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Poster Session Abstracts

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Poster #: 1 *Highlighted Oral Presenter

Are we close to finding a Cure for Diabetes? Stem Cell Transplantation reverses hyperglycemia in Diabetic Mice

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Human embryonic stem cells programmed to differentiate into insulin producing cells (hESC-IPCs) represent a potentially limitless source of tissue for islet transplantation. In collaboration with Novo Nordisk LLC, we are evaluating hESC-IPC's technologies for treatment of Type 1 diabetes. The aim of this study was to evaluate in vitro and in vivo function of alginate encapsulated hESC-IPCs. Athymic Nude mice (AN), rendered diabetic with 180 mg/kg of streptozotocin (STZ) injected into the peritoneal cavity were maintained on subcutaneous, slow release insulin implants (Linbit Inc, Toronto, ON) 2/mouse). After quality control analysis was performed, 10,000 viable (84±2%), functional (SI=2.27±0.09) SCC were transplanted under the kidney capsule (KC). Approximately 20,000 viable (81±1%), functional (SI=2.63±0.29) stem cell clusters (SCC) were encapsulated in 2.5% ultrapure low viscosity mannuronate (UP LVM) alginate and transplanted in the peritoneal cavity (IP). The mice in the KC and IP groups were monitored for a 180 day period after transplantation. For the first 90 days post transplantation, their blood glucose were maintained using linbits to allow for engraftment under euglycemic conditions. At 30 days post-transplant, blood glucose levels averaged 89±6mg/dL (non-diabetic control), 569±24mg/dL (diabetic, no linbit) and 401±18mg/dL (diabetic with linbit). The transplanted groups (IP & KC, with linbits) showed statistically significant lower blood glucose levels (312±22 mg/dL, 10,000 SCC/KC; 230±15mg/dL, 20,000 SCC/IP) at 90 days [p=0.004]. After 90 days, linbits were removed and the mice averaged blood glucose levels of 409±27 mg/dL (10,000 SCC/KC) and 209±11 mg/dL (20,000 SCC/IP) over a 30 day period. hESC-IPCs survive and function better after transplantation in the peritoneal cavity than under the kidney capsule in diabetic athymic nude mice [p=0.003, ANOVA, P<0.05]. This promising cell therapy can be potentially offered to type 1 diabetic human patients.

Keywords: Type 1 Diabetes; Stem Cell Transplantation; Cell Encapsulation;

Poster #: 2 *Highlighted Oral Presenter

DONOR AND ISOLATION-RELATED VARIABLES PROFOUNDLY INFLUENCE YOUNG PIG ISLET ISOLATION OUTCOMES

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Porcine islet xenotransplantation is rapidly becoming a viable alternative to human islet allotransplantation. Clinical trials of encapsulated porcine islets have begun in several countries worldwide. However, the donor strains used have been highly variable and the outcomes have so far been disappointing. We have targeted our efforts on developing a young pre-weaned pig model as a viable pancreas donor. Following gentle enzymatic digestion and in vitro tissue culture for 8-10 days at 37oC, we have been able to demonstrate yields of >5500 IE/ gm of pancreas, islet purity >75% and viability >80 % (Newport green/PI). We have also recently reported that donor age and weaning status might impact the outcome of islet isolation success. The aim of this study was to demonstrate that donor strain and age are important determinants of successful islet isolation in young pigs and islet yields could be improved by selecting pigs that are under 30 days of age. Pancreases were rapidly procured (<5mins) and then enzymatically digested and then cultured for 8-10 days from either neonatal pigs (<15 days of age; N=32), pre-weaned young pigs (16-30 days of age; N=77) or weaned young pigs (31 days of age or older; N = 7). Two commonly used strains were compared – the domestic Landrace and Yorkshire pigs. Islet yields per pancreas were significantly higher (29x10^3±298 IEq) in the pre-weaned young pigs (<30 age group) compared to the older weaned pigs (18x103±852 IEq) (p<0.001, ANOVA). Islet viability ranged from 84-96% (2.7% variability between isolations) with average viability of 89±0.4%.On further analysis, among pre-weaned young pigs of different strains, Landrace pigs possessed a significantly higher islet yield (30x103±200 IEq) compared to Yorkshire pigs (27x103±352 IEq) (p=0.002, ANOVA). This work highlights the unique ability of porcine islets to produce a scalable process to produce clinical doses of viable islets for transplantation.

