reactions (both hyper- and hypo sensitivity) to sensory stimuli compared to individuals with inattentive type ADHD and healthy controls. Conclusion: The current study results indicate that there are differences in sensory modulation among different subtypes of ADHD in adulthood. The herein results suggest a shift in thinking, emphasizing that contrary to the common perception, which emphasizes the salience of sensory processing disorder only during childhood, it is of utmost importance to identify and regulate sensory disorders also among adults suffering from ADHD due to its effect on their sensory perception and behavior.
Keren	**Aviel-Shekler**	Effects of gestational diabetes on autism-related behavior and gene expression in the brain of offspring Aviel Shekler K. Getselter D. Lukic I. Oron O. Davis L. Malka A. Piran R. Elliott E. Bar-Ilan University, Faculty of Medicine in the Galilee, Safed, Israel Background: Autism spectrum disorder (ASD) is associated with a variety of prenatal, perinatal and postnatal etiologies, and its current prevalence is above 1% of the children born in this decade. ASD is a neurodevelopmental and behavioral disorder which is defined by deficits in social interaction, low communication and repetitive behavior. Recent studies have shown that there is an association between metabolic conditions (MCs) during pregnancy (obesity, gestational diabetes (GDM)) and ASD. There is growing evidence demonstrating effects of GDM on neurodevelopmental behavior disorders and molecular changes in the brain of the offspring. We aim to develop a mouse model of GDM by using pregnant streptozotocin-induced diabetes female C57BL/6 mice and to examine the effects on the offspring, both at the behavioral and molecular levels. Results: After administration of STZ we saw that mice treated with STZ demonstrated higher glucose levels. After conducting behavior tests, the offsprings demonstrated behavioral changes in open field test, grooming test and marble burying test. We determined a significant increase in grooming behavior in males. In addition, the male mice buried more marbles. In the context and cue test of fear conditioning, male offspring of GDM mice demonstrated more freezing time compared to the control group, suggesting that they had a better stress-related memory. Most of the behavioral changes were observed in males which parallel to higher prevalence of neurodevelopmental disorders in male population. In molecular tests, we found different gene expression in the prefrontal cortex and the striatum of the mice. Conclusion: From our results, we can suggest that the GDM offspring demonstrate more autistic like behavior in form of more repetitive behavior and stronger learning after stressful experience. These studies may advance our understanding of the connection between maternal metabolic conditions and neurodevelopmental conditions in the offsprings. <<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<< Phone number: 0545818836 Email: Kitty.sh2@gmail.com PhD student
liron	**davis**	A role for neuronal chromatin organizer CTCF in parvalbumin GABAergic neurons Liron Davis, Evan Elliott. Bar-Ilan University, Faculty of Medicine, Safed, Israel CTCF plays an essential role in 3D genome organization and gene expression and has recently been implicated as a major contributor in neural development. Genetic studies reveal that mutations in CTCF are associated with intellectual disability and autistic behavior. Recent studies in mice models have started to show the importance of CTCF in neuronal morphology and on behavior. Nonetheless, there is little knowledge about the roles of CTCF in CNS in general and in inhibitory neurons in particular. In order to determine the role of CTCF in a subclass of inhibitory neurons, we induced a CTCF cKO in parvalbumin neurons by using the PV-cre /floxed CTCF mice. Adult mice display motor impairments in open field test and abnormal limb-clasping reflex. Moreover, these mice displayed less anxiety-like behavior in dark light test and elevated plus maze test, relative to wild type mice. Immunohistochemistry analysis found a decrease in PV+ neurons and increase in somatostatin+ neurons (neurons which generated from the same precursors as PV). Interestingly, TUNEL staining revealed a lack of apoptosis, suggesting that apoptosis doesn't account for the decrease in PV neurons. Furthermore, to understand how CTCF depletion affects gene expression in PV neurons, we performed RNA- seq on PV+ nucleus isolated from these mice, and WT mice. Gene ontology analysis revealed that ablation of CTCF leads to down-regulation of genes involved in regulation of nervous system development and synaptic signaling, and further identified particular genes involved GABAergic neuron differentiation. Additional research will focus on further understanding of molecular mechanisms and changes in neuronal chromatin structure that underlie this phenotype. Therefore, CTCF-mediated chromatin organization may play an important role in development of locomotion and anxiety impairments. Phone number: 0528-750285 Mail: lironinthesky@gmail.com Student
Vikrant	**Palande**	Introduction Gliomas are the most frequent brain tumors, making up about 30% of all brain and central nervous system tumors, and 80% of all malignant brain tumors. Existing standard diagnostic technique for glioma tumor includes tissue biopsy, which is a highly invasive and hence a risky technique for the patient's survival. 'Liquid biopsy' is a new and recently developed non-invasive cancer diagnostic technique, which includes use of circulating cell-free DNA (cfDNA) fragments for tracing tumor markers. CfDNA fragments are one of those molecular bits that are released into the bloodstream after rapid apoptosis or necrosis of the tumor cells in the cancer patients. Our goal is to do comprehensive study between distinct types of glioma cancer tumors and cfDNA of the respective patients, to elucidate the scope of cfDNA in liquid biopsy technique for glioma diagnosis. Methods We collected 8 different glioma patient's tumor tissue and plasma samples and then isolated tumor DNA from glioma tumor tissue and circulating cell-free DNA(cfDNA) from the respective glioma patient's plasma. Isolated tumor DNA and cfDNA then deeply sequenced on Illumina HiSeq 2500 and then NGS data was analyzed to find out single nucleotide variants (SNVs) as well as structural variants on both cfDNA and tumor gDNA. Results We have successfully detected glioma specific mutations such as IDH1, IDH2, PDGFRA, NOTCH1, PIK3R1 and TP53, from cfDNA isolated from the plasma of glioma patients and could relate this mutations to the different tumor grades of glioma. We are also studying the dynamics of these mutations in response to glioma drug treatment by collecting blood samples at different time intervals. Discussion This study may help in developing liquid biopsy technique for glioma tumor diagnosis and in its prognosis for monitoring the glioma treatment by non-invasive approach, and will eventually help physicians to decide the right treatment on appropriate time while bypassing the existing 'wait-and-see' approach of treatment monitoring.

Ayalla	**Fedida**	A genomic duplication of 83 Kbp is associated with the Mammary-Digital-Nail (MDN) syndrome Ayalla Fedida1, 2, Limor Kalfon1 and Tzipora C Falik-Zaccai1, 2 1Institute of human genetics, The Galilee Medical Center, Nahariya. 2The Azrieli Faculty of Medicine, Bar Ilan University, Safed. Aim & Background Mammary-digital-nail syndrome (MDN) is a unique phenotypic association consisting of anonychia onychodystrophy with hypoplasia or absence of distal phalanges in males and females, accompanied by juvenile hypertrophy of the breast in affected females. Linkage studies and haplotype analysis defined the locus for the phenotype within a 4.3 Mb interval on chromosome 22q12.3-13.1. We aim to reveal the causative genetic variant, underlying the MDN phenotype. Methods Whole genome sequencing (WGS) of two affected and two healthy family members followed by relative quantitative PCR (qPCR) and segregation analysis for validation of the WGS results within the extended pedigree. Reverse transcriptase (RT)-qPCR analysis was used for relative quantification of the transcript abundance of the open reading frames (ORFs) within the genomic variant. Finally, RNA-sequencing was performed for the characterization of the whole transcriptome in breast and skin biopsies. Results WGS revealed a novel heterozygous genomic duplication of 83 Kbp, within the linked interval on chromosome 22 in affected individuals. This duplication contains two ORFs: one encoding the potassium channel protein KCNJ4 and the other encoding an inositol lipid phosphatase pseudogene (LOC400927). Relative qPCR confirmed an autosomal dominant segregation pattern within the family. RT-qPCR analysis revealed a significant increase in the transcript level of KCNJ4 in skin biopsies derived from affected individuals and in breast biopsies of affected females, versus healthy controls. Preliminary results of the RNA sequencing analysis revealed that out of 72 differentially expressed genes 7 significantly down regulated genes belongs to the peroxisome proliferator-activated receptors signaling pathway which mediates the physiological actions of fatty acids (FAs) and FA-derived molecules. How this changes in gene expression leads to the MDN phenotype is yet to be determined. These findings may shed light on a possibly novel signaling pathway affecting the organogenesis of limbs and mammary glands in humans. מס' נייד: 052-3790708 מס' טלפון בעבודה: 04-9107493 כתובת דוא"ל: ayallaf@gmc.gov.il מעמד אקדמי של החוקר המציג: פוסט-דוקטורנטית
Iryna	**Khrystoforova**	Aim & Background: Osteoporosis and sarcopenia are comorbid wide-spread age-related diseases which affects human population tremendously. In human organism after 26 years of age the musculoskeletal system starts to undergo age-related changes. Genome-Wide Association study (GWAS) reveals new candidate genes associated with low bone mineral density (BMD) and complex diseases, such as osteoporosis and sarcopenia. Validation of the role of novel musculoskeletal genes discovered by GWAS is required in purpose to make a bridge between in-silico data and application for improving human life quality. Advanced genome editing technologies such as CRISPR-Cas9 allow the further validation of novel musculoskeletal regulators in animal model. Therefore, the goal of our research is to find novel genes associated with musculoskeletal diseases, based on human GWAS data, and to further validate them in a zebrafish model. Methods: We examined the expression patterns of selected genes (adamtsl3, fam210aa, fam210ab, fubp3, jag1a, wnt4a, wls and srebf1) by in-situ hybridization of specific RNA-probe to zebrafish both in intact and in regenerated 4 dpa (4 days post amputation) fins. We performed the quantitative expression of novel genes in zebrafish different tissues by qPCR. Based on expression assay results we performed the selection of relevant candidate genes for generating stable mutant lines for further functional characterization Results&Cunclusions: The adamtsl3, fubp3, jag1a, mef2ca, wnt4a, wls genes pointed out the involvement in bone homeostasis, during bones regeneration in zebrafish fins. The qualitative analysis in different tissues revealed the significant expression in muscles for fam210aa, fam210ab, mef2ca. The high expression in bone tissues (scales, operculum) was observed for wls. Muscles and bones are developed together and share genetic determinants. Novel candidate genes which expressed in muscle tissue are also relevant for further research. Therefore, we conclude to focus on adamtsl3, fam210aa, fam210ab, fubp3 as relevant candidates for generating mutant lines. Further research is required to identify the role of novel genes in bone homeostasis.
