UC Irvine
ICTS Clinical Translational Science Meeting Abstracts

Title
2017 Pathways to Cures: Clinical and Translational Science Day at UCI

Permalink
https://escholarship.org/uc/item/8kq7s9x2

Author
Institute for Clinical and Translational Science

Publication Date
2017-06-13

2017 Pathways to Cures:
Clinical Translational Research Day at UCI

June 13, 2017

Poster Session Abstracts

Sponsored by:

INSTITUTE FOR CLINICAL AND TRANSLATIONAL SCIENCE
UNIVERSITY of CALIFORNIA · IRVINE

UC·IRVINE
ICTS
from lab to life.

40	Office-Based Ultrasound Guided Percutaneous Renal Mass Biopsy	Okhunov, Zhamshid, Dr.	24
41	Inhibition of the Rho/ROCK pathway as a novel targeted therapy for clear cell renal cell carcinoma	Nelson, Luke	24
43	Mechanically-Coupled Reaction-Diffusion Model of Glioma Growth	Abler, Daniel, PhD	25
44	Magmas inhibition as a potential treatment strategy in malignant glioma	Di, Kaijun	25
45	From Bench to Bedside: Marizomib Activity in Malignant Gliomas - Preclinical Development and Early Clinical Trial Results	Di, Kaijun	26
46	Unusual cardiac paraganglioma mimicking an atypical carcinoid tumor of the lung – Case report with literature review	Spencer, Dean, BS	26
47	Cardiovascular manifestations of feline Sandhoff disease after intravenous AAV gene therapy	Ellis, Lauren, BS.	27
48	Investigation of microbial and viral communities in the cystic fibrosis lung	England, Whitney	27
49	Clinical Comparison of the Mobile Endockscope System and Standard Videocystoscopy using Air and Liquid Irrigant	Abadinaeini, Sina	28
50	Development and Multi-Institutional Evaluation of a Novel 3D-Printed Laparoscopic Trainer: The UCiTrainer	Lu, Sherry	28
51	Selective stimulation of facial muscles following chronic intraneural electrode array implantation and facial nerve injury in the feline model	Ronald Sahyouni, B.A.	29
52	Utilizing consumer photoplethysmography technology to augment the Allen's Test in measuring collateral circulation to the hand: Proof of concept using the Apple Watch	Allison C. Hu, BA	29
53	Development of a Three-Dimensional Kidney Model for Use in a Virtual Reality Environment	Safiullah, Shoaib	30
54	VR/3DP Radiology Lab: A Pilot Project for Single-Platform Integration of Virtual Reality and 3D Printing in Radiology Education	Hernandez-Rangel, Eduardo, MD	30
55	Pathways: Evaluation of an Emerging Digital Nutrition Campaign	Waldeck, Jennifer Ph.D.	31
56	Validation of a Microfluidic Device to Study Patient-Derived Colon Cancer Cells and Determine Clinical Predictive Value	Hachey, Stephanie J MS	31
57	Quantitative Spectral Imaging of tissue function, structure, pathology in (pre-)clinical investigations using Spatial Frequency Domain Techniques	Saager, Rolf B, PhD	32
58	The Impact of Forces Applied during Ureteral Access Sheath Deployment on Ureteral Injury in a Porcine Model	Warner, Anthony, AS	32
59	Telepresence robots for virtual social and academic inclusion: Can they contribute to improved well-being, health, and social outcomes for homebound pediatric patients?	Newhart, Veronia	33
61	Determination of LOXL1 and Fibulin-5 Levels in the Vaginal Secretions of Women With and Without Pelvic Organ Prolapse	Garcia, Bobby MD	34
62	Dose-Response of Rabbit Maxillary Sinus CBF in Lidocaine	Gu, Jeffrey, BS	34
63	Manual Acupuncture, but not Electroacupuncture Stimulate Afferent Nerves through Activation of TRPV1 Receptors to Modulate Pressor Reflexes	Zhi-Ling Guo, MD, PhD	35
64	Optical imaging for diagnostic indices in alopecia	Lin, Jessica	35
65	Therapeutic potential of human preterm umbilical cord mesenchymal stem cells	Fobi, Raissa, MD:	36
66	Mesenchymal stem cell biomakers prevent Bronchopulmonary Dysplasia via suppression of lung inflammation	Aslam, Muhammad, MD 1	36
67	A potential role for group 2 innate lymphoid cells in muscular dystrophy	Jenna Kastenschmidt	37
68	Restore Visual function by Human Embryonic Stem-cell derived 3D retinal organoid transplants in an immunodeficient retinal degenerate rat model	Lin, Bin, PhD.	37
69	Retina organoids derived from hESCs and transplanted to immunodeficient RCS rats	Seiler, Magdalene J., Ph.D.	38
70	Retinal Repair Neural Trace Analysis	Smith, William	38
71	Retinal Degeneration Stem Cell Research - MATLab	Minar, Sydney	39
72	Histological characterization of stem-cell derived 3D retinal progenitor sheet transplants in an immunodeficient retinal degenerate rat model	Mathur, Anu, M.S.	39
73	Electroretinography to determine success of stem cell transplantation in RCS rats	Duong, Jessica	40
74	Modeling epilepsy with isogenic human iPSC-derived neurons	Xie, Yunyao	40
75	Therapeutic Effects of Idebenone on Mice with VCP Disease	Ta, Lac	41
76	Lipidomics Associated Signaling Pathways In VCP Myopathy	Weiss, Lan, MD, PhD	41
77	Analyzing the Muscular and Respiratory Effects of Resistance Training in Patients with Pompe Disease	Bhatnagar, Caleb	42
78	Stable isotope profiles reveal active production of VOCs from human-associated microbes	Phan, Joann	42
79	RNA sequencing of a Cystic Fibrosis isolate identifies genes and novel operons contributing to adaptation to acidic environments	Gallagher, Tara	43
80	Airway Microbe Analysis in Preterm Infants with Bronchopulmonary Dysplasia	Singhal, Meghali, MD	43

81	Mitochondrial regulation of microRNA and implications for macular degeneration	Schneider, Kevin, PhD	44
82	Effects of Anti-angiogenic Drugs on Expression Patterns of Genes Involved in Different AMD Pathogenetic Pathways	Mohamed, Mohamed	44
83	Mapping Dental Plaque Re-Accumulation: an Imaging Approach	Golabgir Anbarani, Afarin	45
84	Developing a Saliva-based Oral Cancer Risk Test for Underserved Population in a Community-Basec Setting	Golabgir Anbarani, Afarin	45
85	Aptamer molecular biosensor for bladder cancer diagnosis and surveillance	Wu, Yi Xi	46
86	Effects of ranibizumab and bevacizumab on phagocytic properties in human RPE cybrids with AMD versus normal mitochondria	Vo, Thomas, BS	46
87	Coevolution of human gut Enterococcus with lytic phage	Wandro, Stephen	47
88	Modulation of epigenetic markers in transmitochondrial age-related macular degeneration (AMD) ARPE-19 cybrid cells	Nashine,Sonali R.	47
89	Targeting the intoxication pathway of Botulinum neurotoxins with heavy-chain camelid antibodies	LAM, KWOK-HO	48

Poster Location: 1

Parent versus teacher ratings of sluggish cognitive tempo; Implications for identifying risk among children with ADHD for poor academic achievement.

Lago, Haley, Social Sciences, University of California Irvine; Abdullah, Maryam, Pediatrics, University of California Irvine, PhD; Schuck, Sabrina, Pediatrics, University of California Irvine, PhD; Cordia, Theresa

Pediatrics, University of California Irvine, M.S

Sluggish Cognitive Tempo (SCT) is characterized by pathological inattention, physical under arousal and slowed thinking often seen in children with Attention Deficit/Hyperactivity Disorder (ADHD). Increasing evidence suggests SCT in children with ADHD contributes to poor academic achievement (Tamm, L. et al. 2016). Sixty-five children, their parents and teachers participated. All child participants attend a school-based behavioral health program for children with ADHD. All participants completed the Strengths and Weaknesses of Attention scale (SWAN) (parent, teacher or self-report versions).Three items from the SWAN, thought to be representative of symptoms associated with SCT were selected to derive an SCT index; "challenges in remaining focused", "having a below average energy level when completing tasks", and "difficulties in engaging in goal-directed activities". Academic achievement for the child participants was measured using the Wide Range Achievement Test, (WRAT4). Teacher ratings of the SCT index were strongly negatively correlated with all academic measures, indicating that children with lower academic achievement are perceived by their teachers to also demonstrate greater impairment from SCT symptoms. Interestingly, parent ratings on the SCT index were not significantly correlated with any area of academic achievement. Similarly, child self-reports of SCT symptoms did not correlate with academic achievement. Results suggest that teacher ratings of children's SCT symptoms are better predictors of risk for low academic achievement than parent ratings and child self-report. Teachers rating of SCT symptoms are likely to be more valuable than parent ratings in assisting practitioners to identify risk for low academic achievement and tailor interventions designed specifically for SCT.

Keywords: Sluggish Cognitive Tempo; Academic Achievement; Attention Deficit Hyperactivity Disorder; Child self-report; Parent and teacher ratings;

Poster Location: 2

The Brain Anatomical Correlates of Attention-Deficit/Hyperactivity Disorder in Young Adults

Gehricke, Jean, Ph.D.; Kruggel, Frithjof, M.D.; Alejo, Sharina, B.A.

Gehricke, Alejo's - University of California, Irvine The Center for Autism & Neurodevelopmental Disorders; Department of Pediatrics Kruggel - Department of Biomedical Engineering

The study examined the structural brain anatomy and connectivity associated with an ADHD diagnosis and child as well as adult ADHD symptoms in young adults. It was hypothesized that an adult ADHD diagnosis and in particular childhood symptoms, are associated with widespread changes in the brain macro- and microstructure, which can be used to develop a morphometric biomarker for ADHD. Voxel-wise linear regression models were used to examine structural and diffusion-weighted MRI data in 72 participants (31 young adults with ADHD and 41 controls without ADHD) in relation to diagnosis and the number of self-reported child and adult symptoms. Findings revealed significant associations between ADHD diagnosis and widespread changes to the maturation of white matter fiber bundles and gray matter density in the brain, such as structural shape changes (incomplete maturation) of the middle and superior temporal gyrus, and fronto-basal portions of both frontal lobes. ADHD symptoms in childhood showed the strongest association with brain macro- and microstructural abnormalities. At the brain circuitry level, the superior longitudinal fasciculus (SLF) and cortico-limbic areas are dysfunctional in individuals with ADHD. The morphometric findings predicted an ADHD diagnosis correctly up to 83% of all cases. An adult ADHD diagnosis and in particular childhood symptoms are associated with widespread micro- and macrostructural changes. The SLF and cortico-limbic findings suggest complex audio-visual, motivational, and emotional dysfunctions associated with ADHD in young adults. The sensitivity of the morphometric findings in predicting an ADHD diagnosis was sufficient, which indicates that MRI-based assessments are a promising strategy for the development of a biomarker.

Keywords: MRI; Brain circuitry; Neurodevelopmental Disorders; Diagnosis; Lifespan;

Poster Location: 3

Parent & Child Perceptions on Handheld Device Use; Implications for Families Affected by ADHD

Jessica Huynh; Maryam Abdullah, Ph.D.; Theresa Cordia, M.S.; Sabrina E.B. Schuck, Ph.D.

Jessica Huynh, UCI Psychology and Pediatrics; Maryam Abdullah, Ph.D., UCI Pediatrics; Theresa Cordia, M.S., UCI Pediatrics; Sabrina E.B. Schuck, Ph.D., UCI Pediatrics

The purpose of this study was to find whether parent's perspectives on handheld devices affected their child's perspective on handheld devices in families affected by Attention Deficit/Hyperactivity Disorder (ADHD). 63 paired surveys (parent and child) about accessibility, use, and beliefs and opinions about handheld devices that were previously collected from families participating in a school-based behavioral health program were analyzed utilizing paired samples t-test. As expected, parents' handheld device accessibility is associated with children's handheld device accessibility and how much parents use handheld devices is linked to parent's beliefs about the importance of handheld devices. Interestingly, there is no statistically significant relationship between parent beliefs and child beliefs but there is a notable negative relationship between them. Thus, we found that further research needs to be done to analyze the relationship between parent's beliefs on handheld devices as compared to children's beliefs on handheld devices.

Keywords: Educational Technology; Handheld Devices; ADHD; Beliefs and opinions;

Poster Location: 4

Perinatal complications associated with Prader-Willi syndrome (PWS).

Singh, Preeti, MD MPH FAAP; Mahmoud, Ranim, MD; Gold, June-Ann, MD; Kimonis, Virginia, MD MRCP

Division of Clinical and Biochemical Genetics, Department of Pediatrics, University of California, Irvine. Division of Neonatology, Department of Pediatrics, University of California Irvine.

Background: Prader Willi Syndrome (PWS) is caused by lack of expression of genes on the paternal chromosome 15 (15q11.2 - 15q13 region). There is an evolving phenotype for those patients with either a deletion, Uniparental Disomy (UPD) or Imprinting Center Defect (ICD). Patients present prenatally with decreased fetal movements, higher pregnancy complications and hypotonia, dysmorphism and feeding difficulties in postnatal period. Objectives: We evaluated the early manifestations of PWS in pregnancy and early neonatal period by their genetic subtype in a large cohort of PWS patients. Methods: Data from 355 patients from a PWS registry were used to analyze multiple clinical variables. SPSS software was used for statistical analysis and p-value of <0.05 was considered statistically significant. Results: Out of 355 patients, 217 had deletion (61%), 127 had UPD (36%), 11 had ID (3%). 190 patients were born by C-section (54%) compared to the general population of 32% (CDC 2014), Fetal movements were decreased in 256 patients (72%). Mean birth weight of PWS babies was found to be 2.71 kg (Range 0.7-5 kg). 254 babies (72%) needed gavage feeding (NG/OG/G-tube), out of which 59 (23%) needed G-tube placement, these values being significantly different than the general population. We found significant difference between deletion versus UPD/ICDs for Maternal age (p=0.00), and Maternal weight pre-pregnancy (p=0.015). Analysis of neonatal variables identified significant difference in weak cry in babies with deletion versus UPD/ICDs (p=0.048). However, no significant differences were found for other maternal and neonatal clinical features, when comparing patients with deletion versus UPD/ICDs. Conclusions: There is a high rate of C-section, low fetal movements and lower birth weight among PWS patients. Babies with UPD were born to older mothers with higher pre-pregnancy weights. Other significant differences included increased incidence of weak cry in the deletion group.

Keywords: Prader Willi Syndrome; Perinatal complications; Genetic subtype;

Poster Location: 5

Temporal and spectral characteristics of hypsarrhythmia in infantile spasms

Smith, Rachel J.; Hussain, Shaun A., MD; Shrey, Daniel W., MD; Lopour, Beth A., PhD

Department of Biomedical Engineering, University of California, Irvine, CA, USA Division of Pediatric Neurology, University of California, Los Angeles, CA, USA Department of Neurology, Children's Hospital of Orange County, Orange, CA, USA Department of Pediatrics, University of California, Irvine, CA, USA

Infantile spasms is a potentially devastating form of epilepsy characterized by clinical spasms and often a chaotic electroencephalographic (EEG) pattern known as hypsarrhythmia. Classic hypsarrhythmia is defined by multi-focal, independent epileptiform discharges on a disorganized background activity with asynchronous large amplitude slow waves. Visual identification of hypsarrhythmia is challenging due to a wide variability in temporal and spectral characteristics and the existence of several variants of the classic pattern. Quantitative measurements of hypsarrhythmia have the potential to improve the accuracy and objectivity of initial diagnostic testing and to expedite successful treatment, but basic amplitude and spectral characteristics have never been reported. Therefore, we quantified hypsarrhythmia with three EEG measurements: the amplitude, the power spectrum, and the autocorrelation function of the amplitude envelope. Empirical cumulative distribution functions of maximum voltage differences in one second intervals of EEG data revealed significantly higher amplitudes in hypsarrhythmia compared to control subjects (Kolmogrov-Smirnov test: $p<0.01$, Wilcoxon rank-sum: $p<0.01$). Further, the power in hypsarrhythmia was significantly higher in all frequency bands, but with the greatest distinction in the lower frequency bands (Wilcoxon rank-sum: $p<0.01$). The long-range temporal structure of hypsarrhythmia was investigated with the autocorrelation of the amplitude envelope. We found significant temporal correlations at longer time lags for data without hypsarrhythmia when compared to data with hypsarrhythmia (Wilcoxon rank-sum: $p<0.01$). This type of objective quantification of hypsarrhythmia can aid clinicians in accurate diagnosis and assessment of treatment response in infantile spasms, ultimately improving treatment outcomes of this catastrophic disease.

Keywords: epilepsy; seizure; quantitative EEG; signal processing; time-frequency analysis;

Poster Location: 6

Investigating postnatal oxytocin as a treatment for Fragile X in a mouse model

Cox, Brittney, PhD; Le, Aliza, BS; Aghazadah, Lida, BS; Lynch, Gary, PhD; Gall, Christine, PhD

Department of Anatomy and Neurobiology

Fragile X syndrome (FXS) is a genetic disorder caused by the silencing of the fragile x mental retardation 1 (Fmr1) gene. FXS is the most common genetic cause of inherited intellectual disability and autism. Both FXS and autism spectrum disorders are characterized by multiple cognitive and social deficits and currently there is no effective pharmacotherapy. Oxytocin, a neuropeptide well known for its role parturition and social behaviors, is in clinical trials in children and adults for treatment of social deficits that occur in FXS and autism disorders. The oxytocin system is important for the normal development of functional networks involved in social and cognitive behaviors. Fragile X model mice (Fmr1-KO) display similar cognitive and social deficits as humans with the genetic disorder. Thus, we used the Fmr1-KO model to examine if oxytocin treatment attenuated deficits in adulthood. Using Designer Receptors Exclusively Activated by a Designer Drugs (DREADDs), with an oxytocin promoter, we tested whether endogenous oxytocin restored social learning in the KO mice. We also tested whether postnatal oxytocin treatment (intranasal, postnatal day 7-14) caused enduring changes that rescue social and cognitive deficits in adulthood. We found that both acute release of endogenous oxytocin and postnatal oxytocin treatment restored various forms of learning in the KOs in adulthood. Current studies are examining how postnatal oxytocin treatment alters the oxytocin system to restore cognitive function. As oxytocin is already being tested in clinical trials with children with autism and other intellectual disabilities, it is important to examine how oxytocin treatment during development effects normal development of functional networks.

Keywords: Fragile X; oxytocin; cognition; behavior; autism;

Poster Location: 7

Role of the Cytoplasmic Polyadenylation Element Binding Protein 3 Ribozyme in Cortical Neurons

Chen, Claire, MS; Li, Xiang, Ph.D; Ke, Ke, Ph.D; Bredy, Timothy W., Ph.D Lupták, Andrej, Ph.D

Department of Pharmaceutical Sciences Queensland Brain Institute, The University of Queensland

Synaptic plasticity is a dynamic process by which neurons alter their synaptic strength in response to neuronal activity. Regulation of mRNA translation and de novo protein synthesis are essential for synaptic formation and neural communication. Cytoplasmic polyadenylation element-binding proteins (CPEB) is sequence-specific RNA binding proteins that have been shown to regulate polyadenylation-induced mRNA stability in dendrites and thereby mediate synaptic plasticity. Previous clinical studies have demonstrated that a single nucleotide polymorphism (SNP) in the intronic sequence of CPEB3 is associated with human episodic memory. Notably, the intronic sequence in which this allele of SNP is located has been identified as a ribozyme, a catalytic RNA capable of efficient self-scission. However, how CPEB3 ribozyme regulates mRNA expression in neurons remains unexplored. In this study, we investigated the role of CPEB3 ribozyme in regulating its mRNA expression in response to neuronal stimulation. Primary cortical neurons were stimulated by potassium chloride (KCl) or glutamate application, and gene expression of CPEB3 was examined at various time points. CPEB3 mRNA expression is up-regulated at two hours after glutamate stimulation, yet it is down-regulated at prolonged time points, which is correlated with the CPEB3 ribozyme expression. Similarly, membrane depolarization by KCl resulted in an up-regulation of mRNA and ribozyme at one hour compared with unstimulated cultures. Repeated KCl-induced depolarization led to a reduction in CPEB3 mRNA expression, whereas, CPEB3 ribozyme expression was elevated. Collectively, those results suggested that the self-cleaving CPEB3 ribozyme might regulate mRNA and protein expression of CPEB3 in neurons, and this activity-dependent induction might contribute to neuroplasticity.

Keywords: CPEB3; Ribozyme; Neuroplasticity;

Poster Location: 8

N-acetylcysteine (NAC) treatment can reverse cisplatin-induced cognitive damage in rats

Lomeli, Naomi, B.S. (1); Di, Kaijun, Ph.D (2,3); Czerniawski, Jennifer, Ph.D. (4,5); Guzowski, John F., Ph.D. (4,5) ; Bota, Daniela A., MD/Ph.D (1,2,3,6)

(1) Department of Pathology & Laboratory Medicine, University of California Irvine (2) Department of Neurological Surgery, University of California Irvine (3) Chao Family Comprehensive Cancer Center, University of California Irvine (4) Department of Neurobiology & Behavior, University of California Irvine (5) Center for the Neurobiology of Learning & Memory, University of California Irvine (6) Department of Neurology, University of California Irvine

Objectives: Chemotherapy-related cognitive impairment (CRCI) is commonly reported following the administration of chemotherapeutic agents and comprises a wide variety of neurological problems. Here we examined the hypothesis that cisplatin-induced neural toxicity and cognitive impairments derive from mitochondrial damage resulting in increased oxidative stress. We also assessed the protective effects of the antioxidant, N-acetylcysteine in mitigating cisplatin-induced damage. Methods: Adult male rats received 6 mg/kg cisplatin in the acute studies. In chronic studies, rats received 5 mg/kg cisplatin or saline intraperitoneally once per week for 4 weeks. N-acetylcysteine (250 mg/kg/day) or saline was administered for five consecutive days during cisplatin treatment. Cognitive testing was performed 5 weeks after treatment cessation. Cisplatin-treated cultured hippocampal neurons and NSCs were tested for changes in mitochondrial function, oxidative stress, caspase-9 activation, and neuronal post-synaptic density-95 (PSD-95) density. Results: Acute cisplatin treatment reduced dendritic branching and spine density, and induced mitochondrial degradation. Rats receiving the chronic cisplatin regimen showed impaired performance in three cognitive tasks and increased hippocampal cell death. Cisplatin induced mitochondrial DNA damage, impaired respiratory activity, increased oxidative stress, and activated caspase-9 in cultured hippocampal neurons and NSCs. N-acetylcysteine treatment prevented free radical production, ameliorated apoptotic cellular death, PSD-95 puncta loss, and partially reversed the cisplatin-induced cognitive impairments. Conclusions: Our results suggest that mitochondrial dysfunction and increased oxidative stress are involved in cisplatin-induced cognitive impairments. Therapeutic agents, such as N-acetylcysteine, may be effective in mitigating the deleterious effects of cisplatin.