Keywords: Islet Transplantation; Xenotransplantation; Porcine Islets; Type 1 Diabetes;

Poster #: 3 *Highlighted Oral Presenter

Probing Metabolism and Growth Changes in Co-cultures of Cystic Fibrosis lung pathogens in concert with oral microbes

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OBJECTIVE: Cystic Fibrosis (CF) patients develop persistent lung infections due to the presence of dense mucus characteristic of the disease. Standard clinical microbiology relies on mono-cultures of the most common pathogens, which does not represent the full microbial diversity and bacterial cross-talk actually present in patients. Given the proximity of the airways to the incredibly dense and diverse microbial communities colonizing the oral cavity, examining opportunistic pathogens of the lung together with oral microbes may capture a more relevant picture of bacterial physiology. METHODS: We are characterizing the interactions between clinical isolates of three Pseudomonas aeruginosa strains, Streptococcus salivarius, and Streptococcus pneumonia to better understand their interactions from multiple angles including metabolomics by GC-MS, comparative genomics, and transcriptomics. These analyses will be contrasted with metabolomics and microbial metagenome sequence data from clinical sputum samples to help place the in vitro results in context with the CF lung in vivo. RESULTS: Preliminary metabolomics profiling performed on S. salivarius and P. aeruginosa indicate a marked increase in trehalose during co-culturing not observed in mono-cultures for either strain. S. salivarius was also found to produce 2,3-butanediol, a volatile fermentation product, in decreased abundance during co-culture than detected in individual culture. Further characterization of these two, in addition to other metabolites is forthcoming. SIGNIFICANCE: By characterizing the effect different microbial species can exert on one another's growth potential, metabolite profile, and transcript abundance, we can better understand the complex interplay between microbial communities and CF patients. This approach may lead to better diagnostics and more effective treatment of polymicrobial infections.

Keywords: Cystic Fibrosis; Metabolomics; Microbiome;

Poster #: 4 *Highlighted Oral Presenter

Conserving Cartilage in Microtia Repair: The Modular Component Assembly approach to rebuilding a human ear

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Objectives: Microtia is a rare abnormality in which the external ear anatomy is either underdeveloped or absent (1:10,000 births). Autogenous auricular reconstruction remains the preferred method for microtia reconstruction, but continues to be one of the most difficult procedures in plastic surgery. Current methods involve carving of multiple ribs, which requires considerable prior surgical experience and creates a large donor site defect. Here, we present a modular component assembly (MCA) approach that minimizes the procedural difficulty and reduces the amount of cartilage to a single rib. Study Design: Ex vivo study and Survey Methods: A single porcine rib was sectioned into multiple slices using a cartilage guillotine, cut into components outlined by 3D-printed templates, and assembled into an auricular scaffold. Electromechanical reshaping was used to bend cartilage slices to create the helical rim. Chondrocyte viability was confirmed using confocal imaging. 10 surgeons reviewed the highest quality scaffold constructed with the MCA approach to evaluate aesthetics, stability, and clinical feasibility. Results: An auricular framework with projection and curvature was fashioned from one rib. Surgeons found the MCA scaffold to meet minimal aesthetic and anatomic acceptability. When embedded under a covering, the helix/anti-helix of the scaffold scored significantly higher on the assessment survey than that of an embedded alloplast implant (t-value=0.01). Otherwise, no difference was found between the embedded MCA and alloplast implants (t-value >0.05). EMR treated cartilage was found to be viable. Conclusion: This study demonstrates that one rib can be used to create an aesthetic and durable framework for microtia repair. Precise assembly and the ability to obtain thin, uniform slices of cartilage were essential. The framework was deemed aesthetically acceptable and clinically feasible. This MCA approach may be an alternative to classic techniques.