Ligat	**Daudi**	Implementing an Intervention Program in a Hospital Setting to reduce ER Visits for Unintentional Child Injuries Ligat Daudi 1, Sivan Spitzer-Shohat 1,2, Anthony Luder1,3, Jumanah Essa-Hadad1, Mary Rudolf 1 1 Department of Population Health, Azrieli Faculty of Medicine, Bar-Ilan University, Zfat 2 Center of Health and the Social Sciences, University of Chicago 3 Ziv Medical Center, Zfat Background & Aim: Unintentional injuries (UI) are a leading cause of child morbidity and mortality worldwide, accounting for 202,000 of ER visits in Israel. One common strategy for reducing UI is home-visitation, conducted mainly by community-based programs. However, interventions' effectiveness is mixed. This may be because studies have not examined the implementation process and its effect on attaining desired outcomes. Our study evaluates the implementation of SHABY, a home-visitation program in Ziv Medical Center, for reducing UI. High-risk families for recurrent UI in children (0-5 years) will be recruited upon ER arrival and will receive two home visits focusing on home-safety counselling over four months. Methods: Evaluation is guided by the Consolidated Framework of Implementation Research assessing the effect of program design, individuals involved and organizational setting on attainment of outcomes. Pilot phase included observations and interviews to assess facilitators and barriers pre-implementation. Evaluation of SHABY uses a mixed methods design, including quantitative data utilizing a home-safety checklist, attitudes questionnaire, and hospital record review; qualitative data involving interviews with hospital and SHABY staff. Preliminary Results: Pre-implementation assessment identified complexities in the intervention's design. Recruitment by ER nurses was found to be difficult and burdensome and home visitation not possible for them to conduct. Hence, we revised the intervention to include designated recruitment nurses and trained nursing students to conduct home visitation. Analysis of the organizational setting identified that while frontline hospital stakeholders were passionate and interested in implementing SHABY, management had difficulty taking ownership, and viewed it as a preventive program which should be conducted in the community setting. Conclusion: High rates of UI visits indicate the hospitals setting important for implementing a preventative program like SHABY, yet implementation in a new setting is a difficult. This evaluative study will increase knowledge regarding factors affecting the implementation process and those important for reducing UI. An abstract for a lecture Ligat Daudi, Ph.D. candidate Phone no. 050-755-4025 E-mail address: Ligat.Daudi@gmail.com
HAGAR	**TADMOR**	Kaposi's Sarcoma Associated Herpesvirus LANA Modulates the Stability of the E3 Ubiquitin Ligase RLIM H. Tadmor, O. Orgil, A. Ahuja, and M. Shamay Daniella Lee Casper Laboratory in Viral Oncology, Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel. * Corresponding Author: meir.shamay@biu.ac.il The Kaposi's sarcoma associated herpesvirus (KSHV) encoded LANA protein functions in latently infected cells as an essential participant in KSHV genome replication and as a driver of dysregulated cell growth. The expression of many cellular genes is modulated in the presence of LANA. In a previous study, we have identified LANA interacting proteins using a protein array screen. Here, we explore the effect of LANA on the stability and activity of RLIM (RING-finger LIM-domain-interacting protein, encoded by the RNF12 gene) a novel LANA interacting protein identified in that protein screen. RLIM is an E3 ubiquitin ligase that leads to the ubiquitination and degradation of several transcription regulators, such as LMO2, LMO4, LHX2, LHX3, LDB1 and the telomeric protein TRF1. Expression of LANA leads to down-regulation of RLIM protein levels. This LANA-mediated RLIM degradation is blocked in the presence of the proteasome inhibitor, MG132. Therefore, the interaction between LANA and RLIM could be detected in co-immunoprecipitation assay only in the presence of MG132 to prevent RLIM degradation. A RING finger mutant RLIM (HH 590, 593 EE) is resistant to LANA mediated degradation, suggesting that LANA promotes RLIM auto-ubiquitination. Interestingly, we find that LANA enhance the degradation of some RLIM substrates, such as LDB1 and LMO2, and prevent RLIM mediated degradation of other substrats such as LHX3 and TRF1. We also show that transcription regulation by RLIM substrates is modulated by LANA. RLIM substrates are assembled into multi-protein transcription regulator complexes that regulate the expression of many cellular genes. Therefore, our study identified another way KSHV can modulate cellular gene expression. phone no: 0528-285603 e-mail address: hagart9@gmail.com post-doc fellow
Olga	**Volodko**	Identification of Acute Coronary Syndrome associated miRNA using an unbiased sequencing approach Olga Volodko1,2, Natalia Volinsky1, Inbar Ben-Zvi1,2, Iddo Magen3, Diab Ghanimb, Fabio Kuzniecb, Nufar Margalit1, Nofar Asulin1,2 and Offer Amir1,2 Cardiovascular Department and Research Center of Baruch Padeh Medical Center, Poria, Tiberias, Israel1. The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel2. Department of Molecular Genetics, Weizmann Institute of Science, Rehovot, Israel3. Abstract Acute Coronary Syndrome (ACS) is a medical condition induced by full or partial blockage of coronary artery(s) and without appropriate treatment it leads to permanent heart damage and heart failure. ACS can be subdivided into several types, whereas the most severe type is associated with ST- segment elevation in electrocardiogram, ST-elevation myocardial infarction (STEMI), and requires immediate medical intervention. MicroRNA (miRNA) are small non-coding RNA molecules of about 22 nucleotides. They mediate regulation of gene expression and are involved in different pathophysiological conditions, including cardiovascular diseases. Our research is aimed to determine differentially expressed miRNA in the serum of STEMI patients, compared with individuals having normal coronary arteries or with chronic arteries disease (CAD) patients who do not require immediate intervention. Blood samples are collected from the study participants twice during the cardiac catheterization procedure: from a peripheral blood vessel and from a coronary artery proximal to the affected area. miRNA will be extracted from blood serum and further detected using the New Generation Sequencing. This is an unbiased approach enabling detection of multiple miRNA molecules, including miRNA that were not previously associated with cardiovascular diseases. Currently, different protocols of samples preparation are compared to enable optimal experimental performance and data acquisition. This study will potentially identify differences between miRNA expressed in serum of STEMI patients compared to healthy individuals or CAD patients, leading to identification of biomarkers for early diagnosis and better understanding of the ACS development mechanisms. מס' נייד: 0545500283 כתובת דוא"ל: olga.volod92@gmail.com מעמד אקדמי של החוקר המציג: סטודנטית למחקר.
דורון	**שגיא**	LEARNING SOCIAL DETERMINANTS OF HEALTH (SDH) THROUGH AN EXPERIENCE-BASED HOME VISITING COURSE IN THE CLINICAL YEARS Introduction- There is broad consensus that medical schools have a duty to impart to students the competences required for tackling social determinants of health (SDH). Such educational programs are usually scheduled in the pre-clinical years, focusing principally on knowledge, attitudes, and basic skills. ETGAR is an experienced-based course designed to enhance students' understanding of health disparities and SDH through post-discharge home-visits conducted with patients whom students recruit while in hospital. Methods- 105 clinical year students working in pairs visited 177 patients living in disadvantaged circumstances in Israel. Their home-visit reports were analyzed employing mixed methodology. A content analysis, using the theoretical framework of biopsychosocial theory, was conducted to classify the topics and concepts raised by students. Reports were compared quantitatively by richness of report (number of items), gender and year of study. Results- Fifteen taxonomy items were identified. Social support and patients' medical conditions were the most prevalent issues followed by personal/emotional related issues; community-related Items were the least prevalent. Richer reports were more balanced and contained significantly more critical thinking. Women and mixed couples provided richer reports. Content analysis demonstrated students' understanding of the relation between SDH and patient health and well-being, the challenges and barriers patients face in the community after discharge from hospital; and action taken by the students. Conclusions- Meeting patients both in hospital and at home enhanced awareness of SDH. Students learned to view the patient comprehensively, and to understand the various factors affecting their health. Students, who essentially had sole responsibility for the home-visit, successfully integrated their skills to take actions that made a difference to patient care. The ETGAR experience provided a means for effective learning about the sort of social determinants that impact on health.

yoav	**bahat**	Structure-function studies of Glycoprotein N (GN) from Tomato spotted wilt orthotospovirus (TSWV) Yoav Bahat and Moshe Dessau The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel. Aim & Background: The Tospoviridae family is a member of the Bunyavirales order, which is the largest known enveloped RNA virus order with incredible diversity in structure, host range, vectors and tissue tropism. Tomato spotted wilt orthotospovirus (TSWV) from the Tospoviridae family is a thrips transmitted virus that infects large number of crops causing global heavy economic burden. Tospoviruses have a lipid-bilayer membrane envelope that protects their tri-partite RNA (-) single-stranded genome. In contrace to mammalian pathogens from the Bunyavirales order, Tospoviruses evolved lacking the race-of-arms against an adaptive immune system therefore they might adapt different evolutionary path to perfect their entry into their host-cell. The two envelope glycoproteins, termed GN and GC, form the envelope spikes that project outward from the viral membrane. It was proposed that of GN and GC form heterodimers, however no experimental evidence exist for neither tospovirus' glycoproteins interactions nor for their organization and function. In light of the substantial gap of structural knowledge, we aim to determine the three-dimensional structure, domain's organization, oligomeric state and biochemical function of TSWV GN. Methods: We expressed TSWV GN, purified it to homogeneity using chromatographic methods and subsequently crystallized it. Using X-ray crystallography, we determined the atomic resolution structure of TSWV GN. With GN structure in hand, we will use structural bioinformatics with structure-based mutagenesis in various biochemical assays to reveal the biological function and relevance of our crystal structure. Results & Conclusion: We successfully purified, crystallized and determined the structure of the TSWV GN. We obtained either diamond or plate shape crystals which diffract to ~3.4 Å and ~2.8 Å respectively. GN crystal structure reveals a novel protein fold that was not previously reported. The crystal structures reveal two potential dimerization interfaces for TSWV GN; A di-sulfide dependent interface, and a non-covalent interaction interface that is responsible for the fold stability of GN. מס' נייד: 054-7896616 מס' טלפון בעבודה: 072-2644904 כתובות דוא"ל: yb911@walla.co.il מעמד אקדמי של החוקר המציג: סטודנט מחקר
Ido	**Lavi**	CRISPR TO GET THERE: A NUCLEAR FACTORS RECRUITMENT TEST BY THE KAPOSI'S SARCOMA ASSOCIATED HERPESVIRUS ENCODED LANA Ido Lavi, Ola Orgil, Nir Avital, Michael Talalai and Meir Shamay Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel Kaposi's sarcoma associated herpesvirus (KSHV, HHV-8) is the etiological agent of Kaposi's sarcoma (KS), and is tightly associated with primary effusion lymphoma (PEL) and multicentric Castleman's disease (MCD). KSHV is a member of the gamma-herpesvirus family and can establish life-long latent infection in human B lymphocytes and endothelial cells. The latency-associated nuclear antigen (LANA) is among the few KSHV encoded genes during latency. In previous studies, LANA was found to be associated with more than 60 host proteins, among them transcription activators and co-activators, as well as transcription repressors and co-repressors. However, it is still unclear if LANA can recruit these proteins to specific chromosomal regions. CRISPR/Cas9 can be targeted to specific chromosomal regions via single guide RNA (sgRNA), and a mutant Cas9 that cannot cut DNA (dCas9) can be repurposed to recruit proteins onto the human genome. Due to the repetitive nature of the telomeres, recruitment of dCas9 results in large protein dots. Combining the CRISPR and Sun-Tag methods, that has the potential to gather up to 10 molecules on single dCas9, we designed sgRNA to the telomeres together with the dCas9 protein fused to SunTag scaffold. We designed a LANA fused to IgG-Fc arm to direct it to the dCas9-SunTag scaffold on the telomeres. Finally, we examined the ability of LANA to recruit several non-telomeric factors and translocate them to the telomere. Here we show for the first time a novel approach to determine the ability of any nuclear protein to recruit any other nuclear factor.
Hossin	**Bouz**	Structural and Evolutional investigation of Phenuiviridae Membrane Fusion Proteins. Hossin Bouz1, Joel Alter1, Moshe A. Dessau1 1The Azrieli Faculty of Medicine, Bar-Ilan University,Safed, Israel The evolution of viruses is mainly influenced by environmental pressures resulting from growing niches of vector transmission, climate, vector and/or host availability, and their immune response. Little is known about the structural basis of the evolutionary processes that cause virus strains restricted to insects or animals to change its host range and infect humans. The entry of the enveloped viruses into their host cells involves receptor binding, followed by internalization and the uncoating of the virus from its lipid envelope, known as membrane fusion. Subsequently, the viral genome is delivered to the cytoplasm of the host cell to initiate replication and assembly of new virions. The mechanistic differences in these steps between human-infecting viruses to insect-restricted viruses will unravel new aspects of the mechanisms of the virus host-range selection. BADU Virus (BADUV) is a newly described virus that belongs to the family of Phenuiviridae (order: Bunyavirales). BADUV is a negative sense, single-stranded RNA virus, divided into three segments. The genome and the proteins surrounding it are contained in a lipid envelope in which the two envelope glycoproteins, Gn and Gc, are anchored at the outer side of the virion. Both of these proteins play an important role in the process of the virus cell entry. In contrast to many closely related viruses from the Phenuiviridae family, BADUV is an insects-restricted virus. Moreover, recent work shows that BADUV is unable to replicate in cultured mammalian and avian cells. We will investigate the structural differences between the BADUV envelope proteins and those of the pathogenic viruses of the same family, in order to understand the mechanistic differences of their entry to the host cell. We successfully purified and crystalized the Gc protein and by using X-ray crystallography, we will determine the three-dimensional structure of the BADUV envelope glycoproteins at atomic resolution. Keywords; BADU Virus, Envelope Glycoproteins, X-ray crystallography. Contact information Hossin Bouz M.S.c Student, The laboratory of Structural Biology of Infected Deseases Moshe Dessau PhD. Azrieli faculty of Medicine in the Galilee, Bar-Ilan University, 8 Henrietta Szold St. Safed, 1311502, Israel. Tel:+97254-3985441 E-mail: hossin.bouz@live.biu.ac.il Office: B104
Regina	**Michelis**	Persistent complement activation is provoked by IgG-aggregates in a sub-population of Chronic Lymphocytic Leukemia patients Regina Michelis1, Tamar Tadmor2,3, Masad Barhoum4,5, Mona Shehadeh6, The Israeli CLL Study Group and Andrei Braester4,5 1Institute for Medical Research, Galilee Medical Center, Nahariya, Israel; 2Hematology Division, Bnai Zion Medical Center, Haifa, Israel; 3The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel; 4Institute of Hematology, Galilee Medical Center, Nahariya, Israel; 5Azrieli Faculty of Medicine, Bar Ilan University, Safed, Israel; 6Biochemistry Laboratory, Galilee Medical Center, Nahariya. Aim & Background: Therapeutic monoclonal antibodies used in Chronic lymphocytic leukemia (CLL) act through complement-mediated cytotoxicity and other mechanisms, and thus depend on the complement (C) availability and activity. Recently we showed abnormal Western analysis pattern of C5 in some CLL patients, associated with high basal levels of C activation markers and decreased activity of the classical pathway (CP). We hypothesized that the CP is constantly activated, and thus exhausted, in the patients with abnormal C5. The aim was to search for potential CP-activators as a mechanism of constant C activation in CLL. Methods: Blood samples were collected from 40 naïve CLL patients and 15 normal controls. C activity and IgM levels were measured using ELISA. C5 and C5a were studied by Western analysis. High molecular weight (HMW), low molecular weight (LMW), and albumin protein fractions were separated from all subjects using gel-filtration chromatography. The C activation potential of the fractions was studied. All data were related to the presence of abnormal C5. Results & Conclusion: The abnormal C5 was identified as an immunoglobulin complex with C5a (Ig-C5a). Baseline levels of C activation markers showed significant negative correlation with the classical, but not the alternative, pathway activity. C activation by HMW fraction from patients with abnormal C5 was significantly higher compared to all other fractions. The data indicated that IgG-aggregates, and not IgM, are the HMW C activating factor. In some CLL patients' serum, IgG-aggregates constantly trigger CP activation, resulting in release of activation products, such as C5a, and formation of Ig-C5a complex. Another result is CP exhaustion and the inability to exert activity that is comparable to normal subjects. The data provides a potential prognostic tool that may help in identifying a sub-group of CLL patients with impaired CP activity, and are likely to be less responsive to immunotherapy.