Keywords: cisplatin; N-acetylcysteine (NAC); oxidative stress; chemotherapy-related cognitive impairment (CRCI); hippocampal damage;

Poster Location: 9

Multimodal optical imaging reveals rapid changes in absorption, scattering, and perfusion in the brain during cardiac arrest and post-resuscitation recovery

Wilson, Robert H., Ph.D.; Crouzet, Christian, M.S.; Torabzadeh, Mohammad, M.S.; Bazrafkan, Afsheen, B.S.; Hosseini-Farahabadi, Maryam, M.D.; Donga, Dishant; Choi, Bernard, Ph.D.; Akbari, Yama, M.D.,Ph.D.; Tromberg, Bruce, Ph.D.

University of California, Irvine Beckman Laser Institute; Department of Biomedical Engineering; Department of Neurology; School of Medicine

Over 565,000 people in the United States are affected each year by cardiac arrest (CA), and only a small percentage of these patients regain neurological function at or near their baseline levels. This poor outcome is largely attributed to the ischemic effect of CA on the brain, as well as the lack of reliable interventional techniques to improve reperfusion following cardio-pulmonary resuscitation (CPR). To obtain increased insight into the relationship between cerebral hemodynamics and electrical activity during CA and post-CPR, we developed a multimodal monitoring platform including optical imaging and electroencephalogram (EEG). We used this instrumentation to continuously monitor the brain in a clinically-translational rodent model of CA and CPR that mimics an intensive care setting. The rapid optical technology includes spatial frequency domain imaging (SFDI) and laser speckle imaging (LSI). SFDI obtains information about tissue hemoglobin concentration, oxygenation, and scattering at frame rates of up to 14 Hz. LSI provides spatial maps of blood flow at frame rates of up to 60 Hz. These techniques allow us to observe the spatiotemporal dynamics of parameters related to tissue perfusion, oxygenation, metabolism, morphology, and composition, throughout the experiment. We can visualize and quantify hyper-dynamic changes in these parameters even at times when the EEG has gone flat and there are no prominent fluctuations in the mean arterial blood pressure. We consistently observe changes in these parameters that coincide with entry into cardiac arrest, initial recovery of cerebral blood flow following CPR, and resumption of EEG activity. Using this data, our multimodal system has the potential to serve as a "test bed" for assessing the response of the brain to clinically-translatable interventional techniques during and immediately after CPR to promote cerebral reperfusion and improve neurovascular outcome.

Keywords: cardiac arrest; resuscitation; brain imaging; optical imaging; cerebral perfusion;

Poster Location: 10

Tinnitus Treatment Using a Novel Web-Based CBT Application: A Pilot Study

Moshtaghi, Omid, BS; Ghavami, Yaser, MD; Sahyouni, Ronald, BA; Giriraj K. Sharma, MD; Jay M. Bhatt, MD; Hossein Mahboubi, MD; Afsheen Moshtaghi, BS; Harrison W. Lin, MD; Hamid R. Djalilian, MD

Division of Otology, Neurotology, and Skull Base Surgery, Department of Otolaryngology – Head and Neck Surgery (All authors), and Biomedical Engineering (RS, HRD), University of California, Irvine, Irvine, CA

Objective: To evaluate the efficacy of web-based cognitive behavioral therapy (CBT) in the management of patients with chronic tinnitus. Study Design: Pilot clinical trial. Setting: Tertiary care medical center. Intervention: The subjects completed an online course spanning 8 to 10 weeks. During the online course, subjects were educated on the pathophysiology and management strategies for tinnitus in addition to cognitive behavioral therapy (CBT). The CBT modules included guided meditation, recognizing and controlling stress, and restructuring negative thoughts. Results: A total of 18 subjects with tinnitus were enrolled with 11 subjects (61%) completing the study. Mean age was 57±17 years. Paired sample t-test analysis of pre- and post-course surveys showed a mean difference of 21 in the Tinnitus Handicap Inventory (THI) (p=0.002). There was no statistically significant change in pre- and post-course psychoacoustic tinnitus measurements, or in depression, anxiety, stress, or post-traumatic stress disorder scores. Conclusions: Internet-based CBT is a potentially effective modality for providing patients suffering from chronic tinnitus a tool to manage symptoms. Our results indicate that web-based CBT helps reduce tinnitus the subjective loudness of tinnitus and impact it has on daily living as measured by the tinnitus handicap inventory.

Keywords: CBT; Tinnitus; therapy; clinical trial; internet based;

Poster Location: 12

90 Year Olds are Less Likely to Fall if they were Physically Active Two Decades Earlier: The 90+ Study

Greenia, Dana R.N., M.S.; Paganini-Hill, Annlia Ph.D.; Sajjadi, S.Ahmad M.D., Ph.D; Kawas, Claudia M.D.; Corrada, Maria Sc.D.

Institute for Memory Impairments and Neurological Disorders Department of Neurology

90 Year Olds are Less Likely to Fall if they were Physically Active Two Decades Earlier: The 90+ Study Dana Greenia RN MS, Annlia Paganini-Hill PhD, S. Ahmad Sajjadi MD PhD, Claudia Kawas MD, Maria Corrada, ScD OBJECTIVE: To determine if physical activity reported 24 years earlier is associated with the risk of falling and to examine factors related to falls in the oldest-old. BACKGROUND: The risk of falls and injuries sustained from falls increase with age. Although risk factors for falls in the elderly have been well characterized, only limited information is available about the oldest-old, people 90 years and older. METHODS: The study included 1536 participants from The 90+ Study, a longitudinal investigation of aging and dementia in the oldest-old. Participants were originally members of the Leisure World Cohort Study (LWCS), an epidemiological study of life style practices. Falls (yes/no) were reported by a participant or informant at the baseline examination of The 90+ Study. Other factors also reported at the baseline examination and known to be related to falls in younger elderly were also examined. Physical activity information was collected in the LWCS 24 years earlier (range: 16-34) and was reported as 15 minutes, 30-45 minutes, or 1+ hour/day. Using logistic regression we examined the relationship between physical activity reported approximately 24 years earlier and falls. RESULTS: At The 90+ baseline visit, participants were on average 94 years (range=90-107), most were women (78%), and had at least a college degree (52%). Falls were reported by 52% (N= 799) of participants and were associated with a higher number of prescription medications, history of TIA or stroke, depression, arthritis, vision disease, heart disease, presence of dementia, and use of assistive devices. After adjusting for potential confounders, and compared to people who reported no physical activity, activity of 30+ minutes/day was associated with approximately a 30

Keywords: Oldest-Old; Falls; Exercise; Physically Active; Risk of Falls;

Poster Location: 13

Variable Clinical Features in Patients with Fabry Disease

Tapia, Daisy, BS; Hall, Katherine, MS, GC; Alandy-Dy, Jousef, BS; Knight, Margaret; Lombardo, Dawn, DO; Pahl, Madeline, MD; Kimonis, Virginia; MD

Division of Genetics and Genomic Medicine, Department of Pediatrics, Division of Cardiology, Division of Nephrology, Department of Medicine University of California, Irvine

We report our experience with Fabry disease in a multidisciplinary clinic in UC Irvine. Our cohort comprises 20 patients (9 adult males, 9 adult females and two male children) ranging in age from 7- 63 y., with age of diagnosis ranging from 3-57. The data shows that 42% of all patients suffer gastrointestinal problems, 53% have reduced sweating, 60% have angiokeratomas, 65% exhibit corneal whorls, 25% have lymphedema, and 90% of the male patients experienced acroparesthesia. 53% of adults have tinnitus, 41% of adults experience hearing loss. There is renal involvement in 35% of patients, most have varying levels of proteinuria but one required a kidney transplant. Thirty-two percent of patients have evidence of cardiomyopathy determined by echocardiogram and MRI studies. One male had a stroke and currently has MRI changes of multifocal encephalomalacia and adjacent gliosis of the left cerebral hemisphere, frontal and parietal lobes. Ninety percent of the males, 44% of the females, and 50% of the children currently receive enzyme replacement therapy (ERT). Each individual demonstrates different response rates to symptom improvement and slowing of organ deterioration. Two individuals developed infusion reactions, one male developed ERT associated meningitis in 2009 which prompted him to end treatment. He re-initiated ERT May 2015 and has continued to tolerate ERT with premedication. ERT will be initiated in the 6 year old male for reduced GFR, a urine GL-3 level of 569µg/mmol Cr. Clinical features are phenotypically heterogeneous, perhaps due to the variety of unique mutations in the GLA gene. Monitoring patients regularly provides insight into genotype- phenotype correlations thus leading to optimization of patient care.

Keywords: Fabry; Clinical Features; Variable;

Poster Location: 14

Variable Clinical Features in Pompe Disease Associated with Novel Mutations

Alandy-dy,Jousef; Wencel, Marie; Hall,Kathy; Julie Simon; Abhilasha Surampalli; Jade Yang; Namita Goyal; Tahseen Mozaffar; Virginia Kimonis;

Division of Genetics and Genomic Medicine, Department of Pediatrics, University of California- Irvine, Orange, CA; Division of Neuromuscular Neurology, Department of Neurology, University of California- Irvine, Orange, CA; Dietitian & Nutrition Services, University of California- Irvine, Orange, CA.

Pompe disease is a lysosomal storage disorder caused by the deficiency of enzyme acid alpha-glucosidase (GAA) which results in accumulation of glycogen particularly in the skeletal, cardiac, and smooth muscles. The late-onset form with symptoms presenting in childhood through adulthood, is characterized by proximal muscle weakness, and respiratory insufficiency. We report our experience with 17 adult patients (4 F/13 M) with Pompe disease at one center, several of whom had unique findings and novel mutations. Patients ranged in ages from 18-69 y. (mean 51 y.) and were diagnosed at a range of 11-65 y (mean 37 y.) often after a history of progressive muscle disease of several years duration. Genetic sequencing revealed that 15/17 individuals had the common c.-32-13T>G mutation, and eight had 6 novel mutations: c.1594G>A, c.2431delC, c.2655_2656delCG, c. 1951-1952delGGinsT, c.525_526delTG, and c.1134C>G. A male with the c.1594G>A mutation developed an intracerebral aneurysm at the age of 43 y. treated with surgery. Another male with the c.525_526delTG developed testicular cancer and is in remission. Cardiomyopathy was noted in an adult with the c.525_526 delTG mutation, and peripheral neuropathy in a male with the c. 1951-1952delGGinsT. Two siblings with the c.2655_2656delCG developed very high antibody titers, one of whom developed a severe infusion reaction. Other clinical features included scoliosis and cardiomyopathy in an adolescent, BiPAP requirement in eleven, and tinnitus in five. All patients currently receive alglucosidase alfa with different response rates in their muscle weakness, pulmonary function dynamometry, and functional studies. Our patient cohort illustrates the variable range of clinical features, and alert us to the importance of careful monitoring and early management of these complications. Possible genotype-phenotype associations with these novel mutation will emerge with larger studies.

Keywords: Pompe; Enzyme replacement; myopathy; Genotype-Phenotype; Respiratory insufficiency;

Poster Location: 15

Anti-diabetic Effects of Ileal Transposition Surgery on Obese mice

Shiri Li, PhD; Alessio Pigazzi, MD, PhD

Bariatric surgery (BS) has proved to be the most effective long-term treatment for type 2 diabetes in obese patients independent of the consequent weight loss. However, the mechanisms remain poorly understood. On the basis of the nutrient pass patterns, BS is divided into restrictive and gastrointestinal bypass procedures. It has been postulated that the entry of nutrients into the distal small intestine after roux-en-Y or other intestinal bypass procedures elicits a neuroendocrine response that causes improved glucose homeostasis, which is called "ileal break" mechanism. Ileal transposition (IT), one type of BS, which is exclusively a hindgut procedure to produce weight loss and significantly improve glycemic control, involves translocation of a segment of the distal ileum proximally into upper jejunum without altering the length of gastrointestinal tract or gastric restriction. Several bariatric surgical procedures that mimic clinical setting has been developed on mouse model except IT procedure due to restrictions imposed by surgical technical issues. In this study, we aimed to improve surgical technique in order to successfully establish IT surgical procedures on mouse model and examine the anti-diabetic effects of IT surgery on high-fat diet (HFD) induced obese mice. By performing side-to-side fashion of enteroenterostomy with a single layer continuous 10-0 suture, we succeeded in establishing IT surgical procedure on HFD-induced obese mice. IT group showed significantly body loss and improved daily blood glucose after surgery compared to IT sham group. An intraperitoneal glucose tolerance test (IPGTT) was performed at week 2 and 4 after surgery and a significant decrease in total area under the curve for blood glucose was noted in the IT group in comparison to IT Sham group. This successful procedure of IT surgery will open a novel avenue and opportunity to further study the possible mechanisms underlying IT surgery by using specific knockout mice.

Keywords: Bariatric surgery; Diabetes; Obese mice; Ileal transposition;

Poster Location: 16

Development of novel biologic and nanotechnology-based therapeutic agents to enhance insulin secretion and counter beta cell dysfunction and loss in diabetes

Chessler, Steven, MD, Ph.D.; Gruzman, Arie-Lev, Ph.D.; Lee, Abraham, Ph.D.; Donald Lee; Anna Munder; Michelle Shih-Hui Lee, Jean-Paul Lellouche, Derek Vallejo

UC Irvine, Department of Medicine, UC Irvine, Dept of Biomedical Engineering Bar Ilan University, Dept. of Chemistry and Institute for Nanotechnology

Dysfunction and loss of the insulin-secreting pancreatic beta cells are central to the development of diabetes. In type 2 diabetes, ever more aggressive therapy and then insulin treatment become necessary in the face of worsening beta-cell failure and depletion. In type 1 diabetes, insulin therapy is necessary at the outset. Only two classes of drugs target the beta cell: sulfonylureas (and meglitinides) and GLP-1-related agents. These increase insulin secretion but do not act on the key pathogenic mechanisms: beta cell dedifferentiation and loss. Neuroligin-2 (NL2) and neurexin (Nrxn) are transmembrane proteins originally identified in the brain. There they engage in trans-cellular interactions essential for GABAergic synapse formation and function. We have found that NL2 and Nrxn are present on the beta cell surface and, through similar extracellular interactions, promote beta-cell proliferation, function, and resistance to injury. NL2 activates the protein gephyrin and triggers the formation of GABAergic signaling mechanisms, both recently found to be potent drivers of beta-cell regeneration and promising therapeutic targets. To test the utility of targeting the NL2-Nxn interaction, we designed an NL2 peptide based on the Nxn binding site and also produced a recombinant protein incorporating the NL2 extracellular domain. These were separately clustered by attachment to nanoparticles and artificial lipid vesicles. Dose-response and time course studies with beta cells showed that these reagents increase insulin secretion, insulin content and resistance to oxidative stress. The candidate agents also increase beta cell proliferation, expression of maturational markers and, in a pilot study with diabetic mice, reduced blood glucose levels. In summary, we have developed and tested promising therapeutic agents based on a novel mechanism—the neuroligin-neurexin interaction—and provided proof of principle for the value of this mechanism as a therapeutic target.

Keywords: Diabetes; Insulin; Nanotechnology; Nanoparticles; Therapy;

Poster Location: 17

A Novel Approach to Calculate Work Rate on a Treadmill (TM) in Early-and Late-pubertal Children

Ronen Bar-Yoseph MD; Shlomit Radom-Aizik PhD; Dan Cooper MD; Janos Porszasz MD, PhD; Pearl Law

1) Pediatric Exercise and Genomics Research Center, Department of Pediatrics, UCIrvine 2) Rehabilitation Clinical Trials Center, Division of Respiratory & Critical Care Physiology & Medicine, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, USA 3) UCI Institute for Clinical and Translational Science

Childhood obesity and children who survive previously fatal diseases and conditions highlight the need for rigorous metrics of fitness in children and across the lifespan. Cardiopulmonary exercise testing (CPET) data in children must be scaled to the magnitude of the metabolic perturbation. In CPET using cycle ergometry (CE), the external work (WR) is readily determined. With TM testing WR is hard to estimate from its key elements of speed, incline, and body mass (S, I, M) given the complexity of the mechanics of energy cost as S and I change. PURPOSE: To estimate WR associated with TM exercise (S,I,M) in early and late pubertal boys. METHODS: Our strategy involved: 1) Using CE to establish the regression coefficient (a) and intercept (b) from the linear equation $V?O2=a?WR+b$; 2) assuming the same relationship we estimated work rate (WR') from the $V?O2$ measured on TM using S, I, M (Fig A) and S2, I, M (Fig B); 3) analyzed the regression parameters from the function $WR'=a?(S2,I,M)+b$ in 10 early pubertal (mean age 9.8 y/o, tanner stage 1-2) and 10 late pubertal boys (15.8 y/o, tanner stage 4-5), performed CPET on CE and TM. RESULTS: WR' was moderately and non-linearly correlated with $S?I?M$ (mean $r=0.61$, Fig A). However mean $r=0.96$ and linear relationship was found with $WR'=a?(S2?I?M)+b$, (Fig B). Further, the slope (a) was significantly higher in the younger (0.0395 ± 0.006) compared with the older boys (0.0316 ± 0.008 ($p=0.017$). CONCLUSION: This approach enables CPET data interoperability between TM and CE. WR' seems to be a square function of S, making it a linear function of kinetic energy ($MS2$). CPET slopes (e.g., $?V?O2/?WR$ or $?HR/?WR$) can be calculated and provide useful insights into disease mechanisms and progression in children and adults, when maximal efforts are questionable. The maturational related differences between WR' and SIM suggest a biological difference in the efficiency of muscular work as children grow and develop. Supported by NIH P01HD-048721 & P

Keywords: Work rate; Cycle ergometer; Treadmill;

Poster Location: 18

Improving Parental Satisfaction with Children's Surgery using A Tailored Web-Based Surgical Preparation Program (WebTIPS)

Vivero, Marla, B.A.; Fortier, Michelle, Ph.D.; Stevenson, Robert, B.A.; Dina Khoury, B.A.; Eva L. Maurer, B.S.; Zeev N. Kain, M.D., M.B.A.

Anesthesiology & Perioperative Care, University California-Irvine School of Medicine

Behavioral preparation programs are effective in decreasing preoperative anxiety and postoperative pain. Healthcare delivery and reimbursement systems are under reorganization with a particular focus on improving the health of populations, individual experience, and reducing the costs of care using the Triple Aim Model. The purpose of this pilot study was to examine the impact of a newly developed, web-based, tailored behavioral preparation program (WebTIPS) on parent satisfaction with pain management when compared to usual care. A total of 14 parent-child dyads participated. Eligible children were English-speaking, between the ages of 2 to 7 years, American Society of Anesthesiologists status I or II, and underwent outpatient elective surgery and general anesthesia. Parents of children scheduled for surgery accessed WebTIPS at least two days prior to surgery and completed items from the National Research Corporation to assess satisfaction with pain management following surgery. Current NRC data were compared to NRC data collected from parents of children who had outpatient surgery in the last 12 months. Compared to usual care, a greater percentage of parents in the WebTIPS group were satisfied with their child's pain control (20.4% increase) and with how the hospital staff cared for their child (11.2% increase). Qualitatively, parents were highly satisfied with WebTIPS, providing feedback such as WebTIPS "really helped him [child]", "helped answer a lot of questions and [made me] feel more prepared", and "made a great difference in our experience." Results from this pilot study showed that use of a tailored, web-based behavioral preoperative preparation program (WebTIPS) resulted in improved parental satisfaction with pain management compared to standard hospital care. Because the items impacted are among the top predictors of overall patient satisfaction, we conclude that WebTIPS has the potential to improve overall parent satisfaction with children's surgery.

Keywords: pediatrics; perioperative pain; web-intervention;

Poster Location: 19

Four months of a School Based Exercise Intervention Improved Fitness in normal weight and overweight/obese Children with Asthma in a minority, low SES population - a pilot study

Lu, Kim MD; Cooper, Dan MD; Haddad, Fadia PhD; Lakes, Kimberley PhD; Radom-Aizik, Shlomit PhD

Pediatric Exercise and Genomics Research Center

Rationale: Fitness can improve asthma management. However, children from poor minority communities engage less in physical activity, and have increased asthma disease burden. The goal of this pilot study is to evaluate 1) the feasibility of an exercise intervention in a school setting; 2) the effect of the intervention on fitness and asthma outcomes in children with asthma. Methods: Nine children, ages 7-11 years, from 2 elementary schools in Santa Ana, CA, a population with high percentage of Hispanic and low socioeconomic status, participated in the study. Training sessions occurred at the schools during afterschool hours (3 sessions per week, 45mins long) for 4 months. Before and after the intervention, evaluations included pulmonary function testing, cardiopulmonary exercise testing, assessments of habitual physical activity, body composition, and executive function testing. Blood was obtained at baseline and after training . Results: All 9 participants completed the study. Average attendance of exercise sessions was 84.5%. Three of the participants were normal weight, 3 were overweight and 3 were obese. Four of the 9 participants had persistent asthma. Aerobic fitness levels improved significantly with 9.4% (SE±1.7) improvement in peak VO2 after training. There was a significant improvement in lean body mass of 9.2% (SE±0.5). Two of the 4 participants with persistent asthma were able to decrease their controller medications. Participants improved significantly on a computer administered executive function (EF) task that measures inhibitory control and shifting, [t (6) = -4.324, p=.005]. Conclusion: By designing a pilot school based exercise intervention for children with asthma with significant engagement from the schools and families, we showed good evidence of feasibility and acceptability in a predominantly poor and minority population. The exercise intervention was effective with improvement in aerobic fitness, setting the stage for larger studies.

Keywords: asthma; exercise; obesity; children;

Poster Location: 20

Team KiPOW Lite: A Replicable School-Based Academic-Community Partnership to Improve Pediatric Health Behaviors

Nagpal, Nikita, MD; Narayanan, Nisha, MD; Nam, Jennifer; Alexa Love; Hillary Zieve; Leesa Li; Heather Wright; Candice E. Taylor Lucas; Lishi Zhang; Aashay Vyas

1. Pediatrics, UC Irvine-Children's Hospital of Orange County, Orange, CA, United States. 2. Pediatrics; Pediatric Exercise and Genomics Research Center, University of California Irvine, School of Medicine, Irvine, CA, United States. 3. University of California, Irvine School of Medicine, Irvine, CA, United States.