Keywords: Microtia; Auricular Repair; Costal Cartilage; Modular Component Assembly; TPFF;

Poster #: 5 *Highlighted Oral Presenter

Targeted Investigation of Novel Mesenchymal Stem Cell Biomarkers of Bronchopulmonary Dysplasia in Prematurely Born Infants

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Background: Bronchopulmonary dysplasia (BPD) is a chronic disease of preterm infants caused by oxygen toxicity, inflammation, and ventilator use leading to arrested alveolar development. Current therapies lack effectiveness and have undesirable side effects. Our work has shown mesenchymal stem cell conditioned-media to have protective effects in mouse BPD models. Analysis identified Osteopontin (Spp1) and Macrophage colony stimulating factor 1 (Csf1) as key in suppressing the TGF-B surge in the lungs, leading to protection against BPD. Aim: Determine the association between Spp1, Csf1 and BPD by quantifying Spp1, Csf1 and TGF-B levels in tracheal aspirate fluid (TAF) of preterm infants. Method: Infants under 32 weeks gestational age 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 1st TAF sample was obtained at intubation, before surfactant dosing. The 2nd was obtained at extubation or the 4th day if still intubated. Spp1, Csf1, TGF-B and IgA levels were analyzed using ELISA. IgA was used as control to correct for TAF volume. Infants were followed prospectively for development of BPD. Results: A feasibility study was performed on 10 preterm infants to quantify Spp1, Csf1, TGF-B and IgA and to generate standard curves. Then, 6 infants were enrolled and TAF obtained. They were similar in baseline maternal and neonatal characteristics. 3 of 6 developed BPD and had either declining Spp1 and Csf1 levels or rising TGF-B levels post-ventilation. The other 3 had stable Spp1, Csf1 and TGF-B levels and did not develop BPD. Conclusions: Our pilot study showed that quantification of Spp1, Csf1 and TGF-B in the TAF of preterm infants is feasible. Spp1, Csf1 and TGF-B levels are associated with BPD. Ongoing data collection is underway to reach study power. Further studies are needed to confirm this association and will guide targeted BPD therapy.

Keywords: bronchopulmonary dysplasia; mesenchymal stem cells; biomarkers; preterm infant;

Poster #: 6 *Highlighted Oral Presenter

Using Small Molecules to Reactivate of Oncogenic p53 Mutants through DNA-binding Domain Stabilization

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The tumor suppressor p53 is an important cell-cycle regulating transcription factor that is mutated in 50% of human cancers. Most of these oncogenic p53 mutations create a single amino acid substitution in the DNA-binding domain (DBD), leading to continued expression of full-length but nonfunctional p53 protein. The most common of these p53 mutations, R175H [Arg at position 175 mutated to His], causes the DBD to become thermodynamically destabilized, losing its DNA-binding activity, and becoming nonfunctional at physiological temperatures. A pharmaceutical that can restore wild-type p53 function to R175H, or any of these single amino acid mutants, could have an enormous impact on our ability to treat cancers with p53 mutations. We identified a novel class of small molecules that are able to stabilize the R175H DBD and G245S DBD (another oncogenic mutation) in vitro and induce p53R175H- and p53G245S-dependent cell death in cancer cells, suggesting that these small molecules have the potential to target many oncogenic p53 mutants for reactivation. Our objective is to understand the molecular mechanism that allows this class of small molecules to restore function to oncogenic p53 mutants, from atomic-level interactions with the p53 DBD to the changes in the biochemical functions of the p53 DBD.