Boris	**Brant**	Dual function of Polycomb group proteins in T-helper (Th) cells Boris Brant, Yiftah Barsheshet, Moran Titelbaum, and Orly Avni. The Azrieli Faculty of Medicine, Bar-Ilan University, Safed. Aim & Background: The immune system distinguishes between self and non-self but also between different types of non-self, such as bacteria, viruses and worms. Th cells have a fundamental role in that challenge. Following antigen recognition, naive Th cells can differentiate toward one of the several effector lineages, each expressing a distinctive transcriptional profile of cytokines and other lineage specific genes, which eventually instruct the strategy of the immune response. In our lab, we are interested in understanding the mechanisms underlying differentiation and stimulation of these cells. My work is especially focused on exploring in a genome wide manner the binding activity of- and the epigenetic regulation by the polycomb group (PcG) proteins such as the Ezh2 in differentiated Th cells. More specifically, I investigate the involvement of RNA and transcription factors in the differential recruitment and function of PcG proteins. Methods: We performed ChIP-Seq, RNA-Seq and RIP-Seq in in vitro differentiated Th1 and Th2 cells derived from normal and Ezh2-conditionally deficient mice. Results& Conclusion: We demonstrated that Ezh2 has a dual function as a positive and a negative transcriptional regulator in Th cells; Ezh2 is required for robust expression of the signature transcriptional programs of differentiated Th1 and Th2 cells. We further revealed that Ezh2 possesses a differentiation- and stimulation-dependent binding activity in Th cells, and its binding is correlated with Th1 and Th2 specific transcription factor motifs. We found that Ezh2 is associated also with nascent RNA, and we currently studying potential functions underlying this activity. Altogether our results demonstrated the importance of Ezh2 in decision making during Th cell differentiation and stimulation. Cell: 0526412418 Lab: 0722644922 E-mail: boris.brant@gmail.com PhD student
Guy	**Journo**	Detection of lymphoma based on a novel herpes virus methylation assay Epstein-Barr virus (EBV) is the causative agent of infectious mononucleosis and has been associated with several human malignancies. Over 90% of adults are latently infected with EBV worldwide. In the majority of infected individuals, EBV infection is asymptomatic, but in certain cases it can lead to the development of several malignancies. EBV is associated with 30-50% of Hodgkin lymphoma (HL) cases, and over 90% of nasopharyngeal carcinoma (NPC) cases. Viral copy number in the blood as a diagnostic tool for the detection and monitoring of EBV-associated NPC is already in practice. The major challenge of viral copy number in the blood is to draw the threshold line to distinguish between healthy EBV-carriers and patients with EBV-associated malignancies, since it varies significantly between individuals. In latently infected cells, including tumor cells, the viral episomal genomes are CpG methylated, as opposed to the un-methylated virion associated viral DNA. We hypothesized that CpG methylated EBV genomes will be present preferentially in the blood of patients with EBV-associated malignancies. The use of paramagnetic beads linked to methyl CpG binding domain (MBD) protein allowed separation of virion from cell-derived EBV DNA. We followed CpG methylation of EBV sequences in cell-free (cf) DNA isolated from the plasma of patients with EBV-negative HL, EBV-positive HL and NPC. Methylated CpG DNA was the predominant form of EBV DNA in the plasma from patients with HL and NPC. Although lower levels of EBV DNA was detected in the plasma of patients with EBV-negative HL, strikingly only un-methylated EBV DNA could be detected in plasma from these patients. This study suggests that in addition to measuring EBV copy number in the plasma, CpG methylation analysis is a potential biomarker for EBV associated malignancies.
Anuj	**Ahuja**	Kaposi's sarcoma associated herpesvirus (KSHV, HHV-8) is a gamma herpesvirus associated with several human malignancies such as Kaposi's sarcoma (KS), primary effusion lymphoma (PEL) and multicentric castleman's disease (MCD). Human endogenous viral elements (EVE) or transposable elements (TEs) are mobile genomic sequences of viral origin that are able to change their position within the genome. TEs have been linked with a variety of disorders and malignancies, though the precise nature of their contribution to many of them has yet to be elucidated. The effect of KSHV on cellular gene expression was extensively studied, but our knowledge regarding the effect of KSHV on TEs is very limited. Here, to study the modulatory effect of KSHV on the expression of TEs, we have done transcriptome analysis of KSHV-associated primary effusion lymphoma (PEL) cells (BCBL1 and BC3), and following de-novo infected B-cell lymphoma (BJAB219) and primary endothelial cells (TIME219), by next-generation RNA sequencing (RNA-seq). We found that large numbers of TEs are differentially expressed in PEL cell lines and de-novo infected cells which includes LTR transposons, Long Interspersed Nuclear Elements (LINEs), Short Interspersed Nuclear Elements (SINEs), DNA transposons and DNA repeat elements. A vast number of TEs were up-regulated than down-regulated in PEL cell lines. The two PEL cell lines, BCBL1 and BC3, shared ~45% upregulated and ~76% downregulated TEs. In de-novo infected BJAB cells, we also detected differentially expressed TEs compared to un-infected controls, although to a lesser extent. The expressions of several TEs were validated by RT-qPCR. In conclusion, our results demonstrate that KSHV infection modulates the expression of many TEs, and in chronically infected PEL cells many more TEs are upregulated. Up-regulation of these mobile elements during chronic infection might contribute to enhanced transposition events and its impact on the human genome.

Moran	**Titelbaum**	The involvement of Ezh2 in chromatin organization in differentiating T helper Cells Moran Titelbaum, Boris Brant, Yiftah Barsheshet and Orly Avni. Faculty of Medicine Bar-Ilan University Aims & Background: Following their first interaction with the antigen, naive T-helper (Th; CD4+) cells can differentiate into distinct lineages of effector or regulatory cells characterized by specific profile of cytokines. These cytokines instruct eventually the strategy of the immune response. Previous studies in our lab showed that the polycomb group (PcG) proteins function in differentiated Th cells as both negative and positive transcriptional activators. The mechanisms underlying this dual function have not yet fully understood. Considering the known involvement of the PcG proteins in the regulation of chromatin structure and transcription on one hand and cytoplasmic actin polymerization on the other, we hypothesized that these epigenetic regulators harness the actin machinery for their nuclear functions. Methods: We used Chip assay, biochemical methods and confocal microscopy to assess the function of Ezh2 in differentiating Th1 and Th2 cells. Results & Conclusions: Here we demonstrate a peak in the presence of nuclear F-actin 24 hours following stimulation of naïve Th cells, in correlation with nuclear enlargement. F-actin and the regulators of actin polymerization machinery were partially co-localized with Ezh2 in the nucleus. The methyltransferase activity of Ezh2 was necessary for methylation of nuclear actin and for the F-actin-dependent nuclear chromatin reorganization in differentiating Th cells. All together our study suggests a model in which Ezh2 regulates chromatin structure by modulating actin polymerization. Moran Titelbaum Mobile phone: 050-4411154 Laboratory phone: 072-264-4921 Email: Moritltle@gmail.com M.Sc. student Presented as a Lecture
mor	**zigdon**	Social stress-responsive microbiota jeopardizes self-tolerance Mor Zigdon1, Michal Werbner 1, Yiftah Barsheshet 1,Rachel Haupt1, Iva Lukic1,Evan Elliot1, Omry Koren1, Orly Avni1 Bar-Ilan University Faculty of Medicine1 Aim & Background: Autoimmune diseases combine genetic predisposition and environmental cues. Stressful life events are considered a risk factor for autoimmune disorders, though the mechanisms are unclear. Stress-triggered neuroendocrine hormones lead to immune dysregulation, but considering the recently appreciated gut-brain-microbiome axis, and the well-known microbiome-immune interactions, we asked whether and how the brain-microbiome-immune triangle is involved in stress-promoting autoimmunity. More specifically, how the microbiome is affected in response to stress, the way it is affected, and why these changes cause susceptibility to autoimmune diseases and other disease such as depression. Methods: To answer these questions we used the chronic social defeat (SD) model in wild type C57BL/6 mice and Myelin Oligodendrocyte Glycoprotein (MOG)-specific T cell receptor transgenic (2D2) mice. To profile the microbial composition we performed 16S rRNA gene sequencing of feces, to assess depression we performed behavioral tests, and to investigate immune response we purified the mesenteric lymph nodes and exam the differentiation and function of T helper (CD4+) cells. Results& Conclusion: Together our results delineate a model in which the immune reaction to stress-responsive bacteria compromises tolerance to self, and therefore may increase the risk for autoimmune diseases and depression especially in susceptible individuals. מס' נייד: 052-5278464 מס' טלפון בעבודה: 072-2644922 כתובת דוא"ל: Morzigdon@gmail.com מעמד אקדמי של החוקר המציג: סטודנט מחקר
Yara	**Hamshawi**	Stabilizing the pancreatic α to β-cell transdifferentiation by inhibiting neogenic δ-cell formation and somatostatin secretion. Yara Hamshawi, Ron Piran. Bar-Ilan University Faculty of Medicine. Aim & Background: Both type 1 (T1D) and type 2 (T2D) diabetes are characterized by having an inadequate supply of functional β-cells over time, therefore β-cell regeneration could represent an unprecedented therapeutic approach for diabetes. Previous researches have shown that β-cells could arise by neogenesis from α-cells as a result of pancreatic injury consisting of caerulein plus alloxan which led to islet cell transdifferentiation, but the result was a large amount of δ-cells resulting from α- to β- and then to δ-cell transdifferentiation. In this study, we aim to use these findings to explore ways to stabilize the β-cell intermediate during the α- to β- to δ-cell transdifferentiation process by inhibiting neogenic δ-cells formation and somatostatin secretion. Methods: We hypothesize a model in which the β-cell intermediate could be stabilized and mature in order to become a diabetes treatment if the transition to δ-cell is being inhibited. To this end, we have obtained Somatostatin knockout (SstKO) mice. These mice underwent the alloxan plus caerulein treatments. Thus, by eliminating the δ-cell fate or preventing δ-cell maturation we hope to generate stable β-cells. Results & Conclusion: Alloxan-mediated ablation of β-cells in mice led to severe hyperglycemia in all groups. Surprisingly, female SstKO mice highlighted an advantageous phenotype compared to SstKO males, in which the females were practically cured from diabetes, providing evidence that there is an unexpected effect of the combination of somatostatin and sex hormones on glycemic levels. Somatostatin-secretion inhibitor drugs are already available. These results highlight the possibility to cure diabetes if somatostatin secretion is inhibited in diabetic patients.