Team Kid Power (KiPOW) is an academic-community partnership that increases healthcare provider face-time with children to combat pediatric obesity. 10-week pilot programs in Washington DC and Orange County schools demonstrated improved weight, blood pressure, and health behaviors. The replicability of KiPOW is challenged by unique school curricular requirements, thus the impact of an abbreviated 5-week program (KiPOW Lite) was evaluated. n=90 5th graders from a Title 1 school [Intervention: 53 (55% female); Control: 37 (60% female)]. Medical and college students visited the intervention group for 70 minutes weekly over 5 weeks. They ate school lunch with them, taught health lessons, and lead active play during recess. Pre-post weight, height, BMI, and BP were obtained. Health behaviors were assessed via a modified HABITS questionnaire. Two-sample paired t-test was used to detect pre and post intervention change. A generalized linear mixed model was used to test the difference of pre-post change between intervention and control groups adjusting for gender and baseline. Random effect for each class was included in the model to account for within-class correlation. KiPOW Lite was implemented in 5 weeks. Mean baseline BMI was the 80th percentile. In unadjusted analyses, significant reductions were noted in the intervention group for weight (p=0.0462), and BMI (p=< 0.0001). A decreased trend in diastolic BP in the intervention group (p=0.0555), and an increased trend in systolic BP in the control group (p=0.0715) were noted. Pre-post changes in weight and BMI were not significant after adjusting for gender, baseline, and within-class correlation. Team KiPOW is a replicable model that may be a feasible adjunct to reinforce wellness policy in many school districts. Its ability to affect weight, BMI, and health behaviors in 5 weeks is limited. Further evaluation of the dose-effect during full-length implementation of KiPOW in three Orange County schools is needed.

Keywords: Obesity; School-based intervention; Health coaching;

Poster Location: 21

The Collective Impact of California's Approach to Smarter Lunchrooms

Mills, Mary Ann MPH; Young, Shannan RDN, SNS; Reed, Heather MA, RDN; Robertson, Trina MS,RDN

UC CalFresh Nutrition Education Program, UC Davis Dairy Council of California California Department of Education

Background: The mission of the Smarter Lunchrooms Movement of California (SLM of CA) is to provide training and technical advising for school foodservice in California on the Smarter Lunchrooms Movement theory and practices created by Cornell's Center for Behavioral Economics in Child Nutrition Program funded by the USDA. Smarter Lunchrooms Movement (SLM) uses evidence-based strategies for the promotion of healthful eating behaviors using low- and no-cost practices. Objectives: The SLM of CA objectives are to train 300 school districts in California on the SLM principles and practices, engage 50% of these school districts in implementing at least one SLM principle by 2016 with help from TAPs, and link SLM principles to ongoing nutrition education programs. Methods: The SLM of CA collaborative trained foodservice staff on how to implement SLM principles in cafeterias, created a team of TAPs who provide SLM consultation to school and foodservice staff, and provided ongoing support to the SLM community through webinars, newsletters, website resources and best practices. Results: The SLM of CA collaborative has trained 272 California school districts and approximately 800 school district staff through a highly rated two-part workshop series. In addition, 85 UC CalFresh and Dairy Council of California TAPs were trained between 2013 - 2015. Conclusion: SLM of CA facilitates trainings to school districts throughout the state and expects to exceed the goal of training 300 school districts. School districts that have implemented SLM principles reported success in increased selection of targeted entrees, fruit, milk, and salad bar participation. The collaborative has also successfully linked SLM principles and practices to nutrition education programming while providing a comprehensive approach to obesity prevention.

Keywords: Behavioral economics; School meals; Childhood obesity; Nutrition; School-based health;

Poster Location: 22

Governing Drug Metabolism: Rational Design of CYP3A4-based Pharmacoenhancers.

Samuels, Eric

Department of Pharmaceutical Sciences, University of California Irvine

Human cytochrome P450 3A4 (CYP3A4) is the most abundant and clinically relevant drug metabolizing enzyme. In particular, CYP3A4 is involved in the metabolic clearance of most commonly used anticancer agents, including taxanes, topoisomarase I and II inhibitors, vinca alkaloids, hormonal therapies, and newer targeted treatments such as gefitinib and imatinib. Carefully controlled inhibition of CYP3A4 can increase the bioavailability and efficacy of drugs that would otherwise be rapidly metabolized. Controlled inhibition is already being exploited in HIV and HCV treatment, where ritonavir and its derivative cobicistat (Figure 1) are used as pharmacoenhancers for antiviral drugs. Both ritonavir and cobicistat have multiple side effects and neither were designed based on the CYP3A4 structure. Our goal: to design more specific and potent CYP3A4 inhibitors that can serve as pharmacoenhancers for the treatment of long-term pathological conditions such as cancer, organ transplants, and viral infection.

Keywords: None

Poster Location: 23

Revisiting the Model Minority Myth among Asian Americans: Assessing Indicators of Physical Health Status and Social-Emotional Wellbeing of Cambodian Americans Residing in Southern California.

Sharif, Mienah Zulfacar, Ph.D.; Biegler, Kelly, Ph.D; Mollica, Richard, MD, M.A.R.; Susan Elliot Sim Ph.D ; Elisa Nichols MD ; Maria Chandler MD, MBA ; Quyen Ngo-Metzger MD, MPH; Kittya Paigne MD; Sompia Paigne LCSW; Dara H. Sorkin PhD

Sharif, Biegler, Sorkin: University of California, Irvine, Department of Medicine Mollica: Harvard Medical School, Department of Psychiatry Sim: University of Toronto, Faculty of Information Nichols and Chandler: University of California, Irvine, Department of Pediatrics Ngo-Metzger: US Preventive Services Task Force, Agency for Healthcare Research and Quality Paigne: The Community Medical Wellness Center in Long Beach

Background: Asians are largely understudied in health research and are often aggregated into one homogenous group thereby disguising disparities prevalent across subgroups. Cambodian Americans are one of the largest refugee communities in the United States and may be at high risk of adverse health outcomes considering their pre-and post-migration low socioeconomic positions. This study provides a profile of the health status in the largest community of Cambodian Americans in North America. Methods: Data were collected via questionnaires and medical records from two community clinics in Southern California (n=383). Cambodian American patients 18 years of age or older were invited to participate. Results: The results yielded mixed findings. Overall, respondents reported poor health outcomes, suboptimal health behaviors, and low levels of health-related quality of life. However, participants overwhelmingly held positive perceptions of their experience within the healthcare setting. Discussion: There is a need for more health promotion efforts among Cambodian Americans in order to improve their health behaviors, perceived wellbeing and health outcomes.

Keywords: immigrant health; disparities; Cambodian Americans; pyschosocial factors;

Poster Location: 25

Racial and Socioeconomic Disparities in Bladder Cancer Survival: Analysis of California Cancer Registry

Martin, Jeremy; Youssef, Ramy, MD; Bettir, Kheira; Jenny Chang, MS, Rahul Dutta BS, Simone L. Vernez, BA, Argyrios Ziogas, PhD, Hoda Anton-Culver, PhD, Nguyen, Nobel B.S.

1. Department of Urology, University of California, Irvine 2. Department of Epidemiology, University of California, Irvine

Objective: Herein, we examined the California Cancer Registry (CCR) to determine bladder cancer survival disparities based on race, socioeconomic status (SES), and insurance type in California patients. Methods: The CCR was queried for bladder cancer cases in California from 1988 –2012. Survival analyses were performed to determine prognostic significance of racial and socioeconomic factors. Results: 72,452 cases were included (74.5% men, 25.5% women). Median age was 72 (range 18-109). 81% were white, 3.8% black, 8.8% Hispanic, 5.2% Asian, and 1.2% others. SES was stratified by quintile. In black patients, tumors presented more frequently with non-urothelial histology, advanced stage, and high-grade and in females. Medicaid patients tended to be younger and had more advanced stage and high-grade tumors compared to patients with Medicare or managed care (p < 0.0001). Kaplan-Meier analysis demonstrated significantly poorer 5-year DSS in black, low SES, and Medicaid patients (p < 0.0001). Multivariate analysis revealed that black race (DSS HR 1.295, 95% CI: 1.212 – 1.384), lowest SES (DSS HR 1.325, 95% CI: 1.259 – 1.395), and Medicaid insurance (DSS HR 1.349, 95% CI: 1.246 – 1.460, p < 0.0001) were all independent prognostic factors (all p < 0.0001) after controlling for stage, grade, age, and gender. Conclusions: Analysis of California Cancer Registry demonstrated that black ethnicity, low SES, and Medicaid insurance portend poorer disease-specific survival, after adjusting for classic clinicopathological features.

Keywords: bladder cancer; tumor; females;

Poster Location: 26

Clinics' Clientele Characteristics

Vo, Baotran N., M.D.

The An Lanh student-run free clinic began operation in Spring of 2014 to serve the under served community in Garden Grove. The clinic has been gathering patient demographics with the hopes of better serving the Garden Grove community. It was found that the majority of patients surveyed at the free clinic had a household income of less than $40,000 along with an employment status of either unemployed or holding a part-time position. Results also revealed that 72% of this population had high school level of education or lower and only 38% of the population had proof of citizenship in the United States. 22% of the patients surveyed reported having diabetes, 10% with back complications, and 10% with arthritis. These results provide insight into characteristics of patients served in Garden Grove; however, the researchers felt the data was insufficient to represent the entirety of the disadvantaged demographic. As a result, the researchers decided to turn this project into a community health assessment in conjunction with the Flying Samaritans that operate free clinics in Mexico.

Keywords: Family Medicine; Health Assessment; Demographics; Orange County;

Poster Location: 27

Clinic in the Park: A One-Stop-Shop Model Bridging Medicine to Public Health

Agran, Phyllis, MD/MPH; Murray, Sandra, MD; Billimek, John, PhD; Tam Au, BS; Hae In Kim, BA

University of California, Irvine, School of Medicine and UC Irvine Health Clinic in the Park, OneOC fiscal project

Background: Founded in 2011, Clinic in the Park is a pediatrician-led project of The Federal and AAP Healthy Tomorrows Partnership for Children. We are a multidisciplinary health collaborative designed to connect children to services, perform screenings, and deliver health education. Using public space, Clinic in the Park offers a 'one stop shop' model of health promotion within under-served neighborhoods in OC. Goals & Objectives: (1) Increase Access to health and social services in trusted community settings: parks, schools, resource centers. (2) Provide Venues where health professionals; public, academic institutions/ organizations; community agencies; and individuals collaborate to provide one-stop-shop services. (3) Develop Sustainable Community Service to collectively improve individual and community health. Methodology: Clinic in the Park works with our network of collaborators to provide a 'one stop shop' that includes a wide spectrum of resources and services. Each Clinic, through data collection and analysis, we review community needs, estimate cost savings/impact and produce outcomes reports. Results: Over 5 years, Clinic in the Park has increased from 15 to 50 collaborators and provided 71,398 services to 26,216 visitors. These services include connections to services and resources (including legal aid); health screenings; and child/adolescent safety education/tools. This year, we implemented and evaluated 4 new venues in under-served OC communities. An example is with Hoag Center for Healthy Living where 7,573 services were provided to 481 visitors. Most of our families do not have the opportunity to learn about their health outside of traditional medical offices. Conclusion: Clinic in the Park bridges medicine and public health, taking traditional health promotion into the community. We continue to increase capacity through new venue and service collaborators. Determining how to integrate this model into the health care system is our ultimate goal.

Keywords: None

Poster Location: 28

Developing capacity to conduct large-scale testing of an explanatory model of clinical nurse leader integrated care delivery: leveraging health system stakeholders

Bender, Miriam, PhD RN; Banks, Darla, MSN RN; Check, Dana, MSN RN; Houser, Andrea, PhD RN Marshall, June, DNP RN Murphy, Elizabeth, MBA RN Spears, Paula, DNSc RN Spiva, LeeAnna, PhD RN Williams, Marjory, PhD RN

Bender, UCI, Sue & Bill Gross school of Nursing Banks, Texas Health Resources Check, Gundersen Health System Houser, Gundersen Health System Marshall, Texas Health Resources Murphy, Mercy Health Saint Mary Hospital Spears, Texas Health Resources Spiva, WellStar Health System Williams, Central Texas Veterans Administration

Background: Clinical nurse leader (CNL) integrated care delivery is an innovative systems-oriented approach to catalyze patient care quality and safety, but lacks a generalizable evidence base, justifying a program of research that is feasible, scalable, and capable of translating this care delivery innovation into reliable and usable evidence for practice. Objective: We leveraged existing community-stakeholder and scientific connections to establish the research capacity to conduct multi-site studies designed to test an explanatory model of CNL integrated care delivery. Specific aims were to: identify variables that measure CNL model constructs; achieve consensus on key variables for inclusion in model testing research; and confirm variables can be operationalized with strong fidelity across diverse health systems. Results: The study team identified 82 instruments with the potential to measure CNL model constructs. There were general concerns about the sensitivity of instruments to measure CNL constructs, with consensus that further validation was required. The study team also reached consensus that the National Database on Nursing Quality Indicators (NDNQI) outcomes metrics, including falls, infection rates, staff turnover, and pressure ulcers, were valid metrics for measuring CNL outcomes. However, concerns were raised about the frequency of mandated changes in NDNQI metric definitions over time, which limits longitudinal research across settings. Implications: This capacity building research phase identified and addressed challenges inherent in measuring and comparing models of nursing care delivery across diverse care settings and linking them to improved patient quality and safety outcomes. Additional research on CNL Model operationalization is indicated to validate and develop metrics and instruments that support generalizable evidence on CNL practice integration.

Keywords: participatory research; nursing models; quality and safety; stakeholder engaged research;

Poster Location: 29

Exploring Multifactorial Aspects of Plaque Removal

Ho, Jessica BS; Ngo, William BS; Khasahi, Fatima BS; Forghany, Ali BS; Sahni, Karan BS; Wilder-Smith, Petra DDS, PhD

University California Irvine, Beckman Laser Institute

Objectives: To evaluate the effects of a novel anti-plaque formulation on the removal of dental biofilm. Specific aim was to elucidate the role of dessication vs mechanical forces on dental biofilm using a novel debriding solution and "static" vs "dynamic" treatments. Methods: Twenty-five extracted teeth underwent standard biofilm incubation over 4 days[1]. Then samples were randomized into 5 groups of 5 teeth each, stained with GUM®Red-Cote® (Sunstar Americas,Inc., Chicago, IL) plaque disclosing solution and imaged with high-resolution multi-photon microscopy (MPM) prior to treatment with HYBENX® Oral Decontaminant (EPIEN Medical Inc., St. Paul, MN, USA). Group 1 samples received a "static" 30s water dip; Group 2 a 20s "dynamic" exposure to a dental high pressure air/water syringe; Group 3 a "static" 30s dip rinse in the test agent followed by a "static" 30s dip rinse in water; Group 4 a "static" 30s dip rinse in the test formulation followed by 20s "dynamic" exposure to a high pressure air/water syringe; Group 5 a 20s "dynamic" application of test agent (20 seconds high pressure syringe at 10ml/s) followed by 20s "dynamic" exposure to a high pressure air/water syringe. Results: MPM images demonstrated the persistence of thick layer of biofilm on the tooth surface after water dip treatment. Similarly, test agent dip plus water dip only removed a few small irregular partial-thickness patches of biofilm. Samples exposed to air/water spray alone showed some disruption of the biofilm, leaving large heterogeneous residual biofilm areas over >50% of surface. Test agent dip treatment plus air/water spray left very small, thin, mostly partial-thickness scattered islands of biofilm. Application of dynamic test agent spray plus air/water spray removed the biofilm almost entirely. Conclusions: Test agent desiccant effect alone causes mild disruption of dental biofilm.Additional dynamic rinsing is required to achieve complete removal of dental biofilm.

Keywords: mulit-photon microscopy; biofilm; anti-plaque;

Poster Location: 30

Recent Epidemiological and Metabolic Trends in Stone Disease: Rising Hypocitraturia and Hyperoxaluria

Youssef, Ramy, MD; Martin, Jeremy; Bettir, Kheira; Khashayar Sakhaee, John Poindexter, Simone L. Vernez, Charles D. Scales, Glenn M. Preminger, Michael E. Lipkin

University of California, Irvine Department of Urology

Introduction: Metabolic factors underlying the recent increase in stone prevalence are unknown. Herein, we evaluate metabolic risk factors in stone patients from two different decades, comparing changes in metabolic profiles of stone formers over time. Methods: A retrospective review was performed of patients who underwent metabolic evaluation of urolithiasis with 24-hour urine collections at a single institution. There were 309 stone patients evaluated from 1988-1994 (group 1), and 229 patients from 2007-2010 (group 2). A comparison between both groups was performed to assess changes in demographics and metabolic profiles. Results: Comparing group 1 to group 2, the male: female ratio decreased from 1.3:1 to 0.8:1, obese patients (BMI ≥ 30) increased from 22% to 35%, and patients ≥ 50 y increased from 29% to 47% (all $p < .005$). A greater percentage of patients had hypocitraturia in the recent cohort (46% to 60%, $p = .001$), with hypocitraturia significantly more frequent in obese patients ($p = .005$). Hyperoxaluria was also increased in group 2 compared to group 1 (23% to 30% $p = .07$), a finding that was significant in males (32% to 53%, $p = .001$). Conclusions: Urolithiasis has increased in females, obese, and older patients, consistent with population based studies. We report a rising incidence of hypocitraturia and hyperoxaluria in the contemporary cohort, particularly in obese patients and in males, respectively. Further studies are needed to better characterize the metabolic changes corresponding to the increase in stone disease.

Keywords: Hypocitraturia; Hyperoxaluria; Obese; Females; Gouty Diathesis;

Poster Location: 31

Mortality outcomes in advanced chronic kidney disease associated with warfarin use: a retrospective cohort study

Lin, Mark, BS; Hanna, Medhat, BS; Streja, Elani, PhD; Melissa Soohoo MPH; Wei Ling Lau MD

University of California, Irvine Department of Medicine, Nephrology Division Harold Simmons Center for Kidney Disease Research and Epidemiology

Controversy exists regarding the benefits of warfarin therapy in chronic kidney disease (CKD) patients. CKD patients are at high risk for stroke and cardiovascular events, but are also prone to bleeding complications. Warfarin is also independently associated with arterial calcification acceleration. Our study aims to assess mortality outcomes associated with warfarin treatment in patients with stage 3-6 CKD needing anticoagulation therapy. In a retrospective matched cohort study, we identified 59 adult patients with stage 3-6 CKD initiated on warfarin from 2011-2013 at the University of California, Irvine Medical Center. Upon matching for gender and age+/-5 years 134 patients with stage 3-6 CKD who had indications for anticoagulation therapy but were not initiated on warfarin were identified. All-cause mortality risk associated with warfarin treatment was estimated using Cox regression analysis. Hazard ratios were adjusted for comorbidities and use of antiplatelet agents. At 5.6 years follow-up, use of warfarin in CKD/dialysis patients was associated with higher risk of all-cause mortality (hazard ratio [HR] 2.26; 95% confidence interval [CI] 1.35-3.78) compared to the warfarin-naïve group. This difference remained significant after multivariate adjustment for comorbidities (HR 2.39; 95%CI 1.42-4.03), use of antiplatelet agents (HR 2.55; 95%CI 1.51-4.31) and CKD stage (HR 2.80; 95%CI 1.63-4.82). After stratification based on CKD stage, warfarin had no effect on the risk of death for stage 3-4 CKD patients (HR 0.93; 95%CI 0.39-2.21). For stage 5 pre-dialysis patients and stage 6 chronic dialysis patients, warfarin use correlated strongly with higher all-cause death risk (HR 7.11; 95%CI 3.49-14.5). In this study, we report an association between warfarin use in CKD patients and increased all-cause mortality. After multivariate adjustment, this association remained strongly significant in end-stage renal disease patients but not in patients with stage 3-4 CKD.

Keywords: mortality; chronic kidney disease; warfarin; stroke; bleeding;

Poster Location: 32

Pregnancy Care Choices: Who Cares for You During Pregnancy, Labor, and Delivery?

Vo, Baotran N., M.D.

Multiple studies in the United States have shown that the number of deliveries performed by family physicians has declined. Family medicine physicians are often easier to have access to than specialists, but many individuals are unaware of the services that a family medicine physician can provide. The objective of this study was to observe if a change in patient perception on the prenatal and postnatal care services that can be provided by a family physician, through a short interventional survey. Research assistants gave interventional surveys to patients, eighteen years and older at clinics in the local Orange County clinics. Surveys questioned participant's preference with which health care professional they trust for prenatal care. Included after was an educational questionnaire with six yes or no questions assessing patient's knowledge about the care provided by family medicine doctors. Then they were reassessed with which type of health care provider they would go to for prenatal care. With over 400 responses collected, 32% chose a family medicine doctor initially. However, after the intervention, this percentage increased to 51%. Analysis was done with a two-tailed t-test, with a p value of 7.2×10^{-14}. Showing a significant increase in patients who are willing to choose a family medicine doctor for pre-and postnatal care, due to this short interventional survey.

Keywords: None

Poster Location: 33

UCI Consent-to-Contact Registry (C2C): A new tool for accelerating clinical research recruitment at UCI

Klein, Kirsten, BA; Cox, Chelsea G, MPH, MSW; Gombosev, Adrijana, MS, CCRP; Hoang, Dan, BS; Witbracht, Megan, PhD; Pierce, Aimee L, MD; Grill, Joshua D, PhD

Institute for Memory Impairments and Neurological Disorders (UCI MIND); Alzheimer's Disease Research Center (UCI ADRC); Institute for Clinical and Translational Science (UCI ICTS); Department of Neurology; Department of Psychiatry and Human Behavior

Background: The most consistent barrier to improved medical care is slow recruitment to clinical research. To help clinical investigators at UCI overcome this barrier, we developed a potential participant registry. The UCI Consent-to-Contact Registry (C2C, c2c.uci.edu) is an online repository of individuals who have given permission to be contacted about studies for which they may be eligible. We aim to enroll 1,000 adults in the C2C in the first year and 10,000 adults overall. Methods: The C2C is an IRB-approved source for study recruitment. Interested community members can enroll at one of two levels: (1) email only—to receive information on studies in general; (2) full enrollment with electronic informed consent—to be matched with suitable studies. Full enrollees self-report demographic, diagnostic, and medical information, and complete validated scales assessing diet, exercise, subjective memory performance, and research attitudes. They also describe the types of studies about which they are willing to be contacted. Enrollees are invited to update information annually and can withdraw at any time. Engagement and retention strategies include e-newsletters and promotional items. UCI investigators with IRB-approved protocols can submit study information to be emailed to level one registrants or request a query of level two registrants. Results: As of April 1, 2017, 757 adults have registered in the C2C, of which 285 provided email only and 472 provided demographic and health data. Two thirds of enrollees are female and 86% are white. The mean age is 64 years (Range: 18-96). UCI investigators have requested C2C queries resulting in 232 eligible registrants from which 53 have been matched and enrolled in four IRB-approved studies. Conclusions: The C2C is an important tool to facilitate recruitment to clinical research at UCI. To learn more about the C2C, contact Adrijana Gombosev (agombose@uci.edu) or Kirsten Klein (kleinkm@uci.edu).