Keywords: p53; cancer; tumor suppressor; protein stabilization; reactivation;

Poster #: 7

Clinico-Biological Prognostic Score for Prediction of Oncological Outcomes After Radical Cystectomy for Squamous Cell Carcinoma of the Bladder

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INTRODUCTION:Clinico-pathological and molecular profiles were correlated to clinical outcomes in patients treated with radical cystectomy due to squamous cell carcinoma (SCC) of the urinary bladder to identify a model that combines both clinical and pathological prognostics.METHODS:Immunohistochemistry for 14 biomarkers were performed on tissue microarray sections of 151 cystectomy specimens with pure SCC. A 3 risk category molecular score was defined based on number of alterations. A 3 risk category clinical score was defined based on disease free survival (DFS), estimated by MSKCC post cystectomy nomogram merging 7 clinico-pathological parameters. The sum of 2 scores was used to state a poor prognostic score (PS) (>3) and was correlated to DFS.RESULTS:The study included 151 patients with pathological stages: T2 in 50%, T3 in 38%, T1 and T4 in 6% each; low grade in 53%; LN metastasis in 30.5%, and LVI in 16% of patients. Median follow-up was 63.2 months. The best prognostic panel of markers include: COX-2, FGF-2, P53, and Bax via Kaplan-Meier analyses. COX-2 was linked with advanced stage and high grade; FGF-2 was associated with high grade, LN, and LVI; and p53 with high stage ($p = 0.05$). The marker score was defined as 1 or low risk, no or 1 marker altered, 2 or intermediate risk if 2 markers were altered, and 3 when >2 markers were altered. Scoring was defined as 1 or low risk if DFS probability is > 80%, 2 or intermediate risk if DFS is 60-80%, and 3 when DFS < 60%. Poor PS were defined if the sum of 2 scores were > 3. The poor PS was associated with disease recurrence ($P < 0.001$); and was an independent predictor of disease recurrence (HR 3.2, and p=0. 02, CI 1.168-8.524).CONCLUSIONS:Biomarkers can help classic clinico-pathological prognostics for prediction of poor outcomes after radical cystectomy for SCC. A PS combining clinical and molecular prognostics can be utilized for patient counseling, selection for adjuvant therapies, and design of clinical trials.

Keywords: Prognosis; Outcomes; Biomarkers; Radical Cystectomy; Squamos Cell Carcinoma;

Poster #: 8

Prognostic Biomarkers for Bilharzial and Non-Bilhrazial Related Bladder Cancer: Immunohistochemistry Study of 14 Markers

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OBJECTIVES: Herein we define the best prognostic biomarkers in bilharzial and non-bilharzial related bladder cancer (BBC and NBBC) after a radical cystectomy (RC). We also determine the clinico-pathological differences between BBC and NBBC. METHODS: Immunohistochemical (IHC) staining for 14 markers (p53, p21, p27, cyclin E, ki67, COX-2, EGFR, FGF-2, VEGF, Bcl-2, Caspace-3, Bax, ERK, TSP-I) was performed in 315 patients treated with RC. Patients were divided into 2 groups: Group 1 comprised 205 patients (65%) with BBC and group 2 comprised 110 patients (35%) with NBBC. Clinico-pathological differences were compared and markers were correlated to clinical outcomes in both groups. RESULTS: The study included 315 patients (239 males and 76 females) with median age 54y (range 31-79). There was a significant difference in histological types, tumor stage, grade, and architecture between both groups ($P < 0.05$). BBC was presented with lower grade, higher stage, and non-papillary non-urothelial carcinoma. COX-2 expression was the best independent predictor of disease recurrence (HR 1.9, CI 0.99-3.626 and P= 0.05) and cancer specific mortality (HR 2.8, CI 1.155-6.73 and P= 0.023) in BBC. Ki-67 was the only marker associated with disease recurrence in NBBC in Kaplan-Meier survival analyses (HR 4.2, p =.038) CONCLUSIONS: BBC differs pathologically and biologically from NBBC. BBCs present more frequently as low-grade, high stage non-papillary, and non-urothelial cancers. Our findings support the need for further evaluation of COX-2-targeted prevention and therapies in bladder cancers developing on top of chronic inflammation. Ki-67 might represent a good prognostic marker regardless to histological type of BC in Western countries, but this should be further studied.