Shilo	**Dadon**	Hyperbaric oxygen therapy For attenuation of neuropathic vulvodynial pain in a rat model Shilo Dadon1,3, Eilam Palzur1, Jacob Bornstein1,2,3 The Gynecology research laboratory, institute for medical research, Western Galilee Hospital, Nahariya1, Department of Obstetrics and Gynecology, Western Galilee Hospital, Nahariya2, The Azrieli Faculty of Medicine, Bar-Ilan University, Israel3 Background: Vulvodynia, defined as: "vulvar pain of at least 3 months' duration, without clear identifiable cause, which may have potential associated factors" is still an enigma, since the etiology and pathophysiology are still discussed. Unlike any other body pain, vulvodynia has a special significance, because it involves the intimate parts and as a result of the vulva being a sexually function organ. Recent works have described proliferation of intradermal and intraepithelial nerves, in women with vulvodynia. To further study the pathogenesis of the neuroproliferation, and possible treatments, a search for an animal model seemed warranted. Recent studies suggested the use of hyperbaric oxygen therapy (HBOT) as a treatment for Fibromyalgia which share common features with vulvodynia, yet no evidence have been proposed for its mechanism. Aims: Establishing a novel rat model of vulvodynia presenting behavioral (pain) and neuroproliferative alterations in order to study the effect of HBOT as a vulvodynial therapy. Methods: Female Sprague-Dawley rats will be used in this study. Initially, baseline pain threshold will be measured, each rat will examine compared to her initial values. In order to induce vulvodynia, the inflammatory factor Zymosan will be injected into the lower vulvar area. Rats will be classified to two groups zymosan Injected- vulvodynia and saline Injected-sham group. After three repetitions of this process, rats develop a chronic vulvar pain - Vulvodynia. Vulvar pain measurements will be obtained by "Electronic von Frey" device. Rats will be followed for a total of 11 weeks. Neuro-proliferation will be measured by the density of unmyelinated sensory C fibers, peptidergic fibers and sympathetic innervation. 15 consecutive HBOT will be administrated at 2.5 ATA for 90' 24h following vulvodynia. Results & Conclusions: After repeated exposures to Zymosan, rats developed persistent vulvar pain. מס' נייד: 0549437286 מס' טלפון בעבודה: 04-9107538 כתובת דוא"ל: ShiloD@gmc.gov.il מעמד אקדמי: סטודנט מחקר
Itai	**Yechezkel**	Structural and Functional Investigation of the Nucleocapsid (N) protein of the Fig Mosaic Virus (FMV). Itai G. Yechezkel1, Joel Alter1, Moshe A. Dessau1 1The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel The Fig Mosaic Virus (FMV) infects a mass of agricultural produce, from figs to mulberries, and is the known cause of Fig Mosaic Disease (FMD). FMD not only affects the foliage of these plants, it also causes the production of smaller and mottled fruits. Coupled with the fact that global hunger is on the rise – this year being an estimated 124 million people facing crisis food insecurity (Global Report on Food Crises 2018) it is becoming increasingly important to protect all food sources. FMV is part of the Fimoviridae family and shares multiple similar proteins, including the Nucleocapsid (N) protein. N proteins of a variety of viruses are known to encapsulate the viral RNA and have a handful of functions for viral viability. Whilst N protein structures have been solved for various other viruses, there are numerous differences between these N proteins and therefore uncovering the tertiary structure of FMV N will contribute towards an understanding of its specific function in FMV. We hypothesise that the N protein binds to RNA in an oligomeric fashion. We expressed and purified multiple constructs of FMV N in an E. coli bacterial vector system and set up a broad range of crystal screens, that resulted in numerous hits displaying various microcrystals morphologies. We use Mass Spectroscopy and N-terminal sequencing to gain further understanding to the constructs we made and we hope to optimise the conditions for crystal growth to allow us to use X-ray crystallographic techniques to solve a three-dimensional structure helping to unravel the mechanisms by which FMV N protein encapsulates the RNA genome of FMV, and by that will reveal new structural, evolutionary and functional insights on this new and unique plant virus. Keywords; Fig Mosaic Virus; Fig Mosaic Disease; Viral viability; Nucleocapsid; X-ray Crystallography Contact information Itai G. Yechezkel, M.Sc. Student, The laboratory of Structural Biology of Infectious Diseases, Moshe Dessau PhD. Azrieli Faculty of Medicine in the Galilee, Bar-Ilan University, 8 Henrietta Szold St. Safed, 1311502, Israel. Tel: +972-50-266-3838 E-mail: itaigershon.yechezkel@live.biu.ac.il Office: B104

sagi	**hamo**	P8 of High Plains Wheat Mosaic Virus Structure and Function Sagi Hamo, Joel Alter and Moshe Dessau The Azrieli Faculty of Medicine, Bar Ilan University Food security is a growing concern in the western world as well as in developing countries. High Plains wheat mosaic virus (HPWMoV) is a member of the newly discovered Emaravirus genus, transmitted by the wheat curl mite (Aceria tosichella Keifer). It is the causative agent of the High Plains disease in wheat, maize and other cereal grains, resulting in substantial economic burden. RNA silencing is an important mechanism by which organisms fight against viral infections through transcriptional and post-transcriptional gene silencing. To bypass this mechanism, viruses have developed viral suppressors of RNA silencing that reduce or inhibit this defense pathway. These viral suppressors vary in terms of structure and effect, and their diversity suggests that they may function by different unknown mechanisms. HPWMoV is a negative sense single stranded RNA virus with an octa-partite genome comprising segments S1 – S8, that encode proteins P1-P8 respectively. The P8 protein was found to be a suppressor of RNA silencing that shows no significant sequence identity/similarity to any other protein. Structural and biochemical information on RNA silencing suppressor proteins is scarce, particularly on those encoded by Emaraviruses. In this study, we aim to determine the crystal structure of HPWMoV encoded RNA silencing suppressor protein (P8), using X-Ray Crystallography, and elucidate its molecular mechanism of action. In our preliminary results, we show the expression and purification of P8 to high degree of homogeneity. We discovered that P8 oligomerizes in solution. We verified our findings using both cross-linking methods and Mass spectroscopy. Finally, we were able to crystallized P8 and obtain diffracting crystals suitable for X-ray studies. Once the structure of P8 will be in hand, we will biochemically investigate the underlying mechanism of siRNA suppression during HPWMoV infection. Phone number- 0528666366 Email – sagi.hamo@gmail.com Academic Status: graduate research student
Zohar	**Hamo**	Aim & Background: This research focuses on characterization of the host immune response to Clostridium difficile infection (CDI) in order to identify potential immunological biomarkers for determining CDI severity. It is important to recognize patients with severe disease due to high risk of complications and death. Methods: Fifty-four patients diagnosed with C. difficile infection were enrolled in the study. Serum samples were obtained within a median time of 24-48 hours after the laboratory confirmation for presence of C. difficile. Cytokine and chemokine concentrations were measured using the MILLIPLEX®MAP kit, based on fluorescent-coded magnetic beads. Demographic, clinical, and prognostic data concerning the patients were retrospectively collected from medical records. The illness severity score was determined according to "Score indices for Clostridium difficile infection severity". Results& Conclusion: Thirty-eight (70%) of the patients had a mild disease and 16 (29.8%) of the patients had a moderate disease. Significant correlation was found between a moderate disease and the following seven cytokines-GM-CSF ($p = 0.01$), IL-1β ($p = 0.004$), IL-8 ($p = 0.009$), IL-12p70 ($p = 0.01$), INF-α ($p = 0.02$), IL-15 ($p = 0.001$), and IL-2 ($p = 0.003$). Additionally, the ratio of IL-12p70/IL-5, IL-12p70/IL-10, and IL-12p7/IL-17A was significantly higher ($p < 0.05$) in the moderate disease group, indicating increased Th1 response in more severe cases of CDI. The cytokines that we have found to correlate with disease severity may serve as biomarkers for early prediction of CDI severity. Measurement of these biomarkers is easy and quick. It is important to recognize patients with severe disease due to the high risk of complications and death. An earlier assessment of illness severity will contribute to a better adjustment of medical treatment, including monitoring and follow-up.
Nehora	**Amar**	Examining the use of Debates in Medical Ethics Teaching of Medical Students Nehora Amar, Dr. Miriam (Miri) Bentwich Bar-ilan University Faculty of Medicine ABSTRACT AIM & BACKGROUND: Medical ethics concerns the moral dilemmas faced by physicians. It is recommended that medical ethics would be taught in small groups since they supposedly increase the students' critical thinking. "Debate" is a pedagogical tool that is taken to enhance critical thinking, while bolstering enthusiasm among its participants regarding the discussed subjects. This study examines whether the use of the debate tool, within small-groups learning of medical ethics among medical students, strengthens their engagement with this subject and enhances their critical thinking. METHODS: An intervention study using a mixed-methods research approach. Videotaped small-groups learning sessions in medical ethics were used, along with questionnaires administered at the beginning and end of the year regarding students' attitudes toward small-groups learning of medical ethics. 68 (90%) first-year students completed the questionnaires, out of which, 44 students also participated in the qualitative videotaped sessions. Four groups of students were compared: no intervention at all, no intervention and videotaped, partial intervention, full intervention (use of the debate tool). Statistical analysis along with microanalysis based on Kamin's critical thinking model were used to analyze the data. RESULTS & CONCLUSION: In the quantitative part the "full intervention" group showed the highest number of attitudes changed for the better (5/9) and lowest number of attitudes changed for the worse (2/9). In comparison, the "partial intervention" and "videotaped without intervention" groups exhibited only a change for the worse in all attitudes. The debate tool encouraged students to increase their participation in the discussions, however, this increase did not reflect an enhancement in the overall critical thinking they expressed. The gaps found between the attitudes of students and the critical thinking they demonstrated raise a question regarding the extent to which students' subjective perceptions should be trusted in evaluating the success of medical ethics teaching in small groups. מס' נייד: 052-8979860 כתובת דוא"ל:nehoramar@gmail.com מעמד אקדמי של החוקר המציג: סטודנטית לתואר שלישי העדפה להרצאה*
Tom	**Domovitz**	Using inhibitors to revert the epigenetic and oncogenic signature induced by Hepatitis C virus infection in liver cells after virus eradication. Tom Domovitz1, Shira Perez1,2, Ateret Davidovitz1, Tomer Meirson3, Assy Nimer4, Salomon M Stemmer5, Izhak Haviv2 and Meital Gal Tanamy1. 1Molecular Virology Lab, Azrieli Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel. 2Cancer Personalized Medicine and Diagnostic Genomics Lab, Azrieli Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel. 3Cell Migration and Invasion Laboratory, Azrieli Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel. 4Internal Medicine Department A, Western Galilee Medical Center, Naharyia, and Azrieli Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel. 5Davidoff Center, Rabin Medical Center, Beilinson Campus, Petach Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. Abstract: Background: Hepatitis C virus (HCV) is a major public health problem. It infects about 3% of the world's population and it is estimated that 30% of patients eventually develop liver diseases such as Hepatocellular carcinoma (HCC). HCC is the fifth most common cancer in men and the seventh in women worldwide with poor prognosis mainly because high rate of tumor recurrence or metastasis. The therapy against HCV infection was for many years Interferon (IFN), with side effects and low sustained virological response (SVR), about 50%. The current therapy is direct acting antiviral (DAAs) that results in high SVR rates (>90%), shorter treatment duration (8 or 12 weeks) compared to IFN and high safety. However, evidences show that DAAs treatment reduces but not eliminate HCC development. Aim: to evaluate the epigenetic signature induces by HCV infection and remain following DAAs treatment and to explore whether following IFN or specific inhibitors treatment the signature is revers. Results: We have demonstrated in our lab that HCV induces epigenetic alteration in histone modifications following HCV infection that correlated with changes in gene expression. These epigenetic alterations remain persistent as epigenetic signature following virus eradication with DAAs- a "hit and run" mechanism. The signature caused by HCV infection associated with oncogenesis and invasive phenotype of the host cell. In contrast, we found that following IFN treatment, there is a reversion of the epigenetic signature. Importantly, we found that treatment with specific inhibitors (HAT, HDAC, EGFR inhibitors) following DAAs reduce the invasive and metastasis features by reverting epigenetic alterations induced by HCV. These results were also observed in mice model. Significance: This study has important implications for understanding the oncogenic signature cause by HCV infection and remains following virus eradication by DAAs and identifying treatment that not only cure HCV but also revers its oncogenic effects. Tom Domovitz 050-9206633 tomdo17@gmail.com PhD student
Wael	**Nasser**	Wael Nasser, Avi On, Ehsan Na, Said Abozed, Boshra N, Haitham M, Mhemad S, Haia Nasser. BARUCH PADEH Medical Center, Department of Pediatric Nephrology, Poriya, Israel.Affiliated to the Faculty of Medicine in the Galilee - Bar Ilan University Introduction: Henoch-Schonlein-purpura is a systemic vasculitis, of small vessels, resulting in skin, joint, gastrointestinal and renal involvement. The pathogenesis of HSP t is postulated that an unknown chronic antigenic stimulus, In children the prognosis is good, as HSP typically resolves rapidly and without complication. Helicobacter pylori is of the most common bacterial infections may cause some extra intestinal manifestations some of which are dermatological conditions, including Henoch-Schönlein purpura. Case Report: A previously healthy 10year-child was admitted to our department , because of-week history of abdominal pain, and purpura on his lower extensor extremities. Physical examination revealed purpuric papules, on the legs, thighs, buttocks,. On admission, his temperature was 37.5°C, , and blood pressure 110/60 mmHg. showed a white blood cell count of 18200/mm3 . The hemoglobin concentration was 11.8g/dL, the platelet count was 400000, while normal results for serum creatinine level Urinalysis revealed microscopic hematuria and proteinuria