Keywords: Accrual; Engagement; Community; Clinical trials;

Poster Location: 34

Engineering Pompe disease models using CRISPR-Cas9 genome editing

Huang, Jeffrey Y, PhD; Wang, Raymond Y, MD

CHOC Children's Research Institute

Pompe disease (PD) is a serious and progressive disorder caused by a genetic deficiency in acid alpha glucosidase (GAA) – an enzyme that recycles stored muscle cell glycogen for energy. PD patients with near-complete GAA deficiency – infantile-onset PD - present within the first few months of life with severe heart enlargement, heart failure, weakness of the muscles, respiratory failure, and demonstrate rapidly progressive, fatal disease. Without treatment, the average age that infantile-onset PD patients require permanent breathing support is about 6 months; the average age of death is about 9 months. Enzyme replacement therapy for Pompe disease using recombinant GAA enzyme (rhGAA) was developed and approved by the FDA in 2006. The treatment is very effective at getting rid of glycogen in heart muscle and reversing the heart symptoms. However, surviving children still have buildup of glycogen in other muscles and struggle with basic activities like talking, walking, eating, or even breathing. Furthermore, the outcomes of infantile-onset PD vary according to cross-reactive immunologic material (CRIM) status – one's immunogenic response to rhGAA. CRIM- patients develop significant antibody responses to rhGAA and typically have poorer prognoses, while CRIM+ patients tend to have better responses to rhGAA treatment. Currently, there are no models of PD featuring single nucleotide GAA mutations – which may be amenable to personalized genome editing. The goal of this project is to engineer PD-specific GAA mutations in C2C12 cells - a mouse myoblast line. We will seek to introduce single nucleotide GAA mutations homologous to common mutations found in CRIM- or CRIM+ infantile-onset PD using CRISPR-Cas9 genome editing. This set of experiments will allow us to determine the efficacy and specificity of our CRISPR-Cas9 system in a cultured cell line prior to in vivo testing.

Keywords: CRISPR; Pompe; Genome editing;

Poster Location: 35

Sensitization of DLBCL Cells to ABT-199 by Targeting Translation Initiation Complex

Herzog, Lee-or; Nancy Nguyen; Honyin Chiu; David A. Fruman

Department of Molecular Biology & Biochemistry, University of California, Irvine

The purpose of this project is to investigate the feasibility of using drugs targeting the Translation Initiation Complex (TIC) to improve efficacy of BCL-2 inhibitors in B cell lymphoma. ABT-199 (venetoclax) is a small molecule inhibitor of BCL-2, a key pro-survival protein that has demonstrated impressive responses in chronic lymphocytic leukemia (CLL), and hence received FDA approval for second line treatment of patients with 17p deletion. However, other aggressive hematologic malignancies, such as diffuse large B cell lymphoma (DLBCL), are less responsive to ABT-199 as a single agent - there is an urgent need for new therapeutic approaches in patients with relapsed/refractory DLBCL. We investigated the potential of combining ABT-199 to treat DLBCL with two different types of drugs: 1. mammalian target of rapamycin (mTOR) complex inhibitors (TOR-KI); 2. A drug that specifically targets TIC - a downstream target of the mTOR signaling pathway, named "SBI-0640756" (SBI-756). We hypothesized that DLBCL cells rely on cap-dependent translation, that is facilitated by eIF4E-eIF4G interaction and is promoted by mTOR complex 1 (mTORC1), such that targeting TIC will sensitize DLBCL cells to ABT-199 treatment. By treating DLBCL cells with SBI-756 we discovered profound synergistic induction of apoptosis when combined with ABT-199. Cell viability was reduced even more than with TOR-KI treatment combination. By using Proximity Ligation Assay (PLA) we showed that SBI-756 treatment prevents eIF4E-eIF4G association, and TIC formation in cells. Western blot analyses confirmed that SBI-756 treatment did not change mTOR substrate phosphorylation, indicating that the SBI-756 effect is specific to preventing the eIF4E-eIF4G interaction. Furthermore, polysome fractionation assay of DLBCL cells indicated that SBI-756 treatment reduced polysome formation with a corresponding increase in monosome abundance. This project highlights a novel combination for use in aggressive lymphomas.

Keywords: Diffuse large cell B-cell lymphoma (DLBCL); ABT-199 (venetoclax); SBI-0640756 (SBI-756); Translation Initiation Complex (TIC); B-cell lymphoma 2 (BCL2);

Poster Location: 36

Immunoimaging of Lymphocyte Interactions during Colits Using Two-Photon Microscopy

Skupsky, Jonathan; Othy, Shivashankar; Dong, Tobias; Yeromin, Andriy; Jairaman, Amit; Akunwafo, Chijioke; Angel, Zavala; Said, Hamid M; Parker, Ian; Cahalan, Michael

1. Department of Medicine, Gastroenterology, UC Irvine 2. VA Medical Center, Long Beach 3. Department of Physiology and Biophysics, UC Irvine

Effective treatments for Inflammatory Bowel Disease are limited, and the treatments that are available tend to work systemically with serious potential side-effects. Improving the specificity of treatments that interfere with adaptive immune responses could enhance clinical responses and limit toxicity. To further evaluate immune interactions underlying disease pathogenesis, we have developed a novel, two-photon microscopy method to image dynamic lymphocyte interactions. Two-photon microscopy is superior to standard fluorescence microscopy because lower energy photons are able to penetrate deeper in the tissue, and it is inherently confocal allowing us to generate stunning 3-D, time-lapse movies that illuminate previously unseen interactions. We have generated a CD11cEYFP/Rag2-/- mouse that serves as a host for adoptive transfer of naïve T cells from a DsRed mouse. Adoptive transfer induces colitis and co-adoptive transfer of regulatory T cells from a FoxP3EGFP mouse prevents disease progression. Colonic tissue is explanted and imaged with two-photon microscopy to reveal yellow dendritic cells, red effector T cells, green regulatory T cells, and blue collagen. In the lamina propria, there are effector T cells and dendritic cells interacting and surrounding crypts. Interestingly, in the muscularis layer, which is not typically considered a primary site for inflammation in colitis, dendritic cells are highly elongated and T cells display a unique motility pattern. Overall, this platform technology will allow us to better understand the dynamic interactions between dendritic cells, effector T cells and regulatory T cells in the setting of colitis and in response to various treatments. We are optimistic that direct observation of the cellular targets will facilitate development of novel therapeutics and that we will be able to apply this technique to other inflammatory conditions throughout the GI tract.

Keywords: Two-Photon; Colitis; Immunology; Immunoimaging; Regulatory T cell;

Poster Location: 37

Challenging CD34-positive spindle cell tumor of Nasal Ala: Clinicopathologic Analysis and Immunostains for Tumor Markers

Nowroozizadeh, Behdokht, MD; Deshmukh-Rane, Suvarna, MD

Departments of Pathology, VA Long Beach , UC Irvine

Introduction: CD34-positive dermal fibroma or Medallion-like dermal dendrocyte hamartoma (MLDDH) is a recently described congenital and acquired dermal spindle cell neoplasm. MLDDH and dermatofibrosarcoma protuberans (DFSP) both are CD34-positive dermal neoplasms with overlapping clinicopathologic features and different clinical variants. Clinically, MLDDH presents as a well-demarcated, pigmented, and indurated lesion on the neck, extremities, back, and trunk. MLDDH has mostly been reported in young girls but also there is an acquired type that is common in adults. Histopathologically, MLDDH is characterized by a proliferation of CD34+ spindle-shaped cells or ovoid cells mainly in the reticular dermis and extending into the subcutis in some cases. Case history: We report a case of a 71-year-old male with a history of cancer of the tongue and status post radiation and chemotherapy, who presented to dermatology clinic for evaluation of a round, yellowish colored, lesion measuring 0.5 cm on the right nasal ala. A skin biopsy was performed. Histological examination showed a spindle cell proliferation of fibroblasts in the upper dermis. The lesion spared the subcutaneous tissue, and adnexal structures. There was rare mitotic activity and increased collagen fibers in the superficial reticular dermis. The tumor cells were diffusely positive for CD34 immunostain, and negative for Factor XIIIa, CK903, CD68, S100, melan-A, HMB-45, SMA, desmin, and AE1/AE3 immunostains. Altogether the histology and immunohistochemical studies were neither suggestive of dermatofibrosarcoma protuberans nor neurofibroma. Thus, a diagnosis of MLDDH was considered.Conclusion: It is important to make a distinction between MLDDH and DFSP because they have different surgical managements and wide excision of margins applies only to DFSP. Recognizing different clinical presentations, subtle histopathologic differences, histochemical studies and tumor markers are critical to make the correct diagnosis.

Keywords: medallion-like dermal dendrocyte hamartoma; plaque-like CD34+ dermal fibroma; CD34; dermatofibrosarcoma protuberans; dermatofibroma;

Poster Location: 38

Inhibition of colony stimulating factor-1 receptor signaling mitigates chemotherapy-related cognitive dysfunction

Acharya, Munjal M., Ph.D.; Allen, Barrett, B.S.; Syage, A.R., B.S.; Baulch, J.E., Baddour, A.D., Green, K.N., West, B.L., Parihar, V.K.,

Department of Radiation Oncology (UC Irvine) Department of Neurobiology and Behavior (UC Irvine)

Chemotherapy to combat CNS and non-CNS cancers can elicit severe cognitive dysfunction often referred to as "chemobrain," a condition that can persist long after the cessation of treatment in as many as 75% of survivors. Although cognitive health is a critical determinant of therapeutic outcome, chemobrain remains an unmet medical need that adversely affects quality of life in pediatric and adult cancer survivors. Using a rodent model of chemobrain, we showed that chronic Adriamycin (ADR, doxorubicin) treatment induced significant performance-based decrements on behavioral tasks designed to interrogate hippocampal and cortical function that linked with chronic and persistent elevation in neuroinflammation (activated microglia). We hypothesize that depletion of microglia would have neuroprotective effect against chemotherapy. Adult mice received acute chronic ADR treatment (2 mg/kg IP, once weekly for 4-weeks) and were administered a dietary inhibitor (PLX5622) of colony stimulating factor-1 receptor (CSF1R) to deplete microglia 72 hour post-ADR treatment. Cohorts of mice maintained on a normal and PLX5662 diet were analyzed for cognitive changes using a battery of behavioral tasks 4-6 weeks later. PLX5622 treatment caused a rapid and near complete elimination of microglia in the brain within 3 days of treatment. ADR treated animals given a normal diet caused characteristic behavioral deficits designed to test medial pre-frontal cortex (mPFC) and hippocampal learning and memory and caused increased microglial activation. Animals receiving the PLX5622 diet exhibited no chemotherapy-related cognitive deficits, and showed near complete loss of IBA-1 and CD68 positive microglia in the mPFC and hippocampus. Our data demonstrate that elimination of microglia through CSF1R inhibition can ameliorate chemotherapy-related cognitive dysfunction.

Keywords: Chemobrain; Chemotherapy-related cognitive impairments; Colony stimulating factor 1; Microglia;

Poster Location: 39

Squamous Cell Carcinoma of the Bladder is Associated with Worse Outcomes Compared to Urothelial Carcinoma: Analysis of the California Cancer Registry

Martin, Jeremy; Youssef, Ramy, MD; Bettir, Kheira; Jenny Chang, MS, Rahul Dutta BS, Simone L. Vernez, BA, Argyrios Ziogas, PhD, Hoda Anton-Culver, PhD,

University of California, Irvine Department of Urology

Introduction: While urothelial carcinoma of the bladder (UCB) accounts for the vast majority of bladder cancers, squamous cell carcinoma (SCC) represents the most frequent non-urothelial tumor presentation. There is unclear evidence in the literature concerning whether SCC portends worse survival compared to UCB following covariate adjustment. Herein, we examined the California Cancer Registry (CCR) to compare SCC and UCB survival and define SCC prognostic factors in California patients. Methods: The CCR was queried for SCC and UCB cases in California from 1988 – 2012. Survival analyses were performed to determine prognostics. Results: 67,650 bladder cancer cases (1,390 SCC and 66,260 UCB) were included. Median age was 72 (range 18-109). Male: female ratios in SCC and UCB patients were 0.9: 1 and 3.1: 1 respectively. Kaplan-Meier analysis demonstrated significantly poorer 5-year DSS and OS in SCC patients compared to UCB (p < 0.0001). Advanced stage, grade, female gender and older age (>70) were all predictive of worse survival in UCB patients (all p < 0.0001). In SCC, only stage and older age were prognostic factors (both p < 0.0001). Multivariate analysis revealed that SCC was an independent prognostic predictor (DSS HR 2.617 95% CI: 2.434 – 2.814, p < 0.0001). Conclusions: Analysis of California Cancer Registry showed that SCC portends poorer survival compared to UCB patients in California, after adjusting for clinico-pathological features.

Keywords: urothelial; carcinoma; bladder;

Poster Location: 40

Office-Based Ultrasound Guided Percutaneous Renal Mass Biopsy

Okhunov, Zhamshid, Dr.; Clayman, Ralph V., Dr.; Landman, Jaime, Dr.

In this study, we prospectively evaluated the feasibility, safety, and efficacy of office-based ultrasound-guided percutaneous renal biopsy (USPRB) of renal cortical neoplasms (RCN). A total of 40 patients with RCN were selected based on tumor location found from previous visits to undergo office-based USPRB. After preparing the patients in the prone position, an application of EMLA cream and injection of 1% lidocaine was applied to the flank. Then, an 18G biopsy needle was inserted through a needle guide on the transducer probe. Under US guidance, the needle was advanced to the RCN, and 3 to 5 cores were collected. We assessed patient pain on a ten-point scale (0=none, 10= severe) before, immediately after, an hour after the procedure, and finally at the time of follow up usually one week later. Other variables such as patient demographics, tumor characteristics, perioperative recordings, and histopathological diagnosis were also recorded. The results showed that none of the patients reported pain before the procedure, and the median pain score immediately after was 1/10 (0-3 range), 0/10 (0-5 range) at one hour after, and 0/10 during the follow up visit. The most important finding was that based on histopathological analysis of the USPRB, benign and indolent Renal Cell Carcinomas (RCC) were diagnosed. This averted surgical intervention in 42.5% of the patients enrolled. With this data, urologists can confirm how office-based USPRB is feasible and safe, can reduce pain, and preclude surgical intervention when it isn't necessary in one fourth of their patients.

Keywords: None

Poster Location: 41

Inhibition of the Rho/ROCK pathway as a novel targeted therapy for clear cell renal cell carcinoma

Nelson, Luke; Ma, Mariel; Thompson, Jordan; Razorenova, Olga, PhD

University of California, Irvine, Department of Molecular Biology and Biochemistry

Kidney cancer is the 9th most prevalent form of cancer in the United States, with over 60,000 new cases and 14,000 deaths per year. Clear-Cell Renal Cell Carcinoma (CC-RCC) represents the majority of kidney cancer cases, and usually involves loss of the von Hippel Lindau tumor suppressor (VHL). We find that treatment with Rho Kinase (ROCK) inhibitors specifically targets VHL-deficient CC-RCC cells in vitro and in vivo, whereas cells expressing VHL are resistant to drug treatment. Furthermore, we show that VHL binds to Rho proteins and negatively regulates their expression. Specifically, VHL binds strongly to the GDP-bound, inactive form of Rho. Our current work is investigating the functional relevance of this protein-protein interaction, and how loss of the regulation between VHL and the Rho/ROCK pathway can sensitize these cells to ROCK inhibitors.

Keywords: Cancer; Molecular Biology; Rho; ROCK; Kidney;

Poster Location: 43

Mechanically-Coupled Reaction-Diffusion Model of Glioma Growth

Abler, Daniel, PhD; Büchler, Philippe, PhD

Institute for Surgical Technology and Biomechanics, University of Bern, Switzerland

Glioblastoma multiforme (GBM) are malignant brain tumors that grow rapidly, infiltrate the healthy brain and cause tissue compression. Despite the importance of the biomechanical environment for tumor evolution, most modeling studies of GBM invasion dynamics neglect the tumor's 'mass-effect'. A mathematical model incorporating this aspect of glioma growth was developed and was used to investigate the macroscopic effects of the biomechanical forces caused by the growing tumor in a parametric simulation study. Cell proliferation and invasion were modeled as reaction-diffusion process; the mass-effect was represented by a solid-mechanics model of brain tissue. Both models were coupled by relating local increase in tumor cell concentration to the generation of isotropic strain in the tissue. The model accounted for different brain regions with literature-based values for proliferation, isotropic diffusion and mechanical properties, and was solved using the Finite-Element Method (FEM). Tumors were seeded at multiple locations in FEM models based on the SRI24 human brain atlas. The temporal evolution of tumor cell concentration was simulated, together with the mechanical impact of the growing tumor in terms of tumor-induced tissue displacement. Simulation results for three sets of growth parameters were compared to actual tumors from publicly available GBM datasets. Simulation results consistently reflected parameter choices for different levels of tumor growth and invasiveness. However, statistical evaluation of tumor shape showed the simulated tumors to be more symmetric than their real counterparts. This study confirms earlier findings that tumor shape depends on seed position. It extends these findings by showing that inclusion of tumor biomechanics, using isotropic material and diffusion properties, is not sufficient to reproduce the variety of asymmetric shapes found in real tumors, thus indicating the importance of tissue anisotropy for glioma simulation.

Keywords: glioma; reaction-diffusion model; in-silico oncology; biomechanics;

Poster Location: 44

Magmas inhibition as a potential treatment strategy in malignant glioma

Di, Kaijun; Lomeli, Naomi; Das, Bhaskar C.; Bota, Daniela A.

Di, Kaijun-Department of Neurological Surgery, UC Irvine; Lomeli, Naomi-Department of Pathology & Laboratory Medicine, UC Irvine; Das, Bhaskar C.-Albert Einstein College of Medicine, Bronx, NY; Bota, Daniela A.-Department of Neurological Surgery, Department of Pathology & Laboratory Medicine, Department of Neurology, Chao Family Comprehensive Cancer Center, UC Irvine

OBJECTIVES: Magmas (mitochondria-associated protein involved in granulocyte-macrophage colony-stimulating factor signal transduction) is a nuclear gene that encodes for the mitochondrial import inner membrane translocase subunit Tim16. Magmas is highly conserved and ubiquitously expressed in all mammalian cells, and is essential for cell viability. Its expression levels are increased in a significant proportion of human prostate cancers, independently of mitochondria content. In addition, Magmas mRNA is over expressed in two ACTH-secreting pituitary adenoma cell lines as compared to normal pituitary in mouse, as well as in 47 out of 64 pituitary adenomas compared to normal pituitary in human. Moreover, Magmas silencing sensitizes to pro-apoptotic stimuli and induces a G0/G1 accumulation. Based on the above findings, we believed that inhibition of Magmas by small molecule inhibitors could be beneficial for glioma treatment. METHODS: In this study, we tested the capability of a Magmas inhibitor-BT#9 to cross the blood brain barrier in mice. The anti-tumor effect of BT#9 was investigated using glioma cell lines. RESULTS: Our in vivo results showed that while the plasma level of BT#9 reaches a Cmax within 5 minutes and is obviously eliminated by 720 minutes, brain levels of BT#9 increase over the first 240 minutes after IV exposure and then slowly decrease, indicating that BT#9 may cross the blood brain barrier. In vitro study using glioma cell lines revealed that Magmas inhibition by BT#9 significantly decreased cell proliferation, induced apoptosis along with vacuole formation, blocked migration and invasion. Since Magmas is a ROS regulator, BT#9 treatment resulted in a decrease in respiratory function of glioma cells. DISCUSSION: This is the first study about the role of Magmas in glioma. Our findings suggest that Magmas plays a key role in glioma cell survival and targeting Magmas by Magmas inhibitor has the potential to become an therapeutic strategy in gliomas.

Keywords: Magmas; glioma; anti-tumor effect;

Poster Location: 45

From Bench to Bedside: Marizomib Activity in Malignant Gliomas - Preclinical Development and Early Clinical Trial Results

Di, Kaijun; Chung, Jinah; Lomeli, Naomi; Desjardins, Annick; Trikha, Mohit; Bota, Daniela A.

Di, Kaijun; Chung, Jinah; Lomeli, Naomi; Bota, Daniela A. - University of California, Irvine Desjardins, Annick - The Preston Robert Tisch Brain Tumor Center, Duke University Medical Center, Durham, NC Trikha, Mohit - Triphase Accelerator Corporation, San Diego, California

Background: The proteasome plays a vital role in the physiology of glioblastoma (GBM), and proteasome inhibition can be used as a strategy for treating GBM. Marizomib is a second generation proteasome inhibitor which has a more lipophilic structure, suggestive of potential for penetrating the blood brain barrier. Methods: We investigated in our laboratory at UC Irvine the antiglioma activity of marizomib. Based on these results FDA approval was given to proceed to clinical trials – which were conducted as multicenter, industry-sponsored studies – with UC Irvine serving as the main enrollment site. Preclinical Results: Marizomib inhibited the proliferation, migration and invasion of glioma cells. In animal studies, marizomib distributed into the brain at 30% of blood levels in rats, and significantly inhibited (>30%) baseline chymotrypsin-like (CT-L) proteasome activity in brain tissue of monkeys. Encouragingly, immunocompromised mice intracranially implanted with glioma xenografts survived significantly longer (p<0.05) when treated with marizomib. These preclinical studies demonstrate that marizomib can cross the BBB, inhibits proteasome activity in rodent and non-human primate brain, and elicits antitumor effect in a rodent intracranial model of GBM. Clinical Results and the Pathway to Registration: We conducted a Phase 1B clinical trial of marizomib plus bevacizumab in recurrent GBM patients. The results are very promising – especially for the patients that lack MGMT promoter methylation – with 9 months Progression-Free Survival (PFS) of 23% (0-10% in bevacizumab only studies) and 9 months Overall Survival (OS) of 44% (less than 12% in bevacizumab only studies). A phase III registration study is currently under planning, and will open in the next 9-12 months. Conclusions: Marizomib is a very promising drug for the treatment of GBM. Successful collaborations between academia and industry can increase our ability to develop new molecules for rare malignancies.