Keywords: Prognosis; Bladder Cancer; Biomarkers; Radical Cystectomy; Schistosomiasis;

Poster #: 9

Cultural Sensitivity in Action: A 10-year cancer support group for Korean patients

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The U.S. cultural mosaic is undergoing dramatic change. In the coming decades, it is projected that the number of Caucasians will decrease and there will be a doubling of both Asians and Hispanics. Support for cancer care must always be tailored to the unique needs of the patient and family. Patients who are recent immigrants are highly vulnerable. Culturally sensitive cancer care must address language, information-giving, health beliefs, treatment acceptance, use of complementary approaches, nutrition, family roles, and relationships with health care providers. In 2004, acknowledging the isolation that many Korean women felt during chemotherapy, two Korean oncology nurses began a monthly support initiative. Sensitive to cultural beliefs, they chose to call the meeting a 'Korean Tea Party' rather than a support group. Each meeting consisted of time for the women to share their treatment experiences and guest speakers were invited as were the spouses. Since 2014, 955 women have participated. Success factors include: the participants were highly engaged by giving each other reminder calls prior to meetings and arranging carpools; when a member died, flowers were sent and the entire group of women survivors attended the funeral together; food sharing, a phenomenon central to Korean culture, is included; social times; a nurse and one of the attendees co-facilitate meetings; by having sessions at the cancer center at UCIMC, the women felt highly supported by the hospital. Participants provided evaluation and the results were on three themes: peer support from other women was invaluable; discussions with other enhanced confidence in managing symptoms; and, information shared was very practical and hence highly useful outside of the group setting. By sharing the enduring experience with the provision of this support resource for Korean women with cancer, other oncology nurses may be empowered to initiate a similar intervention in their respective communities.

Keywords: cancer care; cultural sensitivity; patient support; oncology;

Poster #: 10

Investigating the mechanism of CDCP1-activation to inhibit CDCP1-mediated metastasis

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Triple negative breast cancer (TNBC) is a highly aggressive and metastatic form of breast cancer that is characterized by a lack of the estrogen, progesterone, and HER2 receptors, which renders it resistant to targeted and hormone therapies, posing an obstacle for treating TNBC. Recently, it has been found that TNBC expressed high levels of a metastasis-inducing protein, CUB-domain containing protein 1 (CDCP1), which has been correlated with the aggressive nature and poor prognosis of many forms of cancer. CDCP1's role in cancer metastasis is incompletely understood but it can be proteolytically cleaved and phosphorylated, both of which have been correlated with the metastatic potential of multiple cancers. Until recently, it was not clear if phosphorylation and cleavage were the only steps in activation of CDCP1 and its downstream signaling. Using an ectopic expression system we observed a dramatic increase in phosphorylation of cleaved CDCP1 (cCDCP1) compared to full length (flCDCP1). cCDCP1 induced robust phosphorylation of the migration-associated proteins; PKCd, ERK1/2, and p38 MAPK compared to flCDCP1. Also, cCDCP1 induced migration of HEK 293T cells and rescued migration of TNBC cells expressing shRNA against CDCP1. These findings support the necessity of CDCP1 cleavage for its activation and function. Finally, we found that only cCDCP1 is capable of forming a dimer, independently of its phosphorylation status, and are currently working to elucidate the function of this dimer in CDCP1 induced signaling. These studies have important implications for development of a therapeutic to block CDCP1-induced TNBC metastasis.