rachel	**haupt**	A role for the gut microbiome in polycystic ovary syndrome? Rachel Haupt1, Meital Nuriel-Ohayon1, Izhar Ben-Shlomo MD 2, Oren Ziv1, Omry Koren1 1The Azrieli Faculty of Medicine, Bar Ilan University, Safed, Israel. 2Department of Obstetrics and Gynecology, Baruch Padeh Hospital, Poriya Background: Polycystic ovary syndrome (PCOS) is the leading cause of infertility and affects up to 10% of reproductive age women. While PCOS has been extensively studied in the last two decades, the precise mechanisms leading to the clinical complex of PCOS have remained enigmatic to a large extent. It has been shown that diet and physical activity improve the state of women with PCOS and reduce the metabolic syndrome like characteristics and this is often the treatment. Studies in the new field of microbiome research focus on the composition of overall microorganisms in our body and their impacts on our health. Changes in the composition of the gut microbiota (dysbiosis) have been linked with different health states such as pregnancy, obesity, IBD, metabolic syndrome, etc. and have been associated with low grade inflammation and reduced insulin sensitivity. Since it has been shown that the microbiome is affected by both diet and host hormones and in return affects our health status, we believe there is a strong link between the gut microbiome composition, diet, and PCOS. Methods: Our methods include dietary intervention, collection of fecal samples, DNA extraction and PCR amplification, sequencing and identification of 16S rRNA sequences, statistical analyses, clinical measures, microbiota transfer experiments into germ-free mice, and metabolomics. Results: We have tested and analyzed the microbiota of a sample group of lean PCOS subjects vs. controls, and found distinct differences between groups. Metabolomic analysis did not result in significant differences and more samples should be tested. Conclusions: Women with PCOS have differences in composition of gut microbiota. Understanding the meaning of these changes helps us gain insights into the mechanism of PCOS. מס' נייד: 054-3113566 מס' טלפון בעבודה: 072-2644954 כתובת דוא"ל: rachelhaupt05@gmail.com מעמד אקדמי של החוקר המציג: סטודנט מחקר
Dana	**Binyamin**	Aim & Background: Pregnancy may affect the disease course of inflammatory bowel disease (IBD). Both pregnancy and IBD are associated with altered immunology and intestinal microbiology. However, to what extent immunological and microbial profiles are affected by pregnancy in IBD patients remains unclear. Methods: Fecal samples were collected from 46 IBD patients [31 Crohn's disease (CD), 15 Ulcerative colitis (UC)] and 224 healthy controls during 1st, 2nd and 3rd trimester of pregnancy, and pre-pregnancy and postpartum for IBD patients. Bacterial DNA was extracted and the V4 region of 16S rRNA genes was amplified and sequenced using the Illumina MiSeq platform. Microbiome analysis was performed using QIIME2. Results & Conclusion: Pro-inflammatory serum cytokine levels in IBD patients decrease significantly upon conception. Beta diversity analysis and richness measurement did not reveal any significant differences relating to the different pregnancy time points. Microbiome reflects disease type, we could differentiate between CD and UC solely based on the microbiomes with an AUC of 0.75. The microbiota of IBD patients was more similar to one another than that of healthy controls. Microbial diversity in pregnant IBD patients was reduced compared to that in healthy women in the 1st trimester. Pregnancy reduces immunological parameters of inflammation in IBD patients. It seems that the immunological state of IBD patients improves upon pregnancy, while the overall pre-existing altered microbial composition does not appear to be worsened. Intestinal microbiome diversity of IBD patients normalises during middle and late pregnancy. We thus conclude that pregnancy is safe, and even potentially beneficial for IBD patients. מספר טלפון נייד: 050-7343021 כתובת מייל: dsimoni925@gmail.com מעמד אקדמי של החוקר המציג: סטודנט מחקר ברצוני להציג את העבודה כפוסטר
Hagay	**Ladany**	Novel variants in the NARS2 gene causing combined oxidative phosphorylation deficiency 24. Hagay Ladany1,2, Limor Kalfon, PhD2, Ben Harouch S, MD1,2 ,Mandel H, MD2 and Tzipora Falik-Zaccai, MD1,2 The Azrieli Faculty of Medicine, Bar Ilan University, Safed1. Institute of human genetics, Galilee Medical Center, Nahariya2. Aim & Background: NARS2 is a member of a class of enzymes that charge tRNAs with their cognate amino acid called aminoacyl tRNA synthetase. NARS2 encodes the mitochondrial asparaginyl tRNA synthetase. To date, 15 patients with combined oxidative phosphorylation deficiency 24 (OMIM #612803) carrying eight different bi-allelic variants in NARS2 were reported. These patients with variants in NARS2 display wide range of pathologies including myopathy, intellectual disability, hearing impairment, epilepsy, cerebral atrophy, renal disease, and basal ganglia lesions. We have identified a novel homozygous missense variant (c.434T>G) in the NARS2 gene in two siblings who share a similar phenotype. Another homozygous missense variant (c.500A>G) in NARS2 was found in another patient. In both cases the variants were predicted as "disease causing" in-silico. The patients in both families display seizures, hypotonia, global developmental delay, and recessive inheritance pattern. We aim to study the causative effect of these variants on the expression and function of NARS2 and to correlate the variants in this gene with the patients' phenotype. Methods: Skin derived fibroblasts were used for evaluating the mRNA and protein levels by real-time PCR and Western blot respectively. Protein cellular localization was attained by Immunofluorescence staining. Results& Conclusion: The mRNA levels in both cases were found in the range of healthy controls, while the protein expression revealed a ~45% reduction in the patients' fibroblasts. NARS2 in both the wild-type and the variants was co-localized to the mitochondria, but the signal was more disperse in the cytosol in patient's cells. Further studies are required to evaluate the variants effect on the protein function, to understand the mechanism connecting NARS2 with the phenotypic manifestation of the disease. כתובת דוא"ל0545689811 מספר נייד: :hagayladany@gmail.com מעמד אקדמי: סטודנט מחקר - ברצוני להציג פוסטר
Zaher	**Armaly**	Changes in glucose 6-phosphate dehydrogenase in diabetic nephropathy and hemodialysis: Correlation with Haptoglobin Genotype. Zaher Armaly, Safa Kinaneh, Adel Jabbour, and Nayef Habasshi. Department of Nephrology, Nazareth Hospital-EMMS, Nazareth and the Azrieli Faculty of Medicine-Bar Ilan University, Zafed, Israel. Background: Glucose 6-phosphate dehydrogenase (G6PD), the rate-limiting enzyme of the pentose phosphate pathway, is the main source of the essential cellular reductant, NADPH. The latter, is of great importance for tissues actively engaged in biosynthesis of fatty acids. In the kidney, G6PD is important for normal renal physiology, where it regulates tubular salt handling, blood flow, and protects the cells against oxidative damage. Although experimental studies have demonstrated changes in G6PD in experimental diabetic nephropathy (DN), clinical studies are needed to determine whether similar changes occur in diabetic patients and subjects on hemodialysis (HD). Aims: To determine the erythrocyte G6PD activity level in patients with DN and subjects with ESRD on maintenance HD, and to determine the impact of haptoglobin on G6PD activity. Methods: The current study included 32 patients with DN and 24 matched healthy controls; 121 HD patients and 31 matched healthy controls. Single blood sample was drawn from the healthy subjects, patients with DN and HD. G6PD activity, hemoglobin, Haptoglobin phenotype, advanced oxidative protein products (AOPP), and Thiobarbituric acid reactive substances (TBARS) were determined. Results: Erythrocyte G6PD activity of diabetic patients was 9.0±0.5 U/g Hb as compared with the enzyme activity in healthy controls 8.3±0.5 U/g Hb (P=0.299). The activity magnitude of G6PD in HD patients was higher than that obtained in their healthy controls (10.0±0.6 U/g vs 8.5±0.9 U/g Hb U/g Hb, P=0.307). The AOPP levels were significantly higher in HD (211.0±6.2 µM, P=0.015) as compared with their controls (180.4±4.7 µM). In contrast, AOPP was not different between DN (180.0±4.2 µM) and their healthy controls (187.6±2.9 µM). Similarly, TBARS levels were elevated in HD (7.1+0.3 nmol MDA/ml) vs. 4.1±0.2 nmol MDA/ml in their controls (P<0.001). No differences in TBARS were found between DN and healthy controls. 12.5% of patients with DN were Hp 1-1, 43.8% Hp 2-1, and 43.7% Hp 2-2. In their control group, the Hp phenotype was: 8.3% Hp1-1, 50.0% Hp 2-1, and 41.7% Hp 2-2. Distribution of Hp in HD patients was: 12.4% Hp1-1, 48.8% Hp 2-1, and 38.8% Hp 2-2. In their health controls, the Hp phenotype was: 12.9% 1-1, 38.7% Hp 2-1, and 48.4% Hp 2-2. Interesting, the increases in G6PD, TBARS and AOPP were independent of Hp phenotype. Conclusions: This study demonstrates that HD, but not DN patients exhibited higher levels of TBARS and AOPP as compared with healthy subjects, independently to Hp phenotype. Noteworthy, HD and DN were characterized by slight increase in G6PD activity. מס' נייד: 0546693498 מס' טלפון בעבודה: 04-6028888 כתובת דואר אלקטרוני : zaherarmaly@nazhosp.com מעמד אקדמי של החוקר המציג: חוקר ראשי
Hadar	**Mor**	Helminth-Based Product and the Microbiome of Mice with Lupus The hygiene hypothesis claims that the lack of exposure to microorganisms in developed countries correlates with a rise in the incidence of autoimmune diseases. It was also found that helminths are able to modulate the immune response in hosts in order to survive. Consequently, several successful trials using helminths as a treatment for autoimmune patients have been reported. The helminth derivative, phosphorylcholine (PC), was discovered as an immunomodulatory molecule. We examined the effect of TPC in lupus-prone mice when starting the administration after disease onset. TPC treatment altered the gut composition in the mice with active lupus, followed by an increased level of anti-inflammatory interleukin 10 (IL-10), decreased levels of pro-inflammatory mediators, and expansion of the T regulatory cell population. The major effects of TPC treatment on the gut microbiome included decreased abundances of Akkermansia and increased abundance of several genera, including Bifidobacterium, Turicibacter, unclassified Mogibacteriaceae, unclassified Clostridiaceae, Adlercreutzia, Allobaculum, and Anaeroplasma. Importantly, we found that TPC treatment altered the mouse gut microbiome composition, as the increase of Bifidobacterium, in correlation with a significant decrease in protein levels in the urine and improved disease parameters. Bifidobacterium is a widely used probiotic with proven positive effects in numerous disease states. These effects are attributed to short-chain fatty acid (SCFA) production, especially lactate production, which is further metabolized to butyrate. This fits our finding that the butyrate metabolism pathway is over-expressed in TPC-treated than in PBS-treated mice. Butyrate plays protective roles in maintaining the mucus layer of the intestinal barrier. Altogether, our results present the microbiome as an important and novel factor that may mediate TPC treatment, immune changes, and improvement in glomerulonephritis parameters. Since SLE is associated with microbial dysbiosis, it is not surprising that an effective SLE treatment positively affects the microbiome by promoting beneficial populations.
Munai	**Abu_Rahme**	An innovative ultrasound technique for early detecting of renal fibrosis: Superb Micro-Vascular imaging as a reference standard Munai Abu-Rahme, Suheil Artoul, Safa Kinaneh, Nayef Habasshi and Zaher Armaly. Department of Nephrology and Radiology, Nazareth Hospital-EMMS, Nazareth and the Azrieli Faculty of Medicine-Bar Ilan University, Zafed, Israel. Background: Superb microvascular imaging (SMI) (Toshiba Medical Systems, Tokyo, Japan), is an innovative ultrasound image processing technique that shows greater detail and better visualization of small branching vessels by using a unique algorithm that offer high frame rates, less clutter, and fewer tissue motion artifact that were not previously possible without the use of contrast agent. We assume that SMI will provide sufficient information regarding the severity of chronic kidney disease (CKD) and reflecting the fibrotic changes. Aims: To assess the early detecting of renal fibrosis capabilities of SMI imaging in comparison to the reference standard renal biopsy, in order to determine the usefulness of this approach in the early diagnosis of kidney fibrosis even without major changes in SCr. Methods: The SMI was performed in patients with CKD stage 2-4 where some of them underwent biopsy proven chronic renal dysfunction and fibrosis as part of the diagnosis and therapeutic judgment as needed. In addition, biochemical tests were performed in order to obtain the serum parameters of kidney function (BUN, Serum Creatinine), a urine collection test for the assessment of proteinuria, and estimation of GFR by MDRD formula in 45 patients with CKD of various severity and healthy controls (n=17). In addition, all patients underwent SMI US imaging, where vascularity is expressed SMI index (low index reflects low vascularity/fibrosis and vice versa). Results: As expected, SMI index was significantly lower in CKD patients as compared with healthy control (72.2±3.1 Vs 49.1±2.6 %, P<0.001). Interestingly, strong correlation between the SMI index and eGFR was found among the CKD patients (r=0.595, P<0.001). Similarly, a keen inverse correlation between the SCr and SMI index of the diseased subjects. Among those who underwent renal biopsy, SMI index reflects the histological alterations as well as CKD staging. Conclusions: This study demonstrates that in patients with CKD of various stages, SMI imaging may be utilized as a simple and practical method for evaluation of the chronic renal morphological changes and for the differentiation between CKD grades. מס' נייד: 0502641868 מס' טלפון בעבודה: 04-6028888 כתובת דוא"ל: munai.abu@gmail.com מעמד אקדמי של החוקר המציג: סטודנטית לרפואה

Wisal	**Sawaed**	Combination Drug Therapy for Type-1 Diabetes in MICE Wisal Sawaed, Assaf Malka and Ron Piran Bar Ilan University faculty of Medicine Aim & Background: Type 1 diabetes (T1D) is an autoimmune disease characterized by insulitis, a leukocytes infiltration of the pancreatic islets, and β-cell loss. Thus, an effective therapy may require β-cell restoration and immune suppression. Currently, there is no treatment that can achieve both goals efficiently. Previously, it has been shown that each of γ-Aminobutyric acid (GABA), dipeptidyl peptidase IV inhibitors (DPP-4i) such as Sitagliptin, or proton pump inhibitor (PPI) drugs like Omeprazole has beneficial effects in various diabetic mouse models. Therefore, we propose that their combined administration can bring forth an additive therapeutic effect. Methods: We tested this hypothesis in non-obese diabetic (NOD) mice. Diabetic male and female mice were paired and randomly assigned into two groups: non-treatment diabetic control or GABA, Sitagliptin, and Omeprazole, triple treatment. The drugs administered by oral gavage daily. Results& Conclusion: Combined use of GABA, Sitagliptin and Omeprazole administration decreased blood glucose levels and improved the glucose excursion rate as compared to control group. Immunohistochemical analyses revealed that combined therapy managed to maintain β-cell mass. We also noticed that GABA, Sitagliptin, and Omeprazole administration have a survival advantage over matched controls at the beginning of the treatment.