Keywords: marizomib; proteasome; glioblastoma; blood brain barrier; clinical trial;

Poster Location: 46

Unusual cardiac paraganglioma mimicking an atypical carcinoid tumor of the lung – Case report with literature review

Spencer, Dean, BS; Evans, Mark, MD; Wang, Beverly Y., MD; Delrosario, J. Lawrence, MD; Cheng, Timmy, MD; Milliken, Jeffrey, MD

Department of Surgery--Division of Cardiothoracic Surgery, Department of Medicine--Division of Pulmonology and Critical Care, Department of Pathology, University of California, Irvine School of Medicine

Background: Paraganglioma (PG) is an entity of chromaffin cell tumors that often affect adrenal glands and carotid body. PG rarely occurs in the thoracic region, accounting for just 1-2% of all PG. We report an unusual pericardial mass initially misdiagnosed as atypical carcinoid tumor of the lung. The surgically resected mass was proved to be cardiac PG. Proper diagnosis of PG is challenging owing to its rare prevalence, subtle symptoms of presentation, and similar neuroendocrine histopathologic features as atypical carcinoid tumors. These tumors are typically benign and are best treated by surgical resection. Clinical history: A 64 year old female with persistent cough and back pain was found to have a 4 cm x 3cm mass abutting multiple cardiopulmonary structures. A biopsy was performed at an outside institution, and pathology reported "atypical neuroendocrine carcinoma, consistent with carcinoid". The patient was transferred to UCI medical center. Pericardial resection with right pneumonectomy removed a big hemorrhagic pericardial mass 4.3 x 2.9 x 2.2 cm. The mass was occupying pericardial sac with adherence to the right hilar area. Cross sections revealed the mass pushing into right middle lung parenchyma. Pathology Diagnosis: Histology of the mass was that of PG with multiple ethanol embolizations. Immunohistochemical examination revealed that type I (chief) cells were positive for neuroendocrine markers (Chromogranin and Synaptophysin, while type II (sustentacular) cells were positive for S100. There was no evidence of atypical carcinoid tumor in lung. Conclusion: In our case, accurate diagnosis by pathology was provided after successful surgical resection. Cardiopulmonary related symptoms, physical exam findings, radiographic imaging, and laboratory results should be utilized for proper diagnosis of PG. Our experience highlights the importance of an interdisciplinary approach between specialties to provide quality clinical patient care.

Keywords: Cardiac Paraganglioma; Neuroedocrine tumor; Interdisciplinary Medicine;

Poster Location: 47

Cardiovascular manifestations of feline Sandhoff disease after intravenous AAV gene therapy

Ellis, Lauren, BS.; Winter, Randolph, DVM.; Gray-Edwards, Heather, DVM, Ph.D.; Maitland, Stacy; Randle, Ashley; Edwards, Robert; Sena-Esteves, Miguel; Martin, Douglas; Wang, Raymond

1) College of Veterinary Medicine, Auburn University, Scott Ritchey Research Center 2) University of Massachusetts Medical School, Gene Therapy Center 3) University of California-Irvine School of Medicine, Department of Pathology 4) CHOC Children's Specialists, Division of Metabolic Disorders 5) University of California Irvine School of Medicine, Department of Pediatrics

GM2 gangliosidosis is a fatal neurodegenerative disorder caused by a deficiency of lysosomal ß-N-acetylhexosaminidase (Hex) and includes both Tay-Sachs and Sandhoff disease. Feline models of Sandhoff disease recapitulate the human condition and are utilized to assess safety and efficacy of adeno-associated viral (AAV) gene therapy. A monocistronic AAVrh8 vector encoding the Hex ß subunit (deficient in Sandhoff disease) was delivered intravenously at a dose of 5e12 vg/kg body weight. Despite attenuation of neurologic disease, treated cats demonstrated valvular dysplasia and dilatation of the aorta. Cardiovascular manifestations in treated cats were further investigated. Myocardium, carotid artery, ascending/descending aorta, and mitral/aortic valves were obtained at necropsy from normal (n=2; 2.1 months), untreated GM2 (n=6; 1.4 months), and AAV-treated GM2 cats (GM2+AAV) (n=2; 4.8 months). Tissues were stained with hematoxylin & eosin or Verhoeff-Van Gieson (for elastin). Vascular intima-media thicknesses were measured using ImageJ and reported as (mean±SD). Carotid artery thickness of GM2 (0.034±0.0072 μm) and GM2+AAV (0.039±0.00044 μm) cats was increased compared to normal (0.023±0.00044 μm). Ascending aorta thickness of GM2 (0.12±0.020 μm) and GM2+AAV (0.092±0.022 μm) cats was decreased compared to normal (0.167±0.004 μm). Descending aorta measurements were lowest in GM2+AAV cats (0.075±0.014 μm), while untreated GM2 cats (0.13±0.023 μm) and normal cats (0.11±0.028 μm) were comparable. Arterial media of GM2 cats contained 'clear cells' with prominent storage, causing widening of the spaces between elastin laminae. Elastin fragmentation was noted in the untreated GM2 aortas. Abnormalities of the arterial tunica media, also reported in human mucopolysaccharidoses, may explain aortic dilatation in GM2+AAV cats. GM2 cats had increased carotid intimal-medial thickness compared to normal cats. Future studies will include additional cats to increase statistical power.

Keywords: GM2 gangliosidosis; Lysosomal Storage Disorder; Gene Therapy; Outcomes;

Poster Location: 48

Investigation of microbial and viral communities in the cystic fibrosis lung

England, Whitney; Blancaflor, Angelo; Whitaker, Rachel; Whiteson, Katrine

Department of Molecular Biology and Biochemistry, University of California, Irvine Department of Pharmaceutical Sciences, University of California, Irvine Institute of Genomic Biology and Department of Microbiology, University of Illinois at Urbana-Champaign

The cystic fibrosis (CF) airway is home to dense mucus, preventing effective mucociliary clearance and leading to colonization by a variety of microbes. These chronic microbial infections lead to debilitating respiratory disease in CF patients. While bacterial communities within CF lungs are well studied, viral communities and their interactions with bacterial communities in CF lungs are largely uncharacterized. Microbe-virus interactions are critical in the evolution and ecology of microbes. These interactions can have dramatic impacts on communities through predation and introduce genetic diversity through resistance and adaptations. Shotgun sequencing of paired microbial and viral metagenomes from clinical samples enables culture-independent comparison of clinical samples through time and across patients. Sputum samples were collected from patients at the UCSD Adult CF Clinic from one to three time points over the course of treatment for clinical exacerbations, and viral and microbial DNA were prepared independently for sequencing. Virus-like particles were obtained using CsCl gradients, while intact microbial cells were harvested using hypotonic lysis. Twelve metagenomes and eleven viromes were sequenced from six patients. Draft assemblies were constructed, and high levels of diversity were found within and between viral and microbial communities. Replication rates of important species in microbial metagenomes were analyzed to establish which species are most actively replicating, and if there are shifts in replication over time. Comparison of viromes to existing databases reveals few matches, indicating that many of the viruses present in the CF lung are outside the set of sequenced viruses. To further elucidate microbe-virus interactions in the CF lung environment, future work will include investigation of lytic and temperate lifestyles in viromes, including comparison of virome and microbial metagenome assemblies to identify integrated prophages.

Keywords: microbiome; cystic fibrosis; metagenomics; host-virus interactions;

Poster Location: 49

Clinical Comparison of the Mobile Endockscope System and Standard Videocystoscopy using Air and Liquid Irrigant

Abadinaeini, Sina; Yoon, Renai; Dutta, Rahul; Patel, Roshan M.; Spradling, Kyle; Okhunov, Zhamshid; Sohn, William; Lee, Hak J.; Landman, Jaime; Clayman, Ralph V.

1. University of California, Irvine, Department of Urology 2. Rutgers New Jersey Medical School, Department of Surgery, Division of Urology 3. Stanford University, Department of Urology 4. Kaiser Permanente, Fontana, Department of Urology 5. Gordon Hospital, Gordon Urology

Introduction and Objective: Standard videocystoscopy (SVC) requires a cystoscope, light source, monitor/camera system, and fluid irrigant. The high associated cost precludes the widespread use of videocystoscopy in underserved communities. We developed the Endockscope (ES); a low cost, mobile videocystoscopy system which employs a mobile phone for image display and a LED light source. We compared the clinical performance of the ES by comparing the system with SVC utilizing both air and liquid irrigant. Methods: Patients receiving in-office cystoscopy for bladder tumor surveillance or stent removal underwent SVC using standard saline and cystoscopy equipment. Without removing the cystoscope, the ES was secured to the eyepiece of the cystoscope using an iPhone 6S as the video monitor/camera and the LED light source. The cystoscopy was then repeated via liquid irrigant (Endockscope-Liquid, ES-L) followed by air irrigant (Endockscope-Air, ES-A). All three exams were recorded and sent to 11 expert endourologists for grading/analysis on image quality/resolution, brightness, color quality, sharpness, overall quality (1-5 scale, 5 being best), and whether the video was satisfactory for diagnostic purposes. Results: Ten patients underwent SVC, ES-L, and ES-A cystoscopy. Six of 10 patients had SVC videos determined to be adequate for diagnostic purposes and were compared with the Endockscope system. The SVC videos scored higher relative to both the ES-L and ES-A ($p < 0.05$) on every metric analyzed. A trend of higher ratings was noted among ES-L videos compared to ES-A on all metrics. However, none achieved statistical significance ($p > 0.05$); 52% and 44% of the ES-L and ES-A videos, respectively, were deemed satisfactory for diagnostic purposes ($p = 0.384$). Conclusions: In settings with limited access to both electricity and standard videocystoscopy equipment, the Endockscope mobile cystoscopy system utilizing a fluid irrigant may be a viable alternative.

Keywords: Endoscopy; Minimally; Invasive; Cystoscopy;

Poster Location: 50

Development and Multi-Institutional Evaluation of a Novel 3D-Printed Laparoscopic Trainer: The UCiTrainer

Lu, Sherry; Yoon, Renai; Okhunov, Zhamshid; Safiullah, Shoaib; Lama, Daniel J.; Dolan, Benjamin; Kaler, Kamaljot; Clayman, Ralph V., Landman, Jaime

Introduction and Objective: Current laparoscopic trainers are costly and of limited access to trainees. With the advancement of new techniques in minimally-invasive surgery and the increased cost of surgical training tools, we aimed to create a low cost, easily accessible laparoscopic trainer that would aid trainees in building surgical skills. In this study, we evaluate the feasibility of the 3D printing manufacture of the UCi Trainer (UCiT) and compare the performance to a standard laparoscopic trainer (SLP) for surgical skills development. Methods: The UCiT was developed using Solidworks software to create a computer aided design (CAD). The CAD was imported into 3D-printing software (Makerbot Industries) and printed using a Flashforge 3D-printer. Once assembled, a tablet computer was utilized as both the monitor and camera to simulate an endoscopic environment. Urologists from four institutions were asked to print, assemble and use the UCiT. Participants performed two tasks, peg transfer and intracorporeal knot tying, on both the UCiT and SLP and were scored on their performance. A questionnaire was given to each participant to rate their experience 3D printing, assembling, and using the UCiT compared to SLP. Results: All participants were urologists with no previous experience with 3D-printing. There was no significant difference in performance scores for both the peg transfer and intracorporeal knot tying tasks when using the UCiT and SLP. However, the SLP scored significantly higher than the UCiT ($p<0.05$) in trainee experience for image quality, display lag, comfort, and overall performance. Of the eight participants who assembled the UCiT, six were successful in building the trainer, and all participants in the study agreed that 3D-printing would be an effective tool for surgical education. Conclusions: The UCiT can be easily manufactured in a cost-effective manner and serves as additional resource for laparoscopic training for trainees.

Keywords: Laparoscopy; Surgical Education; Minimally Invasuve Techniques; Simulators; 3-D Printing;

Poster Location: 51

Selective stimulation of facial muscles following chronic intraneural electrode array implantation and facial nerve injury in the feline model

Ronald Sahyouni, B.A.; Yarah M. Haidar, M.D.; Omid Moshtaghi, B.S.; Beverly Y. Wang, M.D.; Hamid R. Djalilian, M.D.; John C. Middlebrooks, Ph.D.; Harrison W. Lin, M.D.

Medical Scientist Training Program (R.S.), Department of Otolaryngology-Head & Neck Surgery (Y.M.H., H.R.D., J.C.M., H.W.L.), School of Medicine (O.M.), Department of Pathology (B.Y.W.), University of California, Irvine, Irvine, CA, USA

Background: Our group has previously shown that activation of specific facial nerve (FN) fiber populations and selective contraction of facial musculature can be achieved through acute intraneural multi-channel microelectrode array (MEA) implantation in the feline model. Hypothesis: Selective stimulation of facial muscles will be maintained in the setting of (1) chronic and (2) acute MEA implantation following FN injury and subsequent recovery. Methods: This study included seven cats. In three cats with normal facial function, 4-channel penetrating MEAs were implanted chronically and tested biweekly for six-months. Electrical current pulses were delivered to each channel individually, and elicited electromyographic (EMG) voltage outputs were recorded for each of several facial muscles. For FN injury experiments, two cats received a standardized hemostat-crush injury, and two cats received a transection-reapproximation injury to the FN main trunk. These four underwent acute implantation of MEA and EMG recording in terminal experiments four months post-injury. Results: Stimulation through individual channels selectively activated restricted nerve populations, resulting in contraction of individual muscles in cats with chronic MEA implantation and following nerve injury. Increasing stimulation current levels resulted in increasing EMG voltage responses in all cases. Nerve histology showed only minor neural tissue reaction to the implant. Conclusion: We have established in the animal model the ability of a chronically implanted MEA to selectively stimulate restricted FN fiber populations and elicit contractions in specific facial muscles. Likewise, following FN injury, selective stimulation of restricted FN fiber populations and subsequent contraction of discrete facial muscles can be achieved following acute MEA implantation.

Keywords: facial nerve; implant; stimulation; multi-channel electrode array; neuroprosthetics;

Poster Location: 52

Utilizing consumer photoplethysmography technology to augment the Allen's Test in measuring collateral circulation to the hand: Proof of concept using the Apple Watch

Allison C. Hu, BA; Tjoson Tjoa, MD; Brian J.F. Wong, MD, PhD;

1. University of California, Irvine, School of Medicine, Irvine, CA 92617 (ACH) 2. Beckman Laser Institute and Medical Clinic, University of California, Irvine, Irvine, CA 92612 (ACH, BJFW) 3. Department of Otolaryngology – Head and Neck Surgery, School of Medicine, University of California, Irvine, Irvine, CA 92868 (TT, BJFW) 4. Department of Biomedical Engineering, University of California, Irvine, Irvine, CA 92697 (BJFW)

Background: The radial forearm free flap (RFFF) is a reliable reconstructive option for a variety of complex head and neck defects. Advantages include its ease of dissection, tissue match, low complication rates, and high vascularity. Prior to surgery, it is essential to evaluate collateral circulation to the donor hand to prevent post-operative ischemia. Conventional methods use the modified Allen's test (MAT), a qualitative test that measures the time needed for palmar blush refill after release of the ulnar artery compression with occlusive pressure of the radial artery. However, recent studies have demonstrated the inadequacy of the MAT to assess the patency of hand collateral circulation. Objective: To determine whether the Apple Watch, a popular consumer device, can serve as an objective tool to augment the MAT in the assessment of collateral supply to the hand. Design: Apple Watch's heart rate sensor uses photoplethysmography, which illuminates the skin and measures changes in green LED light absorption. The watch was placed on the palm of the hand and a pulse oximeter was attached to the index finger of the same side while performing the MAT. Heart rate was measured for the resting palm, when radial and ulnar arteries were occluded, and when the ulnar artery was recovered. Results: The Apple Watch was precise when compared to the finger pulse ox at measuring resting palmar HR ($p=0.35$) and HR after ulnar artery recovery ($p=0.41$). When both ulnar and radial arteries were compressed, Apple Watch captured a HR significantly lower than the resting HR ($p=0.0030$). When the ulnar occlusive pressure was released, Apple Watch measured a HR significantly higher than the fully occluded HR ($p=0.0016$). Conclusion: Ultimately, this work serves as a proof of concept study, demonstrating the potential use of the Apple Watch as an objective tool to augment the MAT in the assessment of collateral supply to the hand.

Keywords: Apple Watch; Radial Forearm Free Flap; Modified Allen's Test; Photoplethysmography; Pulse Oximetry;

Poster Location: 53

Development of a Three-Dimensional Kidney Model for Use in a Virtual Reality Environment

Safiullah, Shoaib (1); Lama, Daniel (1); Patel, Roshan (1); Patel, Roshan (1); James, Ryan C. (2); Aljadaan, Ahmad (2); Laughery, Mark W. (3); Clayman, Ralph V. (1); Landman, Jaime (1); Ito, Daniela (1)

(1): Department of Urology, University of California, Irvine, Orange, CA; (2): Department of Biomedical Informatics and Medical Education, University of Washington, Seattle, WA; (3): Department of Human Centered Design and Engineering, University of Washington, Seattle, WA

Introduction and Objective: Current advancements in three-dimensional (3D) medical imaging and virtual reality (VR) technology have been used as preoperative tools to improve the basic understanding of human anatomy. This study reports the development of 3D-reconstructed virtual kidney models and their feasibility in preoperative surgical planning and education. Methods: Medical imaging processing software (3D Slicer) was used to convert 64-slice serial axial CT images of 5 patients with small renal mass (SRM) into a 3D computer-aided design (CAD) of the patient's mass and renal anatomy. 3D software (Blender) was used for post-processing and the 3D files were imported into VR software (Bosc, Pear Medical Seattle, WA). A head-mounted display (HMD) was used to view and interact with the VR kidney models by using the user's hands as input. CT images and their corresponding VR models were randomized and reviewed by 3 medical students. The reviewers were required to complete an imaging questionnaire after reviewing the CT image alone and again, after reviewing both the CT image and VR model. The reviewers were asked to score (0-10 scale) their understanding of the SRM's relationship to various renal structures. The location of the SRM on the radiology report and the reviewer's response were recorded and compared. Results: The mean time for the creation of the 3D kidney model was 220.8 minutes (range 177-271 minutes) due to a steep learning curve in using the imaging processing software. There were no complications incorporating the CAD files into Bosc. Although not statistically significant, the VR models improved the user's ability to give the correct location of the SRM compared to CT alone (concordance: 83% vs. 53%, respectively; p=0.371). Conclusions: VR technology is a beneficial tool to view and manipulate a virtual 3D kidney model and may improve a student's ability to understand the location of the SRM and its relationship to the underlying renal structures.

Keywords: Virtual Reality; 3D modeling; small renal mass; surgical education;

Poster Location: 54

VR/3DP Radiology Lab: A Pilot Project for Single-Platform Integration of Virtual Reality and 3D Printing in Radiology Education

Hernandez-Rangel, Eduardo, MD; Houshyar, Roozbeh, MD; Marfori, Wanda, MD; Ushynsky, Alexander

University of California Irvine, Department of Radiological Sciences

The application of virtual reality technologies (VRTs) and 3D printing for medical uses has been studied for decades, from surgical simulations and protests, to the treatment of phobias, pain management, telemedicine and live stream surgeries. Newly designed VTR head-mounted displays (HDMs) and 3D printers have become commercially available and the need to explore and expand its capabilities in any science that requires the sense of presence and immersion is mandatory. We are working in the creation of an open online access platform that contains guidelines and tutorials for the creation of normal or pathologic models in VR and 3D printing. The platform will evaluate the role of these advanced imaging approaches for, medical/radiology education, simulated IR/OR training, and its integration with routine radiological studies. This lab will provide a gateway to improved pre-clinical and clinical education and perioperative evaluation. Objectives: • To implement VR/AR and 3D printing models for anatomy and radiology education with a more immersive and experiential interaction. • To collaborate in a multidisciplinary fashion and integrate advanced imaging tools in clinical decision support VR/3DP Radiology Lab is a preliminary online and mobile platform which integrates Virtual Reality (VR) and 3D Printing. Conclusion: This platform will incorporate radiology into the multidisciplinary treatment team for presurgical support. Moreover, this approach may better inform and educate patients about their medical conditions. The use of VR/AR and 3D printing can be valuable in radiology education as supplement traditional 2D monitor based image review. VR/3DP Radiology Lab provides a novel approach to integrate radiology with other specialties, promoting awareness of the radiologist role, and the possibility for the radiologist to be aligned with the campaign for a patient centered practice.

Keywords: Virtual Reality; 3D Printing; Medical Education; Radiology; Patient Centered Practice;

Poster Location: 55

Pathways: Evaluation of an Emerging Digital Nutrition Campaign

Waldeck, Jennifer Ph.D.; Robertson, Trina MS,RDN

Chapman University Dairy Council of California

This project is a partnership between Dairy Council of California and Chapman University's School of Communication to assess the effectiveness of Dairy Council's Pathways Project which is an e-health initiative designed to help users (those who plan/prepare meals within families with preschool and school age children) create term plans for healthy breakfasts and snacks. The project focused on usability and presentation of Pathways content. Focus group participants (N=11) and survey respondents (N=1742) provided data about Pathways. Results were interpreted using two theories offering insight into message design that can lead to positive outcomes relative to health behavior change (Theory of Planned Behavior and Elaboration Likelihood Model). Thus, evidence-based recommendations for campaign design are grounded in data and established theoretical frameworks. In order to identify strengths, weaknesses, and opportunities for development of Pathways, qualitative data were submitted to content analysis that revealed themes relative to Pathways' readability, usability, and users' recommendations for additional media. Participants' responses regarding these aspects of the program provide evidence of a positive attitudinal disposition to the ideas presented—the first step toward behavioral commitment and change. User feedback relative to desired features and characteristics of the program (that centered on making the site more social, with opportunities for sharing, commenting, and connecting with others) are all consistent with Theory of Planned Behavior. Quantitative data, analyzed using descriptive statistics and ANOVA, provided further evidence of the program's current effectiveness in the areas of social and mobile capabilities, readability, and design. The presentation will articulate results of qualitative and quantitative data analysis and provide corresponding evidence-based recommendations for creating a multi-media program that creates behavior change.

Keywords: Health Communication; Behavior change theory; Childhood obesity; Nutrition education; Child and Family Health;

Poster Location: 56

Validation of a Microfluidic Device to Study Patient-Derived Colon Cancer Cells and Determine Clinical Predictive Value

Hachey, Stephanie J MS; Zell, Jason A MPH DO; Hughes, Christopher CW PhD; Sobrino, Agua PhD; Celaya, Elizabeth I; Phan, Duc TT; Klempner, Samuel J MD; Lee, John G MD; Edwards, Robert A MD, PhD

SJH, AS, EIC, DTTP - 1 Department of Molecular Biology & Biochemistry, University of California, Irvine, Irvine, CA 92697, USA. JAZ, JGL, RAE - 2 Department of Medicine, University of California, Irvine, Irvine, CA 92697, USA. SJK - 3 Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, CA 90048, USA. CCWH - 1 Department of Molecular Biology & Biochemistry, University of California, Irvine, Irvine, CA 92697, USA. 3 Department of Biomedical Engineering, University of California, Irvine, Irvine, CA 92697, USA. 4 The Edwards Lifesciences Center for Advanced Cardiovascular Technology, University of California, Irvine, Irvine, CA 92697, USA.