Keywords: CDCP1; triple-negative breast cancer; metastasis; dimer;

Poster #: 11

A phase I dose-escalation and pharmacokinetic study of hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) carboplatin at the time of primary cytoreductive surgery for advanced ovarian, fallopian tube, and peritoneal carcinomas

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Objectives: Hyperthermic intraperitoneal chemotherapy (HIPEC) at the time of cytoreductive surgery (CRS) for ovarian cancer allows immediate regional therapy. Though evidence supporting its efficacy in ovarian cancer is lacking, HIPEC is gaining popularity in the clinical setting. Doses and agents administered are chosen empirically without pharmacokinetic (PK) data. Therefore, we are currently conducting a phase I dose-escalation and pharmacokinetic study of HIPEC carboplatin (NCT02199171) to inform a follow-on randomized phase II study. Methods: Women (n=30) with presumed stage IIC-IVA ovarian, tubal, or peritoneal carcinomas who are planned for CRS are eligible. Those optimally or completely cytoreduced and stable for continued anesthesia receive a 60-minute, closed-abdomen infusion of carboplatin at 41oC according to a novel, continual reassessment dose escalation schema that is flexible to interpret adverse events attributable to surgery vs. those of HIPEC. Serum and peritoneal perfusate are collected for PK studies at time 0 and at every 15 minutes for the duration of the infusion. DNA platinum uptake is measured by inductively coupled plasma mass spectroscopy (ICP-MS). Median, range and interquartile range will be reported for the amount of carboplatin absorbed from the perfusate, the rate of drug absorption from the peritoneal cavity into the systemic circulation, the 0-to-60 min AUC's for peritoneal and plasma platinum concentration curves, the total body clearance, and regional advantage. Three small, easily resectable tumors are left in situ during the perfusion for correlative studies which include direct measurement of tissue temperature in tumors and control avascular mesentery, levels of platinated DNA by ICP-MS in tumors exposed to HIPEC, and expression of heat shock protein (Hsp) 90 in tumors before and after HIPEC. Results: We have accrued 7 patients and achieved dose level 2 as of January 2015.

Keywords: ovarian cancer; hyperthermic chemotherapy; clinical trial (phase I); translational; pharmacokinetic;

Poster #: 12

Diffuse optical spectroscopy probe for therapy monitoring in colorectal cancer: In-vivo optical properties of healthy colon tissue from Yorkshire pigs

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The purpose of this study is to measure and obtain for the first time the optical properties of normal swine colon tissue in-vivo in the near infrared range using a diffuse optical spectroscopy (DOS) instrument and a novel probe designed for endoscopic use. Optical parameters of colon tissue were determined using the diffusion approximation of the radiative transport theory of light propagation. The need of a noninvasive technique arises from the importance of monitoring colorectal cancer response to therapy. Diffuse optical spectroscopy imaging (DOSI) has previously been successful in the prediction of neoadjuvant chemotherapy response in breast cancer, as early as one day after the beginning of the therapy. Rectal cancer is characterized by a low 5-year survival rate. To increase survival, patients with rectal cancer receive similar neoadjuvant chemotherapy and radiation treatments of those with breast cancer. However, very often (up to 30%) such therapies do not reach the desired pathological complete response. Measurements in the rectum pose multiple challenges and constraints to conventional DOSI instruments. The geometry, healthy and tumor tissue properties in the rectum and the requirement of surface contact impose constraints on the probe design. Optical properties of deeper tissue in the rectum are uncertain and may vary, therefore measurement uncertainties are increased. No direct vision is available to the probe operator and the probe must be safe for internal use and easy to clean. In this work we present the first in-vivo colon measurements using an early prototype of a DOS probe. Simulations and phantom measurements have been previously performed to confirm that colon tissue can be characterized reliably using a source-detector separation in the order of 10 mm. We present the prototype of a probe for DOS measurements and colon tissue optical properties obtained on Yorkshire pigs. Using clinically approved components we aim at clinical translation.