Sarina	**Shabso**	The role of the Dermal Papilla (DP) in regulating the hair cycle clock Biological clocks are required to coordinate and synchronize multiple events within complex biological processes. The hair follicle possesses such biological clock that dictates the periodicity of the hair cycle. Hair follicles undergo cycles of growth (anagen), destruction (catagen), quiescence (telogen) and regeneration. Depending on the strain, anagen in mice lasts for around 16 days and the transition from anagen through catagen to telogen requires approximately 2 days to complete. While these time scales persist in every cycle, the length of telogen varies from 2 days to few months, depending on the cycle and gender. Numerous models and theories have been proposed during the last five decades to explain the cyclic nature of the hair follicle. Yet, the components and the molecular mechanisms that underlie the hair cycle clock remain completely unknown. Previous studies have shown that Fgf signaling may play an important role in regulating the hair cycle clock. Fgf5 knockout mice display abnormally long hairs as a result of prolonged anagen, while Fgf5 administration during mid anagen results in premature induction of catagen. In addition to Fgf signaling, canonical Wnt signaling pathway may also play a role in regulating the hair cycle clock. Ablation of b-catenin in the matrix or DP during mid anagen results in premature induction of catagen. We propose that some key components of the hair cycle clock reside in the DP, and both Fgf and canonical Wnt signaling pathways in the DP regulate the expression and activity of these components. 0506304679 מס נייד sarinashabso@gmail.com PhD student
Nitzan	**Biran**	The cytoplasmic side of the nuclear pore complex (NPC) is characterized by distinct architectural features, such as the cytoplasmic ring and filaments, and by a subset of asymmetrically localized nucleoporins. Nup214, localized to the base of the cytoplasmic filaments, plays a key role in nuclear protein export and interacts with the essential DEAD box protein Dbp5, which is critical for mRNA export. Here we report biallelic missense and frameshift pathogenic variants in the gene encoding human nucleoporin NUP214 causing acute febrile encephalopathy. Clinical symptoms include neurodevelopmental regression, seizures, myoclonic jerks, progressive microcephaly and cerebellar atrophy. Although the major affected tissues remain out of reach, we used patient-derived primary skin fibroblasts to determine a set of distinct phenotypic changes at the single cell level. NUP214 and NUP88 protein levels were reduced in patient-derived primary skin fibroblasts, while the total number and density of nuclear pore complexes remained normal. Nuclear transport assays exhibited defects in the classical protein import and mRNA export pathways in patient cells. Direct surface imaging of fibroblast nuclei by scanning electron microscopy revealed a large increase in the presence of central particles (known as "plugs") in the nuclear pore channels of patient cells. This observation suggests that large transport cargoes may be delayed in passage through the nuclear pore channel, affecting its selective barrier function. Exposure of patient-derived fibroblasts to heat shock resulted in a marked delay in their stress response, followed by a surge in apoptotic cell death. This suggests a mechanistic link between decreased cell survival in cell culture and severe fever-induced brain damage in patients. Our study provides the first report of a change observed by direct imaging at the single nuclear pore level being linked to a human disease. Cellphone number: 052-8328892 E-mail: niznaz3@gmail.com Ph.D. student
Fadia	**Zagairy**	Nuclear envelopathies comprise a heterogeneous group of diseases caused by mutations in genes encoding nuclear envelope proteins. Lamina-associated polypeptide1 (LAP1) is a ubiquitously expressed protein located in the inner nuclear membrane. Mutations in LAP1 have been reported to result in two discrete phenotypes of muscular dystrophy and progressive dystonia with cerebellar atrophy. Here we report 7 patients of similar ethnic background who are homozygous for a nonsense mutation in the TOR1AIP1 gene, resulting in the loss of both protein isoforms LAP1B and LAP1C. The patients present at birth with severe progressive neurological impairment, bilateral cataract, growth retardation and early lethality. Patient-derived primary skin fibroblasts exhibit changes in nuclear envelope morphology including reduced anti-lamin A/C nuclear rim staining intensity in addition to the emergence of large channels containing trapped cytoplasmic organelles and traversing the nucleus. The patient fibroblasts also displayed functional cellular impairment demonstrated by decreased and inefficient directional as well as random cell motility. Transduction with LAP1-coding constructs succeeded in rescuing multiple cellular phenotypes and hinted at a differential effect of the two protein isoforms. Our study describes the complete absence of both major human LAP1 isoforms, underscoring their crucial role in early development and organogenesis. LAP1-associated defects may thus comprise a broad clinical spectrum, varying in severity and organ involvement, depending on the availability of both isoforms in the nuclear envelope throughout life.
Inbal	**Mazal-Yeger**	The effect of PAI-1 inhibitor treatment on apoptosis pathway in kidney of rat model of preeclampsia Inbal Mazal-Yeger1,3, Eilam Palzur1, Marwan Odeh1,2,3, Jacob Bornstein1,2,3 The Gynecology research laboratory of the institute for medical research1, Department of Obstetrics and Gynecology, Galilee Medical Center, Nahariya2, The Azrieli Faculty of Medicine, Bar-Ilan University, Israel3 Aim & Background: Preeclampsia is a specific syndrome that occurs in pregnancy and characterized by development of hypertension and proteinuria. It may damage the kidneys, liver, brain and clotting system and leads to eclamptic seizures, placental abruption. Without proper treatment, these characteristics cause to morbidity and mortality of the mother and fetus. Kidney involvement is very frequent. Injury to maternal endothelium is most clearly visualized in the kidney, which reveals the characteristic pathological changes of preeclampsia. The ultrastructural changes in renal glomeruli, including generalized swelling of the endothelial cells and loss of the capillary space, deposits of fibrin within and under the endothelial cells, with modest damage to the podocyte foot processes. PAI-1 inhibitor (PAI-1-DP) is a new peptide that binds to the regulatory region of tPA, but does not affected on the fibrinolysis activity. The aim of this study is to examine the effect of PAI-1-DP on apoptosis pathway in glomeruli cells in kidneys of preeclampsia model. Methods: Pregnant rats were treated with L-NAME causing hypertension and proteinuria, and then with PAI-1-DP. The control group was pregnant rats did not develop signs of preeclampsia. Blood pressure and protein in urine were measured. At day 20 of pregnancy, the rats were sacrificed and their kidneys were harvested for Immunohistochemistry staining with specific antibody to HIF1-alpha, Endoglin(CD105), Cleavage Caspase 3. In addition, MAPK protein family, was examined in a kidney lysate, using multiplex array. Results& Conclusion: Treatment with PAI-1-DP reduced the levels of protein in urine, HIF1-alpha, Cleavage Caspase 3, phospho JNK and increased the levels of Endoglin. From these results, it appears that PAI-1-DP prevented hypoxia and apoptosis of podocyte cells and glomerulus endothelial cells damage. 0507977605 :מס' נייד 04-9107538 :מס' טלפון בעבודה mazall014@gmail.com :כתובת דוא"ל מעמד אקדמי של החוקר המציג: סטודנט מחקר .מעוניינת להציג את העבודה כהרצאה
Chen	**Shochat**	Zebrafish Crispants as a screening tool for bone GWAS candidate genes Chen Shochat Carvalho, and David Karasik Azrieli Faculty of Medicine, Bar Ilan University, Safed, Israel Objective: In recent years, genome-wide association studies (GWAS) have revolutionized the understanding of the genetic architecture of common, complex diseases such as osteoporosis. This approach reveals hundreds of candidate genes which may be involved in the mechanisms of disease. What is needed for post-GWAS exploration is a fast and reliable screen of candidate genes. One of the genes that came up in GWAS for bone mineral density (BMD) was LRP5, a co-receptor in the Wnt-signaling pathway, which controls differentiation and proliferation of osteoblasts. In humans, various LRP5 mutations were shown to affect bone mass. Our lab established a Zebrafish osteoporosis model by lrp5 knockout (KO) and showed it had reduced notochord ossification at 7 days post fertilization (dpf) and lower BMD at adulthood. Here we aimed to evaluate a contribution to candidate gene screening strategy, based on zebrafish "crispants" (CRISPR-derived F0 mutants) of lrp5, a well-established bone effecting gene. Methods: CRISPR-Cas9 was used to create lrp5 crispants: one cell stage zebrafish were injected with Cas9 protein and lrp5 gRNA. At 7 dpf crispants were stained with alizarin red. Notochord ossification in each crispant was analyzed using Fiji software, and the correlation between ossified area of the notochord and genotype (the latter is expected to be mosaic) was established. Results: We found that lrp5 crispants had the same notochord ossification level as injected control and WT fish (p-value>0.05) at 7dpf. Summary and Conclusions: In this study, we show that, unlike stable KO line, lrp5 crispants do not demonstrate less ossification of the notochord compared to controls. These results are in accordance with the fact that crispants are mosaic- carrying various mutation which may have different effect on ossification. In addition, according sequence analysis, most of the crispants still possessed the intact WT allele, allowing the translation of WT lrp5 protein. Keywords: lrp5, bone development, CRISPR-Cas9, BMD, GWAS
Yasmin Ghantous	**Ghantous**	Data pre-processing. Analyzed datasets were retrieved from Gene Expression Omnibus (GEO) and The Cancer Genome Atlas (TCGA) databases. Phenotypic information was manually reviewed and only samples from oral cavity, stage T1 or T2, HPV negative, primary human oral squamous cell carcinoma were considered. Normalized gene expression were processed using the ComBat algorithm for removing batch effects [PMID:16632515]. Classifier development. Our final goal was to develop a classifier to predict node status in clinical settings using RT-PCR. Hence, we normalized our training data accordingly, using the GAPDH housekeeping gene as reference. For classification purposes, we used the "k Top Scoring Pairs" (kTSP) algorithm, which allows sample classification based on the aggregation of votes resulting from expression ordering within a defined set of gene pairs [PMID:25262153]. In order to avoid overfitting, we restricted statistical learning to pairs combining genes promoting metastasis with genes preventing it. We further required our final classifier to be parsimonious (i.e., no more than 6 disjoint pairs), biologically consistent (i.e., higher expression of pro-metastatic genes in node positive patients), and robust across platforms (i.e., based on the intersection of the top scoring pairs identified by RNA-seq and microarray). Before independent validation via RT-PCR, we locked the decision rule, maximizing specificity and sensitivity: a sample was classified as node negative if three or more pairs voted for node negative status. Classifier validation. We validated our classifier using an independent set of 38 patient samples using RT-PCR and 32 Patient Derived Xenografts (PDXs) using RNA sequencing.
Hanan	**Rohana**	Classification of Clostridium difficile STs and examination of correlations between the different strains, disease severity, and the gut microbiome Aim & Background: In recent years, the global incidence of C. difficile infection has increased dramatically with the emergence of hyper-virulent strains. Limited data is available with respect to C. difficile strains that cause a severe disease compared to those which cause a mild diarrhea. Our aim was to understand the different strains' characteristics and the role of such differences in the severity of CDI. Methods: A severity score was calculated for each patient. All stool samples were tested for toxins' presence. Bacteria were isolated from the stool samples, identified by MALDI-TOF and antibiotic susceptibility tests were performed for Metronidazole, Vancomycin, Tigecycline, and Moxifloxacin. Strains were classified by Multi-locus sequence typing (MLST), and the changes they inflict on the gut microbiome were tested. Results & Conclusion: Using MLST analysis, the different Sequence types (STs) were determined. The most frequent strains were: ST04, 37, 104, 42, and 02. The different STs were divided to different clades, i.e. phylogenetic lineages, with clade 1 forming the majority of cases (81.4%, 57/70). We found a significant correlation between ST and age (p=0.024); the lowest mean was of patients with ST104 (n=6), 61.67 ±18.8 years; the highest mean was of patients with ST37 (n=9), 79.67 ±10.6 years. We also found a significant correlation between ST and susceptibility to Moxifloxacin (p=0.001). At the clade level, we found that 93% of the isolates belonging to clade 1 lacked the gene (p=0.002). Significant correlations were found between clade and susceptibility to both Metronidazole and Vancomycin (p=0.024, 0.035, respectively). Differences in intestine microbiome were affected by age, and by clades' distribution and STs. By studying the characteristics of the different strains and clades, clinicians can carry out their medical interventions based on the predicted response or disease severity associated with each strain.