Cancer accounts for 25% of US deaths, and the majority of patients die from metastatic disease that is refractory to current therapies. The low rates of effective preclinical compounds reaching the clinic can be largely attributed to drawbacks in current model systems that are poor predictors of drug response in patients. To address the need for improved preclinical models, the Hughes lab and collaborators designed and fabricated a microfluidics device that supports the formation of a perfused, vascularized micro-tumor (VMT) via co-culture of multiple cell types in an extracellular matrix. This novel platform, truly one of a kind in the field, more accurately mimics the in vivo tumor cell biology and microenvironment than standard drug screening modalities. The VMT represents a major breakthrough in tissue engineering by providing an environment amenable to establishment of perfused vasculature supported by stromal cells in the tissue construct, allowing long-term culture for drug sensitivity and molecular studies. What we propose is to test how an individual patient's tumor cells respond to a set of drugs – a truly personal drug screening methodology. Important questions we aim to address with our pilot study are whether the VMT model is representative of patient tumors and whether findings from the VMT can translate to clinical practice. To determine the clinical relevance of the VMT model, primary VMTs will be established from patient-derived colon cancer samples collected in excess of clinical need as part of a prospective clinical studyand then analyzed for responsiveness to multiple drug combinations. Findings will then be correlated to patient outcomes based on the drug combinations they actually received. The translational infrastructure providing real-time information from patient-derived tumor cells in our VMT will support efforts to improve patient outcomes.

Keywords: Cancer; Microphysiologic system;

Poster Location: 57

Quantitative Spectral Imaging of tissue function, structure, pathology in (pre-)clinical investigations using Spatial Frequency Domain Techniques

Saager, Rolf B, PhD; Torabzadeh, Mohammed; Ghijsen, Micheal; Baldado, Melissa L; Rowland, Rebecca K; Leproux, Anias, PhD; Wilson, Robert H, PhD; Ponticorvo, Adrien, PhD; Kennedy, Gordon T, PhD; Durkin, Anthony J, PhD; Tromberg, Bruce, PhD

UCI, Beckman Laser Institute and Medical Clinic

Spatial Frequency Domain Imaging (SFDI) Technologies are non-invasive optical devices that enable quantitative measurements of tissue structure (scattering) and function (hemoglobin species, oxygen saturation, melanin, water, lipid, and carotenoids). Here, patterns of light projected onto tissue are captured by a camera and analyzed by computer to reveal tissue structure and composition up to 30 times deeper beneath the surface of skin than can be seen by eye. These technologies are developed to enable quantitative longitudinal studies in both preclinical animal models and human subjects. SFDI devices developed at the Beckman Laser Institute are capable of quantitative measurements that allow us to draw comparisons among data collected in serial from a single patient and among patients measured at different sites worldwide. These tools provide researchers with highly versatile, quantitative, cost-effective opportunities to study disease progression and therapeutic response with 1) high degree of fidelity and localization, 2) sufficient spatiotemporal resolution and interrogation depth, and 3) fields-of-view to study events that have broad practical relevance, from surgical guidance to clinical management. We present three different implementations of SFDI: 1) a wide field hyperspectral imager, designed for clinical settings and capable of imaging over 20cm fields of view 2) a spectroscopic imager (SFDS), designed for detailed, depth-segmented spectral characterization of tissues, over limited spatial extent, and 3) a fast SFDI imager, designed to quantify processes like hemodynamics and metabolic activity at rates greater than 14Hz. In addition to device demonstrations, we will present a poster that will summarize results obtained from ongoing collaborative preclinical and clinical studies: assessing the depth and severity of wounds and burns, determining the viability of flaps during reconstructive surgery, and imaging breast cancer response to therapies.

Keywords: Tissue Imaging; Burn wounds; Breast Cancer Imaging; Reconstructive Surgery; Response to Therapy;

Poster Location: 58

The Impact of Forces Applied during Ureteral Access Sheath Deployment on Ureteral Injury in a Porcine Model

Warner, Anthony, AS; Hoang, Long, BS; Kaler, Kamaljot, MD; Roshan M. Patel; Renai Yoon; Daniel Lama; Christina Hwang; Zhamshid Okhunov; Michael Klopfer; Jaime Landman; Ralph V. Clayman

Department of Urology, School of Medicine, UCI School of Engineering, UCI

Introduction and Objectives: Widespread use of the ureteral access sheath (UAS) during ureteroscopy has been slowed by concerns over possible ureteral injury during its passage. In this pilot porcine study, using a novel device developed at UC Irvine, we evaluated the force threshold which would induce ureteral injury. Methods: With IACUC approval, we measured UAS deployment force using a novel Ureteral Access Sheath Force Sensor (UC Irvine Force Sensor) in a female Yorkshire pig (Figure 1). Under fluoroscopic control, force was continuously measured from the time the UAS contacted the urethral meatus until the tip of the UAS had reached the renal pelvis. Ureteral dilators (6-9F), UAS and its obturators (9.5F, 10F, 11F, 11.5F, 12F, 13F, 14F, 15F, 16F) sequentially passed twice into both ureters. Ureteroscopic evaluation was initiated after the 9.5F UAS obturator was passed. Results: No ureteral injury occurred at <4 Newtons (N). Increasing UAS size resulted in greater force over-time (Figure 2) and larger peak forces (Figure 3). First ureteral injury occurred at 8 N (right ureter) and 10 N (left ureter). Figure 4 shows a normal right ureter before and after deployment of a 13F UAS with a peak force of 8N. Conclusion: The UC Irvine Force Sensor can reliably measure force while deploying a UAS. Initial ureteral injury occurred at forces > 8 N.

Keywords: Biotechnology; Medicine; Innovation;

Poster Location: 59

Telepresence robots for virtual social and academic inclusion: Can they contribute to improved well-being, health, and social outcomes for homebound pediatric patients?

Newhart, Veronia

Department of Education, University of California, Irvine

Due to increased survival rates, and reclassification of illnesses once considered fatal, there is a growing population of children who are homebound due to chronic illnesses. This project aims to address the lag between the scientific discoveries that have led to increased survival and needed changes in the treatments and practices afforded to these children for quality of life. Recent technological innovations, such as telepresence robots, may allow for partnerships between the technology, healthcare, and education fields to improve well-being, health, and social outcomes for homebound pediatric patients. These robots allow for real-time, two-way communication and have features that allow for integration of homebound pediatric patients in existing school settings and peer social structures. The goal of robot use is for the patient to engage in social and academic experiences in such a way that they contribute to healthy social emotional development. These social experiences may also contribute to increased adherence to prescribed medial regimens resulting in improved well-being and health outcomes for this population. This project will provide an interdisciplinary partnership between schools of Education, Informatics, and Pediatrics that will provide formal, objective research studies in order to provide recommendations for use of the robots as supported by the psychology, educational, and health care research literatures.

Keywords: TelerDeparobotics

Poster Location: 60

Poster Location: 61

Determination of LOXL1 and Fibulin-5 Levels in the Vaginal Secretions of Women With and Without Pelvic Organ Prolapse

Garcia, Bobby MD; Lechuga, Thomas PhD; Nasiri, Azadeh MD; Chen, Dongbao PhD; Lane, Felicia MD

Garcia, Bobby MD Female Pelvic Medicine and Reconstructive Surgery University of California Irvine Lechuga, Thomas PhD Perinatalogy Research Labs Department of OB/GYN Chen, Dongbao PhD Perinatalogy Research Labs Department of OB/GYN Nasiri, Azadeh MD Lane, Felicia MD Female Pelvic Medicine and Reconstructive Surgery University of California Irvine

Objectives: Pelvic organ prolapse (POP) is a multifactorial disorder associated with vaginal childbirth, aging, and a weakening of the connective tissue in the pelvic floor. Lysl oxidase-like 1 (LOXL1) and Fibulin-5 are two proteins which play an essential role in the synthesis and assembly of elastic fibers. Animal models lacking the Fibulin-5 gene develop POP spontaneously while those lacking LOXL1 develop POP 1-2 days postpartum. Many recent human studies have reported about the changes in gene and protein expression of Fibulin-5 and LOXL1 associated with POP. The most widely used methods have required a tissue sample or biopsy. The objective of this pilot is to determine if LOXL1 and Fibulin-5 can be extracted noninvasively from vaginal secretions, and to determine if levels of these proteins are associated with POP. Methods: A tampon was used to collect the vaginal secretion specimen. A Bicinchoninic Acid (BCA) assay was performed to determine total protein concentrations. The samples were analyzed by western blotting. The resulting membranes were incubated with anti-LOXL1 and anti-Fibulin-5 antibody. In order to compare levels of protein amongst specimens, a densometry analysis was conducted by normalizing the intensity of LOXL1 and Fibulin 5 expression to a standardized nonspecific band on the SDS PAGE gel. The subjects were divided into pre and postmenopausal cohorts, and then further stratified according to stage of POP. The results were reported as an average normalized density. Results: Using this technique LOXL1 and Fibulin 5 proteins were successfully extracted and measured from both pre and post menopausal cohorts. In the premenopausal cohort, LOXL1 decreased with advancing POP stage while Fibulin-5 protein expression increased. In the post menopausal cohort, LOXL1 expression increased while Fibulin 5 expression decreased with advancing POP stage. Conclusions: This is the first published report of non invasive detection of LOXL1 and Fibulin-5.

Keywords: Pelvic Organ Prolapse; LOXL1; Fibulin-5;

Poster Location: 62

Dose-Response of Rabbit Maxillary Sinus CBF in Lidocaine

Gu, Jeffrey, BS; Chen, Jason, BS; Badger, Christopher, BS; Wong, Brian J.F.

Beckman Laser Institute, UC Irvine School of Medicine

Outcome objectives: 1) Recognize the concentration-dependent relationship between lidocaine and CBF, and thus mucociliary clearance. 2) Consider the concentration-dependent effects of lidocaine on ciliary function in clinical practice. Methods: Fresh ex-vivo rabbit maxillary sinus mucosa was obtained, suspended in buffered solution and viewed through phase-contrast microscope. Control videos of each sample of cilia were recorded using iPhone 6 at 60fps. Lidocaine HCL was slowly added to the buffered solution to reach correct final concentration, and filmed. This method was performed on three samples per concentration (0.00002%, 0.0002%, 0.002%, 0.02%, 0.2%, 2%, and 4%). Fast Fourier Transform (FFT) was used to extract frequency information from signal derived from video to determine ciliary beat frequency (CBF). Results: CBF of control sample was 11.42 ± 0.51 Hz. At 4% lidocaine, CBF was 3.56 ± 0.70 Hz. At 2% lidocaine, CBF was 3.67 ± 0.20 Hz. At 0.2% lidocaine, CBF was 4.24 ± 0.12 Hz. At 0.02% lidocaine, CBF was 4.78 ± 0.59 Hz. At 0.002% lidocaine, CBF was 6.23 ± 0.12 Hz. At 0.0002% lidocaine, CBF was 7.98 ± 1.60 Hz. At 0.00002% lidocaine, CBF was 8.48 ± 0.24 Hz. Ciliostasis was not observed at any concentration. Conclusions: Here we determined the dose-response relationship between ex-vivo rabbit maxillary sinus CBF and lidocaine. Although higher concentrations of lidocaine may significantly decrease CBF, ciliostasis was not observed at concentrations as high as 4%. Conversely, even a concentration of lidocaine as low as 0.00002% may decrease ciliary function.

Keywords: Iphone microscopy; Ciliary beat frequency; Cilia;

Poster Location: 63

Manual Acupuncture, but not Electroacupuncture Stimulate Afferent Nerves through Activation of TRPV1 Receptors to Modulate Pressor Reflexes

Zhi-Ling Guo, MD, PhD; Liang-Wu Fu, MD, PhD; Hou-Fen Su, MD; Stephanie C Tjen-a-looi, PhD; John C. Longhurst, MD, PhD

Department of Medicine, School of Medicine, University of California at Irvine, Irvine, CA 92697, USA

We have shown that manual and electroacupuncture acupuncture (MA and EA) at the P5-6 acupoints stimulate afferents in the median nerve (MN) to modulate sympathoexcitatory cardiovascular reflexes. However, mechanisms underlying MA and EA activation of these sensory afferents and their cell bodies in the dorsal root ganglia (DRG) are unknown. A histological study demonstrated that, compared to non-acupoints, transient receptor potential vanilloid type-1 (TRPV1) receptors are expressed in greater quantities in sensory nerves located in the area of the ST36 acupoint. Therefore, we hypothesized that acupuncture stimulates afferent nerves through activation of TRPV1 receptors to modulate pressor reflexes. In rats, we found that single-unit MN activity evoked by MA at P6 was significantly attenuated ($P<0.05$) by local administration of Iodoresiniferatoxin (Iodo-RTX; a selective TRPV1 receptor antagonist, n=12), but not 5% Dimethyl sulfoxide (DMSO; vehicle, n=12) into the acupoint. Administration of Iodo-RTX into P5-6 did not reduce EA-evoked MN activity (n=8). We also observed that MA at P6 and EA at P5-6 induced phosphorylation of extracellular signal-regulated kinases (pERK) in DRG neurons at spinal levels of C6-8 that receive MN inputs. After knocking-down of DRG TRPV1 receptors at these spinal levels with intrathecal injection of siRNA, pERK expression in DRG neurons was reduced by MA, but not EA. Moreover, local injection of Iodo-RTX (n=8), but not 5% DMSO (n=6) into P6 reversed the inhibitory action of MA at this acupoint on pressor reflexes induced by gastric distension. However, the inhibitory effect of EA at P5-6 on pressor responses evoked by gastric distension was not reversed after administration of Iodo-RTX into P5-6 in five separate rats. Thus, these data suggest that MA, but not EA activate sensory afferents through stimulation of TRPV1 receptors to inhibit reflex increases in blood pressure. (Supported by NIH grant AT009347).

Keywords: Acupuncture; Cardiovascular reflex; Afferent; Transient receptor potential vanilloid type-1 receptors; Gastric distension;

Poster Location: 64

Optical imaging for diagnostic indices in alopecia

Lin, Jessica; Valdebran, Manuel; Mesinkovska, Natasha; Michele Van Hal, MD;Griffin Lentsch; Mihaela Balu, PhD; Emon Heidari; Zhongping Chen, PhD

University of California, Irvine, School of Medicine; University of California, Irvine, Department of Dermatology; Beckman Laser Institute

A variety of diseases cause alopecia (hair loss). Early detection and classification of the alopecia type is necessary for appropriate and effective disease management. The gold standard for diagnosing certain types of alopecia requires biopsying the scalp, an invasive and painful procedure for patients. The advent of in vivo optical imaging modalities now allows noninvasive visualization of hair follicles and surrounding structures that can be used to aid histological analysis. This pilot study used multiphoton microscopy (MPM) and optical coherence tomography (OCT) to visualize areas on the scalp in scarring (eg, frontal fibrosing alopecia) and nonscarring (eg, alopecia areata) types of alopecia. 16 patients were imaged using MPM, and 8 patients with OCT. MPM imaging provides intracellular details with endogenous fluorophores. OCT provides real-time imaging and a 3D mapping capabilities to visualize structures around the hair follicles. These laser-based technologies enable examination of the epidermis and dermis. In the results, features seen in histology, MPM, and OCT are compared.

Keywords: alopecia; multiphoton microscopy; optical coherence microscopy;

Poster Location: 65

Therapeutic potential of human preterm umbilical cord mesenchymal stem cells

Fobi, Raissa, MD:; Nalbandian, Angele, PhD:; Bany-Mohammed, Fayez, MD:; Alshammari, Sana, MD: Almadan, Fatimah, MD: Uy, Cherry, MD: Aslam, Muhammad, MD

UC Irvine Medical Center Division of Neonatology Department of Pediatrics

BACKGROUND: Bronchopulmonary dysplasia (BPD) is a chronic debilitating disease of preterm infants leading to arrested alveolar development. Current therapies lack effectiveness and cause undesirable side effects. Our previous work with mesenchymal stem cell secretome (MSC-s) demonstrated protective paracrine effects in mouse BPD models. OBJECTIVES: Objectives of the study were 1) to isolate, culture, immunodeplete and differentiate human preterm and term umbilical cord mesenchymal stem cells (hUC-MSCs), and 2) to analyze the secretome from preterm and term hUC-MSCs relevant to neonatal BPD, utilizing advanced proteomic analysis. METHODS: The human hUC-MSCs from preterm (<28 weeks') and term (37-40 weeks') cord Wharton's jelly were isolated per published protocols. Immunodepletion was performed per published guidelines followed by differentiation potential assessment into osteocytes and adipocytes. The preterm and term hUC-MSC conditioned media generated for identification of active factors via advanced proteomics. RESULTS: We determined that preterm hUC-MSCs have rapid growth compared to term hUC-MSCs (duplication time 10 ± 2 days vs. 21 ± 3 days). Similarly, the differentiation potential into adipocytes and osteocytes was faster with preterm versus term hUC-MSCs (14 ± 3 days vs. 24 ± 3 days). Advanced proteomics analysis identified several peptides related to BPD in both preterm and term group. Preterm hUC-MSC secretome showed higher concentrations of VEGF, HGF, Spp1, M-Csf1, and procollagen, whereas term hUC-MSC secretome depicted higher concentrations of PDGF, FGF, CTGF, KGF, Thromospondin 2, and complement components. CONCLUSIONS: The hUC-MSCs secrete biologically active factors into their conditioned media and can serve as a potential targeted therapy against BPD. Further studies are underway to examine the preterm hUC-MSC secretome for therapeutic efficacy in vitro and in vivo.

Keywords: Mesenchymal stem cell; MSC media; Neonatal chronic lung disease; Human umbilical cord stem cells; Bronchopulmonary dysplasia;

Poster Location: 66

Mesenchymal stem cell biomakers prevent Bronchopulmonary Dysplasia via suppression of lung inflammation

Aslam, Muhammad, MD 1; Singhal, Meghali MD 1; Lagrandeur, Robin MD; Angele Nalbandian 1; Fayez Bany-Mohammed 1, Cherry Uy 1; Peter Donovan 3; Dan Cooper 2

1. Pediatrics, UC Irvine, Irvine, CA, United States. 2. Pediatric Pulmonology, UC Irvine, Irvine, CA, United States. 3. Molecular and Cell Biology, UC Irvine, Irvine, CA, United States.

Bronchopulmonary dysplasia (BPD) is a chronic debilitating lung disease of preterm infants leading to arrested alveolar development with long term morbidity and high mortality. Our work utilizing bone-marrow derived mesenchymal stem cells conditioned-media (MSC-CM) have shown protective effects in mouse BPD models. Analysis of the MSC-CM identified Osteopontin (Opn) and Macrophage colony stimulating factor 1 (Csf1), as key mediators (biomarkers) leading to protection against BPD. Our pilot feasibility study demonstrated feasibility of detection of Opn and Csf1 in tracheal aspirate fluid (TAF) of preterm infants via immunoassay. Objective: We hypothesized that the lack of above MSC biomarkers at birth leads to development of BPD via uncontrolled TGF-b1 activity. Our objectives were to determine the levels of Opn, Csf1, and active TGF-b1 in the TAF of preterm infants in the first week of life and correlate them with later development and severity of BPD. Design/Methods: Infants less than 32 weeks' gestational age and/or less than 1500 gms birth weight who were intubated within 24 hours of life were enrolled into the study. Two samples of TAF were collected pre and post surfactant. Levels of Opn, Csf1, TGF-b1, and secretory IgA were analyzed using immunoassay. Secretory IgA was used as control to correct for TAF volume. Infants were followed prospectively for outcome data including the development of BPD (oxygen requirement at 36 weeks' corrected gestational age). Results: To date, 29 infants have been enrolled and TAF samples obtained. Subjects were similar in their baseline maternal and neonatal characteristics. Standard curves were used from our pilot study to analyze data. 19 of 29 subjects developed BPD. Levels of Opn and Csf1 were lower at birth for BPD infants when compared with infants who did not develop BPD. Conclusion(s): MSC biomarkers, Opn and Csf1, prevent BPD at birth by suppression of lung inflammation (M1 macrophage surge and active TGF-b1).

Keywords: Stem Cell; BPD; Bronchopulmonary Dysplasia; lung inflammation;

Poster Location: 67

A potential role for group 2 innate lymphoid cells in muscular dystrophy

Jenna Kastenschmidt; Ileen Avetyan; S. Armando Villalta;

Department of Physiology and Biophysics and the Institute for Immunology, University of California Irvine, Irvine, CA 92617

Group 2 innate lymphoid cells (ILC2s) are critical regulators of type 2 inflammatory responses, and promote tissue repair and the restoration of homeostasis. However, whether these repair processes include regenerative responses that encompass ILC2 and tissue stem cell interactions is largely unknown. To address this question, we examined the role of ILC2s in regulating muscle regeneration, a tissue with a high regenerative capacity that is dependent on a well-defined muscle stem cell population (i.e. satellite cells). We show that ILC2s are activated and numbers are elevated in skeletal muscle of mdx mice, a model of Duchenne muscular dystrophy (DMD) in which the regulation of disease pathogenesis is controlled in part by the balance between type I and type II immune responses. Gain-of-function studies using IL-2/anti-IL2 complex (IL-2c) showed that this treatment effectively increased the number of ILC2s in mdx skeletal muscle and increased myofiber cross sectional area, suggesting enhanced muscle regeneration. In addition, ablation of IL-13-producing cells, including ILC2s, inhibited the recruitment of muscle eosinophils, an innate immune cell population previously implicated in muscle regeneration. Collectively our data support a working model in which ILC2s regulate mdx skeletal muscle pathogenesis through both direct interactions with muscle satellite cells and by influencing type II immune responses in the skeletal muscle microenvironment.