Keywords: colorectal cancer; therapy monitoring; spectroscopy; probe; in-vivo;

Poster #: 13

Chromatin remodelers HELLS and UHRF1 mediate the epigenetic deregulation of genes that drive retinoblastoma tumor progression

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The Rb family (Rb, p107 and p130) regulates gene expression through interactions with E2F/DP transcription factors. While Rb, p107, and p130 show distinct preferences for particular E2Fs to regulate transcription, they may shift depending on cellular context. Furthermore, there are also distinct mechanisms of action. Rb proteins can directly regulate genes that control cell cycle exit and the expression of genes that control cell fate specification and differentiation through mechanisms including chromatin remodeling and epigenetic control. A major question in the field is how Rb/E2f interactions control proliferation and tumor suppression in coordination with cellular differentiation events. The retina is a good system to study this question because of the role of Rb in tumorigenesis and development. The clearest connection between RB1 inactivation and tumorigenesis is the retina, where RB1 loss is sufficient to cause the epigenetic changes that drive tumor progression. RB1 also plays a role in retinal development. We created a series of genetically engineered mouse models to study the unique and overlapping roles of the E2fs in retinal development and cancer. We found that retinal differentiation defects and tumorigenesis following loss of the Rb family occurs as two independent events that rely on distinct E2fs. Gene expression data from these models identified downstream targets that contribute to tumorigenesis and development. Sox4 and Sox11 may be important for maintaining proper retinal development. Uhrf1 and Hells are overexpressed in retinoblastoma and may be responsible for the epigenetic changes seen in retinoblastoma and required for tumor survival. Furthermore, we showed that upregulation of HELLS is linked to the epigenetic activation of the SYK gene, key for human retinoblastoma survival. We are currently evaluating whether UHRF1 and HELLS are essential for the epigenetic rearrangement that follows RB1 inactivation and promotes tumor progression.

Keywords: genetics; epigenetics; retinoblastoma; pediatric; cancer;

Poster #: 15

Evolution of Stem cell signaling in Colon Cancer

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Cellular plasticity plays a crucial role in colon cancer pathogenesis. We demonstrated by spatiotemporal in situ hybridization data that the prevalent human colon cancer-initiating cells arise from crypt based LGR5+ colon stem cells. Although LGR5 was highly expressed in human colon cancer, it was not a biomarker of colon cancer stem cells and did not predict colon cancer therapy resistance or recurrence. Instead of relying on single-gene biomarker, we defined cellular plasticity based on gene signatures that had been established from purified human embryonic SC, crypt-base LGR5+ intestinal SC, and crypt-top intestinal differentiated cells. To characterize changes in colon cancer plasticity at different tumor stages, we performed Gene Set Enrichment Analysis using these three gene signatures on gene expression profiles from differentiated normal colon mucosa (n = 33) and localized stages I (n = 17) and II (n = 35), lymph node positive stage III (n= 39), and metastatic stage IV (n= 46) colon cancer. We found that maximal embryonic SC program enrichment occurred in stage I colon cancer and decreased dramatically in stages II-IV colon cancer. Tumor progression to higher tumor stages exhibited a heterogeneous tumor differentiation process from an embryonic SC program toward an intestinal SC or more differentiated cell programs. Relative increase in colon tumor differentiation contributed to poor prognosis in moderately differentiated stage IV colon cancer. Understanding of the evolution of cellular plasticity with colon cancer progression is critical to the successful development of therapies that target tumor self-renewal.

Keywords: Colon cancer; Stem Cell Signaling;

Poster #: 16

A novel small molecule Wnt inhibitor preferentially inhibits the in vitro and in vivo growth of castration-resistant prostate cancer by preventing nuclear translocation of LEF1.

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Urology

Nearly 34,000 men are expected to die of castration resistant prostate cancer (CRPC) this year in the U.S. Recent studies have suggested that castration (androgen deprivation) can result in enhanced Wnt signaling, leading to castration resistance. We, therefore, have studied novel Wnt inhibitors for treatment of CRPC. We found that a novel small-molecule Wnt inhibitor, named SULF-1, preferentially and potently inhibited the growth of CRPC cells at nM concentrations (IC50s are from 23 to 95 nM) with minimal effect on the growth of non-malignant prostate epithelial cells. SULF-1 also induced apoptosis by down-regulating the expression of survivin. In addition, SULF-1 significantly inhibited in vivo tumor growth in a xenograft model of CRPC PC3 cells. Most interestingly, SULF-1 treatment of LNCaP androgen-independent (AI) cells resulted in a significantly decreased nuclear localization of the lymphoid enhancer binding factor-1 (LEF-1). This result suggested a novel mechanism of SULF-1 for inhibiting the activation of Wnt signaling and the growth of CRPC cells. Further studies are in progress to identify the exact molecular mechanisms by which SULF-1 cause reduced nuclear localization of LEF1 in CRPC cells.