Elena	**Kirtadze**	Novel variant in COQ4 causes developmental delay, regression, epilepsy and cardiomyopathy associated with CoQ10 deficiency. Elena Kirtadze, B.Sc1,2, Limor Kalfon, PhD1, Ayalla Fedida, PhD1,2 , Ann Saada -Reisch, PhD3, Maha Ajami-Yousef,MD4, Antonia Ribes, PhD5,7 , Daniel J. Moreno Fernandez-Ayala, PhD6,7, Ana Sánchez Cuesta6,7, Gloria Brea-Calvo, PhD6,7, Placido Navas Lloret PhD6,7, Hanna Mandel, MD1, Tzipora Falik-Zaccai, MD1,2 1Institute of Human Genetics, Galilee Medical Center, Nahariya. 2Azrieli Faculty of Medicine, Bar Ilan University, Safed. 3Department of genetic and metabolic diseases, Hadassah medical center, the faculty of medicine, Hebrew University, Jerusalem, 4Clalit Health organization, Haifa and Western Galilee district, 5Department of Biochemistry and Molecular Genetics , Hospital Clínic de Barcelona, Barcelona. 6Centro Andaluz de Biología del Desarrollo, Universidad Pablo de Olavide-CISC, Sevilla, 7Centro de Investigación Biomédica en Red de Enfermedades (CIBERER) Raras Instituto de Salud Carlos III, Madrid, Spain. Aim and Background: CoQ10 is a lipid soluble component of all cellular membranes. It is one of two mobile electron carriers in the mitochondrial respiratory chain (MRC), carrying electrons from complex I and II to complex III. COQ4 is one of ten genes involved in CoQ10 biosynthesis. Its exact function is unknown. Primary CoQ10 deficiencies are phenotypically heterogeneous and can manifest with encephalomyopathy, cerebellar ataxia, isolated myopathy, nephropathy, cardiomyopathy and severe infantile multisystemic disease. To date, 14 patients with primary CoQ10 deficiency due to mutations in COQ4 were reported. We report the clinical, biochemical and genetic defect of twin females who presented with early onset of severe hypotonia, developmental delay and regression, seizures and hypertrophic cardiomyopathy. Plasma and CSF lactate were normal and did not raise the suspicion of a mitochondrial disorder. Methods: Trio WES was performed followed by bioinformatics analyses, Sanger sequencing and segregation analyses of candidate variants. Biochemical studies aiming to confirm the pathogenicity of a genetic variant in COQ4 were performed in patients' fibroblasts (PF) including spectrophotometric study of MRC activities and biosynthesis rate by radioactive precursor incorporation measurements by HPLC. Results & Conclusions: Both sisters are homozygous for a novel missense variant in COQ4, c.437T>G, segregating in an autosomal recessive manner. Western blot and RT PCR analyses revealed no significant reduction of the protein signal nor a decrease in the transcript level of COQ4 respectively. PF showed around 40 pmol CoQ10/mg protein (normal range: 57-121) and reduced activity of complex II+III in the PF. In vivo incorporation of CoQ10 radioactive precursor p-HB showed 80% reduction in CoQ10 biosynthesis in PF. These data confirm the pathogenicity of c.437T>G in COQ4 leading to Primary CoQ10 deficiency. Determining the underlying molecular defect would enable accurate genetic counseling, prenatal or pre implantation genetic diagnosis and screening of high risk populations. Presenting author contact information: 04-9107493 052-6315006 Kirtadze24@gmail.com Msc resaerch student
Yeela	**Tomsis**	Explaining post traumatic symptoms after emergency and elective cesarean section: A structural equation model Yeela Tomsis, Ph.D1., Salam Hadid ,Ph.D.1,2 Nursing school, Zefat academic college1, Galilee Medical Center2 Abstract Aim & Background: Cesarean section (CS) in a lifesaving procedure. Nonetheless, it may involve feelings of helplessness and severe distress. In addition, CS recovery is usually more painful and challenging compared to vaginal birth. Combined with normal post-partum maternal stress, the harsh experience sometimes evolves into greater levels of distress, leading to posttraumatic stress symptoms (PTS) up to full spectrum post-traumatic stress disorder (PTSD). The aim of the study was to compare PTS levels of women who had emergency CS and women who had elective CS, and to build an integrative model which explains the relations between various factors related to post-partum PTS after CS. Methods: As a part of a prospective cohort study, 161 eligible women filled a set of questionnaires four days and six weeks after emergency or elective CS. The questionnaires included demographics, Self-efficacy, perceived difficulty of the labor, perceived control and PTSD questionnaires. PTSD was defined as per DSM-V criteria. Results: Fifteen women (9.3%) had full spectrum PTSD.A significant difference was found between women who had emergency and elective CS in PTS levels, perceived control and perceived difficulty of the labor. Self-efficacy, perceived difficulty of the labor and perceived control explained 43% of the variance in PTS using a structural equation model. Conclusions: Reducing the levels of personal distress by increasing perceived control during CS (a factor that may be externally controlled and manipulated during SC), may reduce the incidence and severity of full spectrum postpartum PTSD and PTS, particularly among women with low self-efficacy and during emergency CS. Author details: Full name: Yeela Tomsis Contact number : 0523750012 E. mail: yeelat@zefat.ac.il Status: Principal Investigator Preferred presentation: oral presentation
Roba	**Dabour**	Identifying novel silent patterns in coding regions of Hepatitis C virus for viral attenuation Roba Dabour1, Ateret Davidovitz1, Tamir Tuler2 and Meital Ga-Tanamy1 1Molecular Virology Lab, Azrieli Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel.2Department of Biomedical Engineering, Tel-Aviv University, Ramat Aviv, Israel. Background & Aims: Hepatitis C virus (HCV) is a leading cause of liver disease. No vaccine is currently available. Live attenuated vaccines contain viruses that have been weakened so that they do not cause serious disease in people with healthy immune systems, but still induce efficient anti-viral immune system. Understanding how viruses co-evolve with their hosts and adapt various genomic strategies to reduce their fitness have essential implications in developing new vaccines. In this study we provide evidence of evolutionary selection for 'silent' patterns of information hidden in the HCV genetic code based on mRNA folding, using a novel genomic analysis. Synonymous mutations directed at these regions are used to weaken the virus. Methods: We used novel bioinformatics tools to analyze HCV genomes from databases to identify synonymous information which are related to mRNA folding. We first constructed various HCV mutants that differ in number and positions of inserted synonymousmutations. To evaluate the effect of the synonymous mutations on viral fitness, we measured the level of HCV replication of these viruses by infecting hepatoma cells and performing qPCR for HCV RNA. We also evaluated the ability of these viruses to spread to adjacent cells by infecting the cells and counting infected cells comprising each focus, using immunofluorescence that detect viral proteins Results: We have generated 4 infectious mutant viruses containing various attenuating mutations. We observed an overall reduction of HCV replication in the mutant viruses compared to the WT. The levels of replication of the different mutants varied with correlation to the level and positions of attenuating mutations inserted. We also observed reduction in HCV spread, also correlating to the level of HCV replication we observed and level of mutations. Conclusions: The findings of this study highlight the potential of synonymous mutations to affect viral infectivity, as a potential tool for viral attenuation for vaccine development. מספר טלפון בעבודה:0722644982 מספר טלפון נייד: 0547874716 כתובת דוא"ל: roba.da1383@gmail.com סטודנטית מחקר פוסטר
erez	**avraham**	The role of HIF1A in modulating the epigenetic and oncogenic signatures induced by Hepatitis C virus infection Erez avraham1, Ateret Davidovich1 and Meital Gal-Tanamy1 1Molecular Virology Lab, Azrieli Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel. Introduction: Hepatitis C virus (HCV) is a major public health issue and it is estimated that 30% of patients will eventually develop liver diseases such as Hepatocellular carcinoma (HCC). It is known that HCV causes hypoxic and increase in reactive oxygen species (ROS) levels due to mitochondrial dysfunction caused by the viral proteins. This malfunction promotes metabolic switch to glycolysis pathway. High levels of ROS contribute to stabilization of hypoxia-induced factor 1 alpha (HIF1A). HIF1A is a master regulator of cellular survival genes. We explore the role of viral proteins in HIF1A stabilization, its role in HCV replication, and expression of HIF1A-induced genes, which facilitates in cellular survival under hypoxia. Methods: To evaluate the ability of HCV to cause hypoxia, we measured ROS production in HCV infected cells following HIF1A inhibitor/activator treatment. To evaluate the effect of HIF1A on the infectivity of HCV, we treated uninfected cells with HIF1A inhibitors/ activators and infected the cells. To evaluate the effect on HCV replication, we first infected the cells and then treated with inhibitors. To evaluate the ability of virus proteins (NS3 and Core) to regulate candidate genes in HIF1A pathway, we generated stable transfection cell lines. Evaluation of gene expression and replication levels for HCV RNA were performed by RT-PCR. Results: HCV infected cells showed higher levels of cellular ROS production after HIF1A activator treatment compared with reduced levels of ROS production after HIF1A inhibitor treatment. Treatment of HCV infected cells with HIF1A inhibitor results in decreased HCV replication and infection, whereas treatment with HIF1A activator resulted in increased HCV replication and infection. For most HIF1A-regulated genes that were increased following HCV infection, we observed significant up also in cells expressing Core protein. Conclusion: These results show that the host master regulator HIF1A has a significant role in HCV life cycle. מספר טלפון נייד: 0525586132. erezbya@walla.com סטודנט מחקר תואר שני פוסטר.
katreena	**yamin**	Analyzing Chromatin Condensation in Yeast by Second Harmonic Generation Microscopy Katreena Yamin1, Michael Assa1, Avi Matityahu1 and Itay Onn1 The Azrieli Faculty of Medicine, Bar-Ilan University1 The DNA in the nucleus is packed by proteins into chromatin fibers. During the cell cycle the interphase chromatin is condensed by members of the Structural Maintenance of Chromosome (SMC) family of protein complexes. Chromosomes reach maximum level of condensation in pro-metaphase. In mammalian cells, condensed mitotic chromosomes are visualized as individual bodies. However, the small size of the nucleus in budding yeast (Saccharomyces cerevisiae) and the low level of condensation make the assessment of condensation in these cells a challenging task. Several methods have been developed to study condensation in yeast. However, all of them suffer from major weaknesses. We developed a new method to study chromatin condensation in live yeast cells that is based on second harmonic generation (SHG) microscopy. SHG is a physical phenomenon of the second order in which the energy of consecutive photons is reflected from isotropic molecules, such as chromatin, One challenge that we encountered in generating second harmonic was the requirement to accurately focus the laser on the cell nucleus. We utilized this method to analyze changes in chromatin density throughout the cell cycle in yeast. Furthermore, we showed that SMCs play a central role in chromatin organization and mediates condensation. This method provides a new tool to study chromatin structure in live yeast cells. מספר נייד: 0546103129 מס' טלפון בעבודה: 072-2644-984 כתובת דוא"ל: yousef_y_r99@hotmail.com מעמד אקדמי: סטודנטית מחקר.

Anjali	**Pathania**	Cohesin loading onto the chromosomes is regulated by the interaction of the core Scc3 subunit with the loader. Anjali Pathania1, Wenjie Liu2,3, Avi Matityahu1, Joseph Irudayaraj2,3 and Itay Onn1* Cohesin is essential for sister chromatid cohesion, which ensures equal segregation of the chromatids to daughter cells. However, the molecular mechanism by which cohesin mediates this function is elusive. Scc3, one of the four core subunits of cohesin, is essential for cohesin activity. Scc3 contains two armadillo repeats and a 90 amino-acid highly conserved domain. The mechanisms by which Scc3 contributes to the activity and the identity of its functional domains is elusive. Here, we describe an in-frame five amino acid insertion mutation after glutamic acid 704 (scc3-R2) in yeast Scc3 that is located in the second armadillo repeat. Cohesin-scc3-R2 complexes are bound to the chromatin but are unable to establish cohesion. Co-immunoprecipitation analysis for cohesin subunits showed differential binding to Scc2 and upon overexpression the growth phenotype of cells carrying the scc3-R2 was partially suppressed. These results imply that Scc3-Scc2 interaction is essential for cohesin loading. Disruption of this interaction, apparently, exposes a DNA binding domain in Scc3 that induces non-specific cohesin-DNA interactions. Finally, we identified two adjacent aspartic acid residues that imitate scc3-R2 allele in viability and loss of cohesion. The results of this study provide new insight into the mechanism by which cohesin is loaded onto chromatin. Furthermore, it uncovers the interplay between Scc3 and the cohesin loader that mediates this activity and enhances our understanding of the mechanisms by which cohesin maintains the integrity of the genome.