Keywords: Duchenne muscular dystrophy; Group 2 innate lymphoid cells; Muscle stem cells;

Poster Location: 68

Restore Visual function by Human Embryonic Stem-cell derived 3D retinal organoid transplants in an immunodeficient retinal degenerate rat model

Lin, Bin, PhD. (1); McLelland, Bryce, B.S. (1); Mathur, Anuradha, M.S. (1); Thomas, Biju (2); Nistor, Gabriel (3); Sigman, Jaclyn (1); Nasonkin, Ignor (4); Aramant1, Robert (1); Keirstead, Hans (3); Seiler, Magdalene (1) (5)

(1) Sue & Bill Gross Stem Cell Research Center, University of California at Irvine, CA; (2) Roski Eye Institute, Department of Ophthalmology, University of Southern California, Los Angeles CA; (3) AiVita Biomedical, Irvine, CA; (4) Bio Time Inc., Alameda, CA; (5) Department of Physical Medicine & Rehabilitation, School of Medicine, University of California at Irvine, CA

Retinal degeneration (RD) diseases such as Age-related Macular Degeneration (AMD) and Retinitis Pigmentosa (RP) affect millions of people worldwide. Most treatment strategies can only delay the progression of the diseases. Our goal is to repair the damaged retina and restore the lost vision by transplanting human embryonic stem cell (hESC) derived 3D retinal organoid (retinoid) sheets. Based on qPCR and immunohistochemistry, we have shown previously that the hESC derived retinoids developed retinal markers and lamination over time. We hypothesize that after transplantation into immunodeficient rho S334ter line-3 RD rats (nude RD rats) the hESC derived retinoid sheets will create new photoreceptors for the host and generate new synaptic connections leading to visual function. To test this, hESC derived 3D retinoids, created based on 2 different protocols, Transplant A (after Zhong et al. Nature Communications 2014) and Transplant B (after Singh et al. Stem Cells & Development 2015), were transplanted unilaterally into the subretinal space of 24-30 day old RD nude rats. Optical coherence tomography (OCT) and optokinetic testing of visual acuity (OKN) were routinely performed after transplantation and superior colliculus (SC) electrophysiology was tested at 4 - 9 months after transplantation (MPS). In OCT imaging, transplants developed layers and photoreceptor rosettes in transplants 4-6 MPS. Histological analysis showed that transplants developed photoreceptors and formed synapses with host. OKN testing demonstrated significant improvement in visual acuity of the transplanted rats at 2-6 MPS. As expected, SC electrophysiology showed no responses in sham surgery rats (n=6) and age-matched non-surgery rats (n=8), while strong responses to the same or dimmer light were found in 11 out of 12 transplanted rats. The data suggested that hESC-derived retinoid transplants in RD nude rats can integrate with the host retina and restore the visual function.

Keywords: retinal degeneration; Human embryonic stem cells; retinal transplantation; electrophysiology; immunohistochemistry;

Poster Location: 69

Retina organoids derived from hESCs and transplanted to immunodeficient RCS rats

Seiler, Magdalene J., Ph.D. (1,2); Lin, Bin, Ph.D. (2); McLelland, Bryce T., B.S. (2);; Mathur, Anuradha, M.S. (2); Nistor, Gabriel, M.D. (3); Aramant, Robert B. , Ph.D. (2); Thomas, Biju B., Ph.D. (4); Keirstead, Hans S., Ph.D. (3)

(1) Dept. Physical Medicine & Rehabilitation, School of Medicine, University of California, Irvine (2) Sue & Bill Gross Stem Cell Research Center, University of California, Irvine (3) AIVITA Biomedical Inc., Irvine CA (4) Roski Eye Institute, Department of Ophthalmology, University of Southern California

The development of retina organoids derived from human embryonic stem cells (hESC) was followed after transplantation to the subretinal space of immunodeficient RCS rats. CSC14 (NIH line 0284) hESCs were differentiated into retina organoids following a protocol modified after Zhong et al. 2014 and characterized by immunohistochemistry (IHC) and qPCR. Dissected sheets of retina organoids (differentiation day 30-63) were transplanted to the subretinal space of nude RCS hosts (1.5-1.9 mo.). Ocular Coherence Tomography (OCT) monitored the development of the transplants at 2 wks to 6 mo. post-surgery. Visual function was accessed by electroretinogram (ERG) before and up to 6 mo. after surgery. Sections through the transplants 20-113 days post-surgery (DPS) were processed for IHC to label human donor, retinal cells and synaptic markers using light and confocal microscopy. Results: Retina organoids showed early lamination and development of retinal cell progenitors. qPCR analysis indicated an expression profile closest to human fetal retina (CHX10+, CRX+, NRL+, LHX2+). OCT imaging revealed the presence of rosettes containing photoreceptors, and provided data on the transplant's distance from optic nerve and volume. Transplanted eyes showed increased B-waves to scotopic stimulation at 2 mo. post-surgery compared to RCS controls. ERG responses were undetectable at 4-6 mo. post-surgery. Transplant histology revealed the development of a rosetted morphology in vivo, with a distinct ONL and photoreceptor outer segments located in the center of rosettes. Transplants showed evidence of migration, and extended processes into the host retina Functional testing of transplanted rats is ongoing. Conclusions: Retina organoids, derived from hESCs were transplanted to the subretinal space of immunodeficient RCS rats. Organoids mature further after transplantation, develop photoreceptors with outer segments, integrate into the host retina, and can improve visual function.

Keywords: retinal degeneration; retinal transplantation; human embryonic stem cell; RCS rat; optical coherence tomography;

Poster Location: 70

Retinal Repair Neural Trace Analysis

Smith, William; Minar, Sydney; ;

Sue & Bill Gross Stem Cell Research Center, University of California at Irvine, CA; 2 Roski Eye Institute, Department of Ophthalmology, University of Southern California, Los Angeles CA; 3 AiVita Biomedical, Irvine, CA. 4 Bio Time Inc., Alameda, CA; 5 Department of Physical Medicine & Rehabilitation, School of Medicine, University of California at Irvine, CA

Retinal degeneration such as Age-related Macular Degeneration and Retinitis Pigmentosa affect millions of people worldwide. Most treatment strategies can only delay the progression of the diseases. Our goal is to repair the damaged retina and restore the lost vision by transplanting human embryonic stem cell derived 3D retinal organoid sheets. Our objective is to document and improve the MatLab code currently used to detect neural activity in the brain of mice. The code currently requires manual influence, and the goal is to fix bugs to make it fully automated and reliable at finding latency, spike count, and spike amplitude of the inputted brain activity. The latency function is used to analyze the time an area of the brain receives an extracellular response from the brain after a stimulus is provided. The spike count function counts spikes over an arbitrary threshold and sums up the different spike responses in a unique location. The spike amplitude function gets the sum averages of the spikes over threshold and this information is useful for determining intensity of response. Since we have been working with a code previously written by other students, we have spent most of our time up until now fully understanding and documenting each step of the code and how it works. We have compiled an extensive amount of work explaining the functions, variables, and processes used in the code. We have moved on to debugging the code's spike count and heat maps. The spike counts works by normalizing the data with high pass filter around zero and finding the number of spikes above a certain threshold during a certain time period. The spike count average per location is put within a 3D-map showing the number of spikes in its respective location. There was a discrepancy between the values shown on heat maps compared to the numbers indicated in the code. We were able to fix this problem so that the 3D map is an accurate representation of the spike count found by the code.

Keywords: retinal degeneration,;

Retinal Degeneration Stem Cell Research - MATLab

Minar, Sydney; Smith, William; ;

University of California, Irvine

Retinal degeneration such as Age-related Macular Degeneration and Retinitis Pigmentosa affect millions of people worldwide. Most treatment strategies can only delay the progression of the diseases. Our goal is to repair the damaged retina and restore the lost vision by transplanting human embryonic stem cell derived 3D retinal organoid sheets. Our objective is to document and improve the MatLab code currently used to detect neural activity in the brain of mice. The code currently requires manual influence, and the goal is to fix bugs to make it fully automated and reliable at finding latency, spike count, and spike amplitude of the inputted brain activity. The latency function is used to analyze the time an area of the brain receives an extracellular response from the brain after a stimulus is provided. The spike count function counts spikes over an arbitrary threshold and sums up the different spike responses in a unique location. The spike amplitude function gets the sum averages of the spikes over threshold and this information is useful for determining intensity of response. Since we have been working with a code previously written by other students, we have spent most of our time up until now fully understanding and documenting each step of the code and how it works. We have compiled an extensive amount of work explaining the functions, variables, and processes used in the code. We have moved on to debugging the code's spike count and heat maps. The spike counts works by normalizing the data with high pass filter around zero and finding the number of spikes above a certain threshold during a certain time period. The spike count average per location is put within a 3D-map showing the number of spikes in its respective location. There was a discrepancy between the values shown on heat maps compared to the numbers indicated in the code. We were able to fix this problem so that the 3D map is an accurate representation of the spike count found by the code.

Keywords: Stem cell; retinal degeneration;

Histological characterization of stem-cell derived 3D retinal progenitor sheet transplants in an immunodeficient retinal degenerate rat model

Mathur, Anu, M.S.; McLelland, Bryce, B.S.; ; Nistor, Gabriel, Sary, Mony; Wan, Jacson; Nasokin, Igor; Aramant, Robert; Keirstead, H.S., Seiler, Magdalene

UC Irvine, Stem Cell Research Center AIVITA Biomedical (Nistor, Keirstead) Biotime Inc (Nasonkin)

Incurable eye diseases such as age related macular degeneration (AMD) and retinitis pigmentosa (RP) are characterized by retinal degeneration (RD). Replacement with retinal progenitor sheets has the potential to restore vision. The current study investigated whether transplants of human stem cell (hESC) derived retinal progenitor sheets could replace the degenerating cells of the host retina and make functionally relevant connections. Our RD model is an immunodeficient (nude) rho SS34ter-line3 rat (will not reject human cells) in which most of the outer nuclear layer (ONL) is absent by P30. hESCs were differentiated into retinal organoids (retinoids) following a protocol similar to Zhong et al. 2014 (Nature Communications 5:4047) or Singh et al. 2015 (Stem Cells & Development 24:2778). These 3D retinoids (differentiation day 30-63) were dissected into sheets and then transplanted into the host subretinal space (P25-30). Transplants 50-300 days post-surgery (DPS) were stained with hematoxylin and eosin (H&E), or processed for immunohistochemistry to label human donor, retinal cells and synaptic markers using light and confocal microscopy. RD sham surgery eyes (150+ DPS) had a complete loss of ONL, however the inner nuclear (INL), plexiform (IPL) and ganglion cell layers (GCL) appeared intact. Transplanted progenitor sheets developed a rosetted morphology in vivo, with a distinct ONL and photoreceptor inner and outer segments located in the center of the rosettes. Transplants (stained with human marker SC-121 or Ku80) extended processes into the host IPL and GCL. Outer segments clearly stained for rhodopsin within the rosettes. The mature retinal markers PKCa (rod bipolar), recoverin (rods and cones, cone bipolar) or rhodopsin (rod outer segments) showed less expression in younger (<100 DPS) than in older (150+DPS) transplants. Neuronal processes of human donor cells (human neurofilament) were dense within the transplant area and extended into the host IPL in all transplants. The labeling of synaptic markers (bassoon and synaptophysin) indicated the presence of functional connections, possibly between the transplant and host retina. In summary, hESC-derived retinal progenitor sheet transplants develop mature retinal cell subtypes including photoreceptors and integrate with the RD host retina.

Keywords: human embryonic stem cells; retinal degeneration; progenitors; transplant;

Poster Location: 73

Electroretinography to determine success of stem cell transplantation in RCS rats

Duong, Jessica; Zhang, Lucy; Monazzami, Marissa; Lin, Bin, Ph.D.; Seiler, Magdalene, Ph.D.

University of California, Irvine; Department of Physical Medicine and Rehabilitation; Stem Cell Research Center

The purpose of our lab is to restore or improve vision of Royal College of Surgeons (RCS) immunodeficient nude rats by transplantation of human embryonic stem cell (hESC) derived sheets. The hypothesis is that hESC-derived sheets can replace degenerated photoreceptors and rescue existing photoreceptors from further degeneration. Development and integration of mature photoreceptors may lead to improvements in visual performance of patients with retinitis pigmentosa and age-related macular degeneration (AMD). To trace the possible improvement in vision via retinal sheet integration, electroretinogram (ERG) tests provide a noninvasive method of measuring vision changes over time. ERG testing was performed on 3 RCS nude rat groups: age-matched control (AMC) rats, hESC-derived transplant rats, and sham surgery rats. In addition, only the left eyes of RCS rats receive transplantation, forming an internal control group. ERG tests were conducted monthly for AMC group; 1 and 2 weeks before surgery then monthly from 1 to 9 months after surgery for transplant and sham groups. As expected, visual responses of AMC and sham groups declined significantly as rats aged. In contrast, there were higher visual responses from transplant rats after surgery. Then degeneration of photoreceptors of RSC rats caused decrease of visual responses began around 4 months post surgery and then became too insignificant to trace. However, significant improvement in vision after surgery supported our hypothesis. The ERG exams supply invaluable data to be integrated into the ongoing research on combating retinal degenerative diseases and its successful results provide a foundation for future clinical trials in humans.

Keywords: stem cell; retinal degeneration; electroretinography; RCS rats;

Poster Location: 74

Modeling epilepsy with isogenic human iPSC-derived neurons

Xie, Yunyao; Ng, Nathan; Safrina, Olga; Konopelski, Sara; Schutte, Ryan; Figueroa, Priscilla ; Schutte, Soleil; Stover, Alexander; Ess, Kevin; George Alfred; Smith, Martin; Schwartz, Philip; O'Dowd, Diane.

University of California, Irvine, Department of Developmental and Cell Biology; University of California, Irvine, Department of Anatomy and Neurobiology; Children's Hospital of Orange County; Vanderbilt University, Department of Pediatrics; Northwestern University, Department of Pharmacology.

Over 1200 mutations in the SCN1A gene, encoding the alpha subunit of the Nav1.1 voltage-gated sodium channel, have been identified and are associated with a wide range of epileptic disorders including genetic epilepsy with febrile seizures plus (GEFS+). How specific SCN1A mutations affect neuronal activity in the human genetic context is not well understood. To address this question we differentiated neurons from three human iPSC lines: 1) patient with K1270T SCN1A mutation (GEFS+ sibling), 2) control (unaffected sibling), and 3) isogenic mutant generated by CRISPR/Cas9 editing of the control line. Three weeks after plating onto astrocyte feeder layers, the large majority of cells with neuronal morphology in all three lines, fired action potentials and received glutamatergic and/or GABAergic synaptic input. Electrophysiological analysis showed a decreased firing frequency and a more depolarized action potential threshold in inhibitory neurons of patient and isogenic mutant lines, while the excitatory neurons remained mostly unaffected with a similar firing frequency and action potential threshold to the control. We identified a cell type-specific impairment of excitability caused by K1270 SCN1A mutation. This isogenic iPSC model will be beneficial to deciphering the links between SCN1A mutations and the impact on epileptic disorders, facilitating the development of personalized anti-epileptic medicine and improved therapies.

Keywords: iPSC; Neurons; Epilepsy; Excitability;

Poster Location: 75

Therapeutic Effects of Idebenone on Mice with VCP Disease

Ta, Lac; Ellur, Sanjanna; Yu, Howard; Avanti, Mahima; Weitz, David; Weiss, Lan; Kimonis, Virginia E.

Division of Genetics and Genomics, Department of Pediatrics, University of California-Irvine School of Medicine, Irvine, CA 92697, USA

Inclusion body myopathy associated with Paget's disease and frontotemporal dementia (IBMPFD) is a complex, autosomal dominant disorder that is caused by mutations in the valosin-containing protein (VCP) gene. Consequently, a mutation in VCP results in decreased production of ATP in mitochondria, and symptoms of VCP disease involve progressive muscle weakness. Since Idebenone is an analog of co-enzyme Q10, the predominant form of ubiquinone in humans, it has potential to treat mitochondrial respiratory chain disorders. Therefore, we hypothesize that Idebenone will produce therapeutic effects within mice with VCP disease due to its role as an antioxidant to restore electron flow in the respiratory chain. This experiment aims to determine the therapeutic potential of Idebenone to ameliorate muscle weakness and pathology of VCP disease. Male and female mice (n=33) were divided into separate groups with treatments of Idebenone, corn oil, and water as a control for several months to determine changes in the muscle strength and endurance measured by Rotarod and grip strength tests. Tissue samples were harvested in order to perform immunohistopathology analysis to detect specific protein markers, such as TDP-43, and autophagy markers, such as p62 and LC3. Based on analysis of the motor tests, there was an increase in Rotarod latency to fall after two months for treatment groups with Idebenone which indicated a therapeutic effect on the mitochondrial respiratory chain within the mice. In addition, we observed that mice with corn oil treatment also had an increase in the Rotarod latency to fall after two months. While Idebenone appears to have produced therapeutic effects and helped improve muscle performance, more analysis and studies are required to fully support the claim that Idebenone is solely the reason for improved muscle strength and endurance. Immunohistopathology analysis is currently on-going to determine if Idebenone directly affects VCP disease pathology.

Keywords: Idebenone; Valosin-containing protein (VCP); IBMPFD; mitochondrial respiratory disorder; muscle weakness;

Poster Location: 76

Lipidomics Associated Signaling Pathways In VCP Myopathy

Weiss, Lan, MD, PhD; Llewellyn, Katrina, PhD; Nalbandian, Angele, PhD; Yu, Howard; Jung, Kwang, PhD; Piomelli, Daniele, PhD; Kimonis, Virginia, MD.

Department of Pediatrics, Department of Anatomy & Neurobiology, School of Medicine, University of California-Irvine

Valosin-containing protein (VCP), a member of the AAA-ATPase super family mediates a network of protein quality control processes including endoplasmic reticulum-associated protein degradation (ERAD), autophagy and mitochondria-associated degradation. Our studies indicate that VCP may also be involved in lipid metabolism. Patients with VCP disease have progressive myopathy and muscle shows presences of TAR-DNA binding protein 43 (TDP-43) positive, ubiquitinated inclusion bodies as well as elevated levels of autophagy markers, LC3-I/II and p62. We have previously generated a mouse model with the common VCP R155H mutation. Homozygous VCPR155H/R155H mice typically die by day 21, however we are able to rescue the disease by a lipid-enriched dietary (LED) diet. A targeted lipidomic analysis of skeletal muscle and liver showed ceramide accumulation in mutant mice fed the normal diet and amelioration in the mice fed the LED. We then utilized pharmacological agents that selectively increase or inhibit (1) the production or (2) the degradation of ceramide to explore the translational potential of modifying the lipidomics-associated cascade. We studied the treatment with ARN 0082, an inhibitor of ceramide degradation to see if it would worsen the phenotype. We saw an increase in the expression of TDP-43 and autophagy markers LC3I/II and p62 expression level in VCP myoblasts. We also studied the selective SPT inhibitors, ARN14494, myriocin and L- cycloserine. These ceramide synthesis inhibitors significantly reduced ceramide biosynthesis in wild-type WT and HZ mouse myoblasts and also VCP patient human induced pluripotent stem cell (hiPSC) derived myoblasts. Treatment also resulted in decrease in expression of TDP-43 and autophagy markers LC3I/II and p62 expression levels. Our studies in understanding the phenomenon of ceramide pathogenesis in neuromuscular disease stem from the observation of the striking rescue of the early lethality in the homozygous VCP mice. We ar

Keywords: Ceramide; Inclusion body myopathy; L-cycloserine; valosin-containing protein (VCP);

Poster Location: 77

Analyzing the Muscular and Respiratory Effects of Resistance Training in Patients with Pompe Disease

Bhatnagar, Caleb; Kimonis, Virginia, M.D.

Pompe disease is a rare inherited progressive autosomal recessive neuromuscular disorder associated with muscle weakness and respiratory insufficiency that can affect all ages, ethnicities, and gender. While the enzyme replacement therapy (ERT) became clinically available and works very well in the cardiac muscle of patients who present in infancy with large hearts due to excessive glycogen storage, it is not as effective in patients who present after infancy with muscle weakness. Stabilization or some improvement has been seen in patients with a later onset, it is worthwhile to investigate other therapies that may slow the progression of their condition and improve quality of life. In this context, exercise/physical activity seems like an obvious choice, because activities like resistance training (RT) are known to be anabolic and produce muscle hypertrophy and improved muscle function in normal individuals. Somewhat shockingly very little is known about the role of physical activity in mitigating the muscle atrophy associated with Pompe disease. To our knowledge, previous studies have not examined the therapeutic efficacy of using RT to blunt/prevent the loss of muscle mass and function in patients with Pompe disease. Hence, the goal of this proposal is to evaluate and document potential benefits of RT in compliant patients and describe the benefit of combining enzyme replacement therapy (ERT) with RT. In the second aim of our study we will be testing and measuring patient respiratory function. We propose analyzing the activity level of the subjects between the baseline period and the exercise study with a health and exercise monitoring device/activity tracker.

Keywords: Pompe Disease; Pediatrics; Genetics; Rare Disease;

Poster Location: 78

Stable isotope profiles reveal active production of VOCs from human-associated microbes

Phan, Joann; Meinardi, Simone; Barletta, Barbara; Blake, Don; Whiteson, Katrine

Department of Molecular Biology and Biochemistry, University of California, Irvine, CA, United States Department of Chemistry, University of California, Irvine, CA United States

Volatile organic compounds (VOCs) measured from exhaled breath have great promise for the diagnosis of bacterial infections. However, determining human or microbial origin of VOCs detected in breath remains a great challenge. For example, the microbial fermentation product 2,3- butanedione was recently found in the breath of Cystic Fibrosis (CF) patients; parallel culture-independent metagenomic sequencing of the same samples revealed that Streptococcus and Rothia spp. have the genetic capacity to produce 2,3-butanedione. To investigate whether the genetic capacity found in metagenomes translates to bacterial production of a VOC of interest such as 2,3-butanedione, we fed stable isotopes to three bacterial strains isolated from CF patients: two gram-positive bacteria, Rothia mucilaginosa and Streptococcus salivarius, and a dominant opportunistic gram- negative pathogen, Pseudomonas aeruginosa. Culture headspaces were collected and analyzed using a gas chromatographic system to quantify the abundance of VOCs of interest; mass spectroscopy was used to determine whether the stable isotope label had been incorporated. Our results show that R. mucilaginosa and S. salivarius consumed D-Glucose-13C6 to produce labeled 2,3-butanedione. R. mucilaginosa and S. salivarius also produced labeled acetaldehyde and ethanol when grown with 2H2O. Additionally, we find that P. aeruginosa growth and dimethyl sulfide production are increased when exposed to lactic acid in culture. These results highlight the importance VOCs produced by P. aeruginosa, R. mucilaginosa, and S. salivarius as nutrients and signals in microbial communities, and as potential biomarkers in a CF infection.

Keywords: Metabolomics; Volatile organic compounds; Cystic Fibrosis; clinical isolates;

Poster Location: 79

RNA sequencing of a Cystic Fibrosis isolate identifies genes and novel operons contributing to adaptation to acidic environments

Gallagher, Tara; Phan, Joann; Whiteson, Katrine, Ph.D.;

UCI Department of Molecular Biology and Biochemistry

Cystic fibrosis (CF) is a genetic disease that affects 30,000 people in the U.S. and 70,000 people worldwide. CF patients have a mutation in the CF transmembrane receptor (CFTR), resulting in reduced ion transport across epithelial cells and accumulation of dense mucus in the lungs. The thick mucus cannot be cleared from the airways, leading to colonization of the CF lungs with microbes. CF pathogens must adapt to complex microenvironments in the lungs that have variations in pH, oxygen levels, metabolites, and microbial composition. The use of culture-independent methods, such as genomics and transcriptomics, contributes to our knowledge of the composition and pathogenesis of bacteria that colonize the CF lungs. In order to determine virulence factors that contribute to colonization of the lungs, we isolated Stenotrophomonas maltophilia from the sputum of a CF patient. S. maltophilia is a Gram-negative opportunistic pathogen that has been identified in the metagenomes from the sputum of CF patients, yet there are little studies on the role of this organism in CF bacterial pathogenesis. In order to identify genes that contribute to S. maltophilia pathogenesis, we sequenced the genome and transcriptome of S. maltophilia. We sequenced the transcriptomes of S. maltophilia cultured in acidic, neutral, and basic pH media in order to identify genes that would contribute to this bacterium's adaptation to different pH in the CF lungs. The transcriptome of S. maltophilia grown in basic pH was similar to when it is grown in neutral pH. In contrast, in an acidic environment, S. maltophilia upregulates multidrug-resistance and macrolide resistance operons. S. maltophilia also upregulates operons with unknown annotations, suggesting these novel operons contribute to S. maltophilia's adaptation to an acidic environment.

Keywords: cystic fibrosis; transcriptome; genome; bacteria; pH;

Poster Location: 80

Airway Microbe Analysis in Preterm Infants with Bronchopulmonary Dysplasia

Singhal, Meghali, MD 1; Aslam, Muhammad, MD 1; Whiteson, Katrine, PhD 2; Angele Nalbandian PhD 1; Fayez Bany-Mohammed, MD 1; Cherry C Uy, MD 1

1. UCI Medical Center, Division of Neonatology. 2. Division of Biochemistry and Microbiology, UCI Main Campus.

BACKGROUND: Bronchopulmonary dysplasia (BPD) is one of the most common chronic debilitating lung diseases among infants and children. BPD predominately affects preterm infants with high morbidity and mortality. Despite advances in preterm care the incidence of BPD remains high. Etiology of BPD is multifactorial with prematurity, infection/inflammation, mechanical ventilation, and maternal chorioamnionitis as the leading causes. With success in whole human genome sequencing and development of affordable ways to study microbiome and metabolomics in humans, the relationship between diverse microbiome and development of diseases has been established. Limited studies are reported neonatal microbiota, mostly limited to skin and GI tract. We hypothesize that lung microbiota will provide useful information regarding development and severity of BPD. Our objective is to analyze microbiota within the tracheal aspirate fluid (TAF) of preterm infants with and without BPD to identify specific metabolites unique to development of BPD. METHODS: Infants less than 32 weeks' gestational age and/or less than 1500 gms birth weight who were intubated within 24 hours of life were enrolled into the UCI IRB-approved study. Those with neuromuscular or congenital anomalies or pulmonary hemorrhage were excluded. The TAF sample was obtained at intubation before any exogenous surfactant administration. Samples are being analyzed for microbial community with 16S rRNA sequencing, and for primary metabolites with GC-MS and lipids/polar compounds with LC-MS. RESULTS: To date, 16 infants have been enrolled into the study and TAF samples collected, processed. The samples are currently being analyzed for the above mentioned markers and clinical data being collected. 6 of 16 infants have developed BPD. We anticipate final data results to be available within the next few weeks which will provide us the opportunity to present this exciting data at the conference. CONCLUSIONS: Analysis of lung microbi

Keywords: Preterm; BPD; microbiome;

Poster Location: 81

Mitochondrial regulation of microRNA and implications for macular degeneration

Schneider, Kevin, PhD; Kenney, Maria Cristina, MD, PhD; ;

University of California Irvine, Ophthalmology

Purpose: The role of microRNA in age-related macular degeneration (AMD) is of great interest for understanding disease progression, and development of possible treatments. This study investigates the role that mitochondria play in regulation of microRNA. We hypothesize that cybrids containing mitochondria from AMD patients will differentially express microRNAs compared to cybrids with age-matched normal mitochondria. Methods: Our experiments utilize a "personalized" transmitochondrial cybrid model in which mitochondria from clinically well-characterized patients, are isolated and fused with human retinal pigmented epithelial cells (ARPE-19) lacking mitochondria (Rho0). The cell lines have identical nuclei, so changes in microRNA levels are attributed to the influence of patient mitochondria. Total RNA including microRNA was extracted from normal (n=5) and AMD (n=5) cybrids. Isolated microRNA were amplified, sequenced and compared with microRNA database MIRbase. MicroRNA expression levels were calculated and normalized to total read number. Statistical analyses by unpaired t-test. Results: Cybrids containing AMD mitochondria exhibited downregulation in mir30d-5p (0.84 fold, p=0.02), and mir338-5p (0.64 fold, p=0.05). AMD cybrids also exhibited upregulation of mir135b-5p (3.03 fold, p=0.007), mir148a-3p (2.09 fold, p=0.02), and mir331-5p (1.42 fold, 0.02). Changes in the above microRNA have been associated with inflammation, oxidative stress, increased vascular endothelial growth factor (VEGF) expression, increased cell autophagy and increased levels of amyloid beta. Conclusions: Our results support our hypothesis that there are a subset of microRNA whose expression is regulated by the mitochondria. Mitochondria from patients with AMD induce expression of microRNA consistent with the inflammatory and angiogenic characteristics of wet AMD. These microRNA could serve as potential biomarkers for AMD, and modulation of their levels could provide therapeutic benefits.

Keywords: Macular Degeneration; microRNA; Mitochondria; Vascular Endothelial Growth Factor; Retina;

Poster Location: 82

Effects of Anti-angiogenic Drugs on Expression Patterns of Genes Involved in Different AMD Pathogenetic Pathways

Mohamed, Mohamed1,2; Moustafa, M. Tarek1,2; Atilano, Shari R1; Memon, Abdul Sami1; Riazi, Mohamed1; Tsao, Sean W.1; Kenney, Cristina M.1; Kuppermann, Baruch D.1

1Gavin Herbert Eye Institute, University of California, Irvine, USA, 2Ophthalmology Department, Minia University, Minia, Egypt

Purpose: Age-related macular degeneration (AMD) is a highly heritable neurodegenerative disease with at least 19 identified risk loci to date. This study examines effects of anti-VEGF drugs on the transcription of genes involved in different AMD pathogenetic pathways in immortalized human RPE cells (ARPE-19) in vitro. Methods: ARPE-19 cells were treated for 24 h with ranibizumab, bevacizumab, or aflibercept in 1X and 2X concentrations of the clinical intravitreal dose. Untreated cells were used as controls. RNA was isolated and quantitative reverse transcription-polymerase chain reaction (qRT-PCR) was performed in triplicates using primers for angiogenesis (VEGFA and HIF1A), apoptosis (BAX and BCL2L13), inflammation (IL18 and IL1B) and oxidative stress (GPX3 and SOD2). ??Ct (differences in cycle thresholds) was obtained and folds calculated using the formula 2^??Ct. Unpaired t test was used for statistical analysis. Results: Aflibercept-treated cells significantly overexpressed GPX3 and IL1B at 1X concentration, and SOD2, BAX, GPX3, and BCL2L13 at 2X concentration compared to untreated cultures. Ranibizumab-treated cells significantly overexpressed SOD2, BAX, GPX3, and BCL2L13 at 1X concentration; and HIF1A, SOD2, BAX, GPX3, and BCL2L13 at 2X concentration. Bevacizumab-treated cells significantly overexpressed VEGFA, HIF1A, SOD2, BAX, GPX3, and BCL2L13 at 1X concentration; and VEGFA, SOD2, BAX, GPX3, IL1B, and BCL2L13. Conclusions: Our results show that anti-VEGF drugs can alter expression of angiogenesis, apoptosis and inflammation genes, which are important pathways involved in AMD pathogenesis. Our findings suggest that in addition to binding vascular endothelial growth factor (VEGF) and blocking receptor interactions for angiogenesis inhibition, these drugs have broader mechanisms of action. That may help us understand patient's variability in response to anti-VEGF drugs.

Keywords: Anti-angiogenic drugs; Age-related macular degeneration; Gene expression;

Poster Location: 83

Mapping Dental Plaque Re-Accumulation: an Imaging Approach

Golabgir Anbarani, Afarin; Vu, Thinh; Ho, Jessica; Ali Forghany, Fatemeh Kashani, Tracie Lam, Karan Sahni and Petra Wilder-Smith DDS PhD

University of California, Irvine

Objectives:To evaluate a simple imaging-based approach to measuring dental plaque removal and re-accumulation after one-time use of a toothpaste or a dental gel. After providing informed consent (UCI IRB 2013-9778),photographs and Plaque Index (PI)(Quigley-Hein with Turesky Modification) were recorded in 10 subjects who subsequently received oral hygiene instructions.Then, subjects brushed with a washout toothpaste (Tom's of Maine Whole Care Toothpaste) for 1 week.Next,subjects were randomly assigned with regard to sequence of toothpaste use-beginning with either 2.6% Livionex Dental Gel (Livionex, Los Gatos, CA) or Colgate TotalR (Colgate-Palmolive,New York, NY) toothpaste.On the evening of Day 7 of week 1,subjects brushed with the first assigned toothpaste.Then they abstained from oral hygiene through the next morning,when PI was recorded, plaque was stained using plaque disclosing solution (2-Tone Disclosing Agent by Young Dental) and standardized intra-oral photographs were taken.Subsequently,subjects brushed for 2 minutes with the same toothpaste that they had used the previous night, and again PI was recorded,and plaque was stained and photographed.After 1 week washout, this was repeated with the second test toothpaste.Using image J,plaque presence expressed as percent of each tooth surface covered was computed. Mean Baseline PI was 2.44 for each leg. Mean increase in Plaque Index overnight was significantly higher for Colgate (1.78) compared to Livionex (0.94) (p=0.002). After morning brushing, the reduction in the PI from Baseline also differed significantly between Colgate (0.24) and Livionex (1.13) (p=0.002).The Area covered by plaque overnight was higher for Colgate (22.3%) compared to Livionex (11.8%) (p=0.02).After morning brushing, the residual Plaque area for Colgate (9.2%) was higher than for Livionex (3.6%) p=0.039.Correlation between imaging and clinical data was 0.6953. A simple imaging-based approach can quantify plaque presence and removal.

Keywords: Dental; Re-accumulation; Imaging; Dental gel; plaque removal;

Poster Location: 84

Developing a Saliva-based Oral Cancer Risk Test for Underserved Population in a Community-Basec Setting

Golabgir Anbarani, Afarin; Lai, Kevin; Islip, Delaney Elizabeth; Betul Ilhan PhD, Cherie Wink RDH, Petra Wilder-Smith DDS PhD

University of California, Irvine

Background Long-term goal is to develop a non-surgical technique based on salivary transcriptomic biomarkers in conjunction with Optical Coherence Tomography (OCT) imaging to diagnose and monitor oral premalignancy in patients with leuko- and erythroplakia. The objective of this study is to identify the relationship between OCT imaging-based biomarkers and 3 salivary mRNAs involved in deregulation of cell proliferation and inherent death in patients with dysplastic leukoplakia and erythroplakia. Study Design/Materials and Method A total of 7 patients with oral dysplastic lesions were monitored over 3 months. Lesions were imaged with OCT and unstimulated saliva samples were collected at 0, 1 and 3 months. Using ABI 7500 real-time PCR system, quantitative polymerase chain reaction was performed to evaluate the expression levels of 3 mRNAs (IL-8, IL1B, SAT) that were isolated from saliva using a commercial kit. Isolated RNA was reverse transcribed into cDNA by means of RNA-directed DNA polymerase and used for amplification with a PCR mix using primers for each biomarker. OCT images were scored on a standard scale of 0-6 and read by a blinded experienced examiner. Histopathology reports were obtained. Results 5 subjects completed this pilot study, their lesions showed considerable internal heterogeneity. OCT image-based diagnoses were in agreement with histopathological diagnosis in 4/5 subjects (kappa value 0.8). In 3/5 subjects, based on OCT, lesions showed progression between visits 2- 3. In these 3 subjects, the up-regulation of IL1B and IL8 were observed, but they were not consistent between patients. 1 patient had progressed to oral squamous cell carcinoma exhibited an up-regulation of SAT and IL-8. Conclusion Salivary mRNAs are promising biomarkers in the early detection and follow up of oral dysplastic lesions. Larger studies are underway to elucidate the role of specific mRNAs as possible predictors for the progression of oral dysplasia.

Keywords: saliva; oral cancer; OCT; translation; dental;

Poster Location: 85

Aptamer molecular biosensor for bladder cancer diagnosis and surveillance

Wu, Yi Xi; Luptak, Andrej

University of California, Irvine; Department of Pharmaceutical Sciences

Biomarkers have the potential to improve the standard care of current medical practices. However, the process from discovery to translation of biomarkers for clinical practices requires labor intensive, time consuming, and expensive procedures; thus, this process remains an enormous challenge. Conventional methods for biomarker discovery rely on analytical techniques to identify biomarkers based on clinical or experimental observations, and once identified, validation and assay development follows. Due to this pitfall, limited reliable biomarkers have been identified and implemented for clinical practices. Therefore, new approaches are in urgent need to improve the effectiveness of biomarker discovery and translation. This project aims to tackle this obstacle by utilizing in vitro selection technique with patient urine samples to evolve and isolate molecular binders that will recognize a panel of biomarkers capable of distinguishing cancerous from non-cancerous urine. Recent research demonstrated that in vitro selection has the capabilities to generate molecular binders highly specific to a microorganism from a complex sample without prior target separation and identification steps. Therefore, we hypothesize this method is also feasible for diseased models. More specifically, we aim to define and profile the molecular biomarkers of bladder cancer in urine utilizing in vitro evolution to generate reliable structure-switching aptamers that recognize disease states. Urine is a strategic bio-fluid for this application since superficial bladder cancer develops within the inner lining of the bladder where it is in perpetual contact with urine, therefore certain molecules and shedding cells are released into urine. Additionally, urine is a readily accessible bio-fluid requiring no invasive means making it ideal for diagnosis and surveillance. Currently, numerous selection rounds have been performed and an enrichment of the library for bladder cancer urine is observed.

Keywords: biosensor; aptamer; bladder cancer;

Poster Location: 86

Effects of ranibizumab and bevacizumab on phagocytic properties in human RPE cybrids with AMD versus normal mitochondria

Vo, Thomas, BS; Abedi, Sina; Chwa, Marilyn, MS; Kenney, Maria Cristina, MD, PhD

Gavin Herbert Eye Institute, University of California, Irvine

Purpose: A critical biological function of RPE cells is phagocytosis of photoreceptor outer segment (POS) disc membranes. Mitochondrial damage and dysfunction are associated with RPE cells of age-related macular degeneration (AMD) retinas. In this study, we used a transmitochondrial cybrid model to compare the phagocytic properties of RPE cells that contain AMD mitochondria versus age-matched normal mitochondria and their response to treatment with anti-VEGF drugs, ranibizumab and bevacizumab. Methods: Cybrids, which are cells lines with identical nuclei but different mitochondria, are made by fusing Rho0 ARPE-19 cells with platelets from AMD and age-matched normal patients. AMD (n = 3) and normal (n = 3) cybrids were treated with both 1μm fluorescent latex beads (1.52 x 107 beads/mL) and either 172 mM of ranibizumab or 140 mM of bevacizumab. These doses of anti-VEGF are equivalent to intravitreal injections given to AMD patients with choroidal neovascularization. Flow cytometry was performed using the ImageStreamX Mark II to assess phagocytic bead-uptake. The average fold values for bead-uptake and SEM were calculated by the GraphPad Prism software. Results: The normal cybrids showed a bead-uptake fold value of 1.091 ± 0.025 (p = 0.076) after treatment with ranibizumab and 1.084 ± 0.045 (p = 0.14) with bevacizumab compared to the untreated normal cybrids (1.000 ± 0.031). The ranibizumab-treated and bevacizumab-treated AMD cybrids had a bead-uptake value of 1.11 ± 0.041 (p = 0.014) and 1.045 ± 0.077 (p = 0.46), respectively, compared to the untreated AMD cybrids (1.000 ± 0.020). Conclusions Our initial findings suggest that cybrids possessing AMD mitochondria respond similarly to normal cybrids when treated with bevacizumab. When treated with ranibizumab, cybrids with AMD mitochondria had an increase in bead-uptake, which was not observed in cybrids with normal mitochondria. This may suggest an additional benefit of treatment with ranibizumab over bevacizumab.

Keywords: macular degeneration; mitochondria; phagocytosis; bevacizumab; ranbizumab;

Poster Location: 87

Coevolution of human gut Enterococcus with lytic phage

Wandro, Stephen; Oliver, Andrew; Gallagher, Tara; Martiny, Jennifer; Whiteson, Katrine

UC Irvine Molecular Biology and Biochemistry UC Irvine Ecology and Evolutionary Biology

Bacteriophages are highly abundant in the human microbiota, but their effect on the abundance and diversity of resident microbes is still unclear. The abundance and ratio of bacterial species, especially in the gastro-intestinal tract, can have important consequences for human health. Phage predation can drive the evolution of bacterial resistance, which can then drive reciprocal evolution in the phage. These coevolutionary dynamics have been extensively studied in few ecological systems, and investigation into other systems is required. We performed experimental coevolution of clinical isolates of Enterococcus faecalis and Enterococcus faecium from healthy human stool with a single infecting T4-like bacteriophage. Each species of Enterococcus and phage were cultured together for eight days by diluting in fresh media every twelve hours. Phage evolution was compared to coevolution in a separate arm where phage were continuously evolved against a naïve host. Both the bacteria and phage genomes were sequenced at a high depth throughout the experiment. Growing phage on either E. faecalis and E. faecium results in mutations in the tail fiber and capsid proteins in the context of both coevolution and continuous evolution to the naïve host. Phage lysis hindered bacterial growth at early timepoints which selected for resistant bacteria with mutations in aggregation promoting factors and surface proteins. In response to initial bacterial resistance, phage coevolving with E. faecium duplicate tail fiber genes to continue lysing the resistant host. Phage coevolving with E. faecalis are unable to overcome the first wave of bacterial resistance and either become extinct or remain at a very low abundance. Bacteria-phage coevolution in the human gut is likely an important driver of bacterial composition and genotype. Further studies will be required to determine the effects on the microbiome and human health.

Keywords: Phage; Enterococcus; Coevolution; Microbiome; Genomics;

Poster Location: 88

Modulation of epigenetic markers in transmitochondrial age-related macular degeneration (AMD) ARPE-19 cybrid cells

Nashine,Sonali R.; Lu, Stephanie; Nesburn, Anthony; Kuppermann,Baruch D.; Kenney, M. Cristina

Sonali R. Nashine1,2; Stephanie Lu1,3; Anthony Nesburn1,4; Baruch D. Kuppermann1; M. Cristina Kenney1,5 1. Gavin Herbert Eye Institute, University of California Irvine, Irvine, CA, USA. 2. Ophthalmology, University of California Irvine, Irvine, CA, USA. 3. VA Medical Center Long Beach Hospital, Long Beach, CA, USA. 4. Cedars-Sinai Medical Center, Los Angeles, CA, USA. 5. Pathology and Laboratory Medicine, University of California Irvine, Irvine, CA, USA.

Epigenetic changes are implicated in the pathogenesis of age-related macular degeneration (AMD). However, the role of AMD mitochondria in mediating those changes has not yet been demonstrated. Therefore the goal of our study was to demonstrate that mitochondria from AMD patients modulate epigenetics in ARPE-19 transmitochondrial cybrids. We observed that methylation and acetylation genes' expression were significantly altered between NL and AMD cybrids. DNMT1 gene, which encodes an enzyme that predominantly methylates CpG residues, and MBD2 that represses transcription from methylated gene promoters, were significantly down-regulated (DNMT1: Fold Change (FC)=0.69, P=0.03; MBD2: FC=0.8, P=0.02) in AMD cybrids compared to NL cybrids. Furthermore, DNMT3A and DNMT3B which function as de novo methyltransferases as well as transcriptional repressors, showed significantly increased gene expression (DNMT3A: FC=1.5, P=0.01, DNMT3B: FC=1.5, P=0.008) in AMD cybrids. MAT2B which catalyzes the biosynthesis of S-adenosylmethionine from methionine and ATP, was significantly up-regulated (FC=1.3, P=0.04) in AMD cybrids. In addition, histone deacetylases, HDAC1 and HDAC6, which are responsible for the deacetylation of lysine residues on core histones, were significantly up-regulated (HDAC1: FC=1.5, P=0.0004; HDAC6: FC=2.63, P<0.0001) in AMD cybrids compared to NL cybrids. In conclusion, since all cybrids differed only in mtDNA content, our results suggest that AMD mitochondria can mediate changes in the methylation and acetylation genes' expression, and regulate the epigenetic machinery in ARPE-19 transmitochondrial cybrids.

Keywords: AMD; Mitochondria; RPE; EPIGENETICS; ARPE-19;

Poster Location: 89

Targeting the intoxication pathway of Botulinum neurotoxins with heavy-chain camelid antibodies

LAM, KWOK-HO; SHOEMAKER, CHARLES B.; JIN, RONGSHENG

Department of Physiology and Biophysics, University of California, Irvine, Irvine, California, USA. Department of Biomedical Sciences, Tufts Cummings School of Veterinary Medicine, North Grafton, Massachusetts, USA

Botulinum neurotoxin (BoNT) is one of the most acutely lethal toxins known to human and its extreme potency poses a major bioweapon threat. Therefore, effective diagnosis and treatment measures of BoNT are urgently needed. Recently, single-domain variable heavy-chain (VHH) antibodies have been examined as a countermeasure because of its high stability and ease of production. Despite efforts have been made to isolate VHHs specific to various BoNT serotypes commonly found in human, the underlying mechanism of inhibition remains poorly understood and therefore limiting their effective uses. Here, we presented a comprehensive structural study to elucidate the structures and inhibition mechanisms of eleven VHHs bound to non-overlapping epitopes across BoNT/A, B, and E. Our data reveals that the VHHs employ diverse mechanisms to achieve toxin neutralization by competing with the protein and ganglioside binding sites, blocking the substrate translocation, or inhibiting the substrate cleavage activities. Knowledge gained from the complex structures prompted us to enhance the potency of the VHHs by linking two VHHs with optimal peptide linker. We created a BoNT/B-specific VHH heterodimer that blocks protein and ganglioside receptors and a BoNT/A-specific heterodimer that simultaneously bound to the enzyme and the translocation domains. Both VHHs demonstrated affinity and potency superior to those by randomly linking two neutralizing VHHs without structural information. This study shed light on future rational design of multi-valent VHHs that can offer therapeutic benefit.

Keywords: Botulinum neurotoxin; Heavy-chain camelid antibody; Toxin; Structure-based antibody design;