Maria	**Elias**	Dissecting cohesin mechanism of action by peptide-based inhibition of head domain engagement Maria Elias1 , Avi Matityahu1, Samar Gani2, Yana Lerner2 Nir Qvit2 and Itay Onn1 1.Chromosome Instability and Dynamics Lab, The Azrieli Faculty of Medicine, Bar-Ilan University 2.Chemistry and Biology of Protein-Protein Interactions Lab, The Azrieli Faculty of Medicine, Bar-Ilan University Cohesin is a chromosome-associated multi-subunit protein complex that tethers the sister chromatids in a process known as sister chromatid cohesion. This process ensures the fidelity of chromosome segregation in dividing cells regulates gene expression and involved in DNA repair. Mutations in cohesin encoding genes are associated with developmental disorders and cancer. The core of cohesin is composed of two SMC proteins called Smc1 and Smc3. SMC proteins are elongated polypeptides with a globular domain at their end, called the head domain. This domain contains two halves of an ABC-type ATPase domain. ATP binding induces the dimerization of the Smc1 and Smc3 heads while ATP hydrolysis induces their disengagement. However, very little is known about the molecular details of this interaction, its dynamics and its functional outcomes. In this project we aim to study the role of head domain interactions by using inhibitory peptide approach. We designed a series of short peptides to inhibit head domain interaction. We express these peptides in cells and assess their effect on cohesin activity. Our results so far indicate that some of the peptides are inhibiting cohesin activity. Next, we will study the molecular outcomes of this inhibition in depth. In addition, we intend to instill synthesized peptides into cells and test their inhibitory effect. This approach will shed new light on cohesin mechanism of action and may lead to the future development of therapeutic peptides for cohesin-related cancer. מספר טלפון נייד : 0509806831 מספר טלפון בעבודה : 072-2644-984 כתובת דוא"ל : maria123566@gmail.com מעמד אקדמי : סטודנטית מחקר
Nomy	**Dickman**	Nomy Dikman1, Basem Hijazi1, Abraham O. Samson1, & Lea Even1,2 Azrieli Faculty of Medicine, Bar-Ilan University1, Western Galilee Hospital, Nahariya2 Aim & Background: Medical students complete clinical rotations during their clinical years. In each department, a junior resident plays the role of a "tutor" that covers medical, logistical and personal aspects. This role has yet to be investigate in depth in the medical education literature. Our experience taught us that good departments typically get good remarks on their tutors. Accordingly, we assessed the contribution of students' satisfaction from their tutors to students' overall satisfaction from the clinical rotations. Aim: to improve the teaching of the medical doctors who teach in the clinical rotations in hospitals. The research's question: is there a correlation between the students' satisfaction of the tutors and their satisfaction of the clinical rotation? Methods: Mixed methods: quantitative and qualitative. A retrospective chart review (2014-2017) - of all students' teaching surveys, on their experience in the clinical rotations, focusing on the tutors' role – was conducted. 710 students in two hospitals completed the questionnaire (102 rotations with 40 tutors) in five departments with long rotations. The perceived satisfaction of the clinical rotation was assessed using a Likert five rank scale. Qualitative written assessment of the tutors was converted into one to three numerical scale. Spearman correlations tested the relationship between perceptions of tutors and satisfaction from clinical rotations. Results: A positive, high significant correlation (rs = .78, p < .01) was found between students' satisfaction of tutors and their overall satisfaction of the clinical rotations. To the best of our knowledge, this is the first time in the literature that the relationship between these variables has been reported. The tutors are not the only teachers in the clinical rotation. Interestingly, when only the tutor in a department was changed, the departmental satisfaction score rose with the tutor's score. Conclusions: It is essential to study in-depth the characteristics of "excellent" tutors and to invest substantial resources in training tutors. Oral Talk מס' נייד: 0506842174 כתובת דוא"ל: nomyd@hotmail.com
Yakir	**Lidani**	A method of teaching students in the clinical clerkship combining two existing methods, TBL and VAKE Perlitz Y.1, Ben Shlomo I.1, Even L.2, Lidani y., Dikman N.3 1Dept. of Ob/Gyn, Padeh Med. Ctr., Poria, 2Dept, of Pediatrics, the Galilee Med. Ctr., 3The Unit for Evaluation & Advancement of Teaching Introduction: Traditionally, the teaching of values has been held secondary to transfer of knowledge to medical student, and was expected to emerge as a byproduct. Currently, many teachers express the desire to deal with moral and ethical dilemmas as central tools for shaping the future practitioners. Values and knowledge education (VAKE) uses dilemmas as a pivot for the active acquisition of knowledge by students. Students split into groups by initial siding as "for" and "against" in a given dilemma, which calls them to find together evidence, supporting their siding. This active search serves to provide the opportunity for active learning. We combined elements from the now widespread TBL method (team based learning) and VAKE to form teaching units for the clinical clerkship. Aim: To compare the usefulness and acceptance by medical students of these combination teaching units in comparison to generic TBL. Method: Clinical clerkship teams were taught by either of the two methods and were asked to fill in knowledge tests as well as opinion questionnaires regarding the method of teaching. The tests and the opinion charts were compared by statistical tests as applicable. Results: Knowledge tests indicated an advantage to the combination method over generic TBL. Opinion charts indicated a significant preference of students to the combined method as compared to generic TBL. In individual, open responses, students pointed to its contribution to their preparation to future dealing with daily dilemmas. Conclusion: Our new method, combining VAKE with TBL should be implemented, as appropriate, during clinical clerkships. Yakir Lidani Medical student Phone: 0522338947 Email: Yakirlidani@gmail.com
Tatyana	**Levinas**	Long-term outcomes of staged non-culprit lesions percutaneous coronary intervention for multivessel disease in patients presenting with ST-segment elevation myocardial infarction
worood	**sirhan**	Towards molecular characterization of pancreatic exocrine and endocrine cells. Worood Sirhan and Ron Piran, Bar Ilan University, Faculty of Medicine Aim & background: Recently researchers showed that by ectopic administration of two morphogens, pancreatic acinar cells (that normally exist in large quantities), transdifferentiate into functional, glucose-responsive, insulin-secreting β-like cells. While these findings shook the islet-cell community, the initial acinar to β-cell conversion was low and except of a few rare reports, most animals remained diabetic. In order to increase the acinar to β-cell conversion process, one needs to understand what makes an acinar cell. Despite of their importance, acinar cells have been poorly studies mainly because of the prevailing characterization methodology. We intend to study what differentiate acinar from β-cells, and use these findings in the future to explore ways to stabilize β-cells in diabetes patients . Methods: To find the differences between acinar and, β-pancreatic endocrine cells we propose to characterize these cell populations, isolate and collect the both different pancreatic cell-type populations from murine samples by using laser capture microdissection technology (leica LMD7), and characterize their proteomic and transcriptomic properties. Results: More than 5,000 cells from each population were gathered in different vials. Cell population were delivered to our collaborators at the Weizmann Institute for proteomic and transcriptomic analysis. מס' נייד: 054-6073601 מס' טלפון בעבודה: 072-2644889 כתובת דואר אלקטרונית: worood.sirhan@live.biu.ac.il מעמד אקדמי של החוקר: סטודנט לתואר שלישי

Adi	**Eshel**	Fecal Microbiota Transplantation Using Orally Administered Capsules for the Treatment of Steroid Resistant and Steroid Dependent Intestinal Acute Graft vs. Host Disease. A. Eshel1, I. Youngster2, M. Geva3, I. Sharon4, A. Nagler3, R. Shouval3, O. Koren1 1 Azrieli Faculty of Medicine, Bar Ilan University, Safed, Israel. 2 Assaf Harofeh Medical Center, Israel. 3 The Division of Hematology and Bone Marrow Transplantation, Chaim Sheba Medical Center, Ramet Gan, Israel 4 MIGAL Galilee Research Institute, Kiryat Shmona, Israel. Background: Steroid-resistant (SR) intestinal acute graft versus host disease (aGVHD) is a devastating complication of allogeneic hematopoietic stem cell transplantation. Preliminary reports suggest that fecal microbiota transplantation (FMT) administered through a nasogastric tube or colonoscopy may be an effective treatment. We report the results of a pilot study using FMT in capsules to treat SR or steroid dependent (SD) intestinal aGVHD. Methods: Participants received a course of 30 frozen capsules produced from healthy unrelated donors over two consecutive days. FMT course was repeated from the same or a different donor if needed. Fecal samples were collected at different time points and DNA was purified for 16S rRNA and metagenomic sequencing. Results: 16S rRNA sequencing of stool samples revealed bacterial domination (i.e, occupation of at least 40% of the microbiota by a single taxon) of Escherichia coli in 4 out of 7 patients prior to FMT, with a major reduction following therapy. FMT was associated with the introduction of new bacterial species and increased bacterial diversity in the patient's stool. Metagenomic and 16S rRNA sequencing of blood culture samples ruled out FMT as the source of bloodstream infections (Patient #1). Conclusion: We are the first to demonstrate the use of orally administered FMT for treatment of aGVHD. The capsules were well tolerated and no treatment related severe adverse events were observed. Two out of seven patients attained complete response following therapy, with no clinical signs for GVHD and minimal steroid treatment suggesting a potential role for FMT in patient management. Phone number: 0507320235 Email: adizimer@gmail.com Title: Research student
zeinab	**usman**	Protein kinase A (PKA) plays critical roles in neuronal function that are mediated by different regulatory (R) subunits. Deficiency in either the RIβ or the RIIβ subunit results in distinct neuronal phenotypes. Although RIβ contributes to synaptic plasticity, it is the least studied isoform. Using isoform-specific antibodies, we generated high-resolution large-scale immunohistochemical mosaic images of mouse brain that provided global views of several brain regions, including the hippocampus and cerebellum. The isoforms concentrate in discrete brain regions, and we were able to zoom-in to show distinct patterns of subcellular localization. RIβ is enriched in dendrites and co-localizes with MAP2, whereas RIIβ is concentrated in axons. Using correlated light and electron microscopy, we confirmed the mitochondrial and nuclear localization of RIβ in cultured neurons. To show the functional significance of nuclear localization, we demonstrated that downregulation of RIβ, but not of RIIβ, decreased CREB phosphorylation. Our study reveals how PKA isoform specificity is defined by precise localization.
nicole	**palant**	Protein kinase A (PKA) plays critical roles in neuronal function that are mediated by different regulatory (R) subunits. Deficiency in either the RIβ or the RIIβ subunit results in distinct neuronal phenotypes. Although RIβ contributes to synaptic plasticity, it is the least studied isoform. Using isoform-specific antibodies, we generated high-resolution large-scale immunohistochemical mosaic images of mouse brain that provided global views of several brain regions, including the hippocampus and cerebellum. The isoforms concentrate in discrete brain regions, and we were able to zoom-in to show distinct patterns of subcellular localization. RIβ is enriched in dendrites and co-localizes with MAP2, whereas RIIβ is concentrated in axons. Using correlated light and electron microscopy, we confirmed the mitochondrial and nuclear localization of RIβ in cultured neurons. To show the functional significance of nuclear localization, we demonstrated that downregulation of RIβ, but not of RIIβ, decreased CREB phosphorylation. Our study reveals how PKA isoform specificity is defined by precise localization.
Atara	**Uzan-Yulzari**	Neonatal antibiotic exposure: the influence on the gut microbiota The establishment and development of the bacterial population during early life have been found to be strongly affected by several factors such as delivery mode, diet and antibiotic exposure. Early life antibiotic exposure causes alterations in the gut microbiota and has also been reported to be associated with the risk of chronic disease including inflammatory bowel disease (IBD), overweight, and asthma. During recent years antibiotics administration has increased dramatically, and it has become the most commonly used drugs in pediatrics in western countries. The long-term impact of neonatal antibiotic exposure remains poorly understood. The current study aim was to examine the impact of neonatal antibiotic administration on gut microbiota up to 24 months from the exposure time compared to control infants. Bacterial populations from fecal samples of antibiotic treated and control infants has been analyzed using 16S rRNA and whole genome shotgun sequencing. In addition, we performed fecal microbiota transplantation (FMT) to germ-free mice from all experimental and control infants in order to further test the microbial changes and their impact on growth. Our results show that penicillin and gentamicin had major effects on infant gut microbiota as long as 24 months after treatment with major impact on Bifidobacterium species. In addition, mice receiving FMT from antibiotic-exposed neonates exhibit long-term microbiota disturbances and gain less weight compared to mice receiving FMT from non-exposed infants. Our data indicate that neonatal antibiotic exposure elicits a long-term impact on gut microbiota development and may be associated with adverse effects on growth.
ariela	**rosenblum**	Abstract: Post-Traumatic Stress Disorder (PTSD) is an anxiety disorder that typically develops following exposure to traumatic events. Following the traumatic event some individuals develop Symptoms that cause significant distress or impairment in social, occupational, or other functioning, negatively affecting quality of life. Participation in satisfying daily activities has a direct positive influence on health perception, personal welfare and quality of life. However, there is not enough research on the relationship between PTSD, participation and quality of life. Objectives: 1. To investigate whether there are differences in levels of participation in daily activities and quality of life among individuals with PTSD and healthy controls, 2. To investigate the correlation between PTSD symptoms, participation in everyday living activities, and quality of life among individuals with PTSD, 3. To investigate the predictive power of PTSD symptoms and participation in daily activities on the perception of quality of life. Measurements: (1) sociodemographic questionnaire; (2) Post Traumatic Stress Disorder Symptom Scale (PSS-SR); (3) The Peritraumatic Dissociative Experiences Questionnaire- Self Report (PDEQ-SR); (4) Activity card sort (ACS); (5) The world health organization quality of life (WHOQOL-BREF) questionnaire. Results: A significant difference was found between the two research groups regarding level of participation. The two main predictors of high perception of quality of life were: 1. high participation in instrumental activities of daily living, and 2. low PTSD symptoms.
Ari	**Meerson**	microRNAs as a functional link between obesity and cancer Obesity is a risk factor for several cancer types, suggesting shared molecular mechanisms. To test the hypothesis that microRNAs play and important role in this molecular cross-talk, we used microarrays, RNA-seq and qRT-PCR to identify cancer-relevant microRNAs that respond to metabolic hormone signaling in cultured cells and/or to metabolic changes in human subjects, and studied the upstream regulation and downstream effects of these candidate microRNAs. Thus, we previously reported that miR-221 was elevated in the fat tissue of obese subjects, but downregulated by leptin and TNFα in cultured adipocytes. MiR-221 directly downregulated the angiogenesis-promoting transcription factor ETS1. In cultured colon cancer cells, we found that miR-4443 was upregulated by leptin and insulin in a MEK1/2-dependent manner. MiR-4443 overexpression decreased invasion and proliferation, and directly downregulated NCOA1 and TRAF4, genes involved in metastasis. Insulin and/or leptin resistance (e.g. in obesity) may suppress this tumor-suppressive pathway and increase cancer risk. Supporting this notion, the miR-4443 locus is frequently deleted in cancers. We also reported that the serum levels of miR-122 (a tumor-suppressive microRNA known to be internalized by target cells where it is biologically active) were elevated 3 months post-surgery in sleeve gastrectomy patients, which may contribute to lower cancer risk. Recently, we showed a stronger down-regulation of miR-10b in the tumors of the obese breast cancer patients, as opposed to the lean. In ductal but not lobular tumors, significant inverse correlations were observed between the tumor levels of miR-10b and the mRNA levels of cancer-relevant target genes SRSF1, PIEZO1, MAPRE1, CDKN2A, TP-53 and TRA2B, as well as tumor grade. Suppression of miR-10b levels in BT-549 primary BC–derived cells increased cell proliferation and invasive capacity, while exogenous miR-10b mimic decreased invasion. Manipulation of miR-10b levels also inversely affected the mRNA levels of miR-10b targets. Our findings suggest that miR-10b may be a mediator between obesity and cancer in post-menopausal women, and that miR-10b expression may have diagnostic and therapeutic implications for the incidence and prognosis of BC in obese women.