Keywords: Wnt; Prostate cancer; apoptosis;

Poster #: 17

Cisplatin causes mitochondrially mediated hippocampal damage

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Chemotherapy-induced cognitive deficits are a major neurological problem. Cisplatin (CDDP) is a commonly used cancer drug, which achieves high concentrations in the brain. We previously reported that CDDP induced non-reversible damage to neural stem/progenitor cells (NSCs) and dendritic spine integrity in the hippocampus. Here we tested the hypothesis that CDDP also alters spine integrity in hippocampal neurons (HN) by a mitochondrial-mediated mechanism. Cultured rat HN and NSCs were treated with CDDP (0.1μM and 1μM). Dendritic spine integrity was studied by quantification of post-synaptic density protein (PSD95) puncta. BDNF mRNA levels were quantified by qRT-PCR. For in-vivo studies, rats were treated with 3mg/kg CDDP i.p. for 2 days. Dendritic branching and spines were quantified by Golgi staining. TUNEL assay and Cleaved Caspase-9 expression ICC was performed to detect apoptosis. Rat hippocampi were harvested and imaged by electron microscopy (EM) 6, 15, and 28 days following CDDP exposure. Mitochondrial respiration was measured using the Seahorse Flux Analyzer XF24. CDDP induced non-reversible damage to dendritic spines and branches in HN. Exposure to 1μM CDDP caused HN apoptosis and severe mitochondrial deficits in the surviving HN. In-vivo CDDP treatment reduced dendritic branching and spine density in CA1 and CA3 HN. EM revealed mitochondrial degradation in the CA3 of the hippocampus 15 days after exposure. CDDP treatment caused a significant decrease in BDNF mRNA. Treatment with N-acetyl cysteine (NAC) partially prevented neuronal apoptosis following Cisplatin exposure. At doses lower than those found in chemotherapy patients, CDDP can potentially induce severe synaptic damage, neuronal cell loss, and mitochondrial damage. Mitochondrially mediated hippocampal damage may be responsible for the cognitive impairment observed after chemotherapy treatment, and might be partially prevented or reversed using clinically available treatments (NAC, ampakines).

Keywords: cisplatin; hippocampus; chemo brain; mitochondrial damage; chemotherapy;

Poster #: 19

IDENTIFYING THE OPTIMAL ALGINATE HYDROGEL AND TRANSPLANT SITE FOR ENCAPSULATED ISLET TRANSPLANTATION

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Islet microencapsulation, where the islets are coated with a biocompatible polymer, has demonstrated various degrees of success in small and large animal trials. We evaluated alginate microcapsules made from two types of alginate hydrogels transplanted to one of two transplant sites into athymic nude mice to characterize changes in microcapsule morphology and foreign body and vascular response post-transplant. Microcapsules made with either Sigma or UP LVM (Ultra-Pure Low Viscosity Mannuronate) alginate solution at two concentrations (1.5% & 2.5%) and crosslinked with 120mM calcium chloride were characterized using an inverted microscope and transplanted at one of two sites in CD1 mice – dorsal subcutaneous space and the peritoneal cavity. The recipients were monitored for a 12 week period after which they were euthanized and the microcapsules were carefully collected for microscopic evaluation, histological and surface analysis. After incubation at 37oC, alginate microcapsules (Sigma & UP LVM) showed a 14±2% decrease in diameter. However, at explant, it was noted that the same microcapsules now showed a 31±4% increase in diameter, which may be attributable to ionic interactions between sodium in the interstitial fluid and calcium in the capsules. Endotoxin & Microbiological analyses of Sigma Alginate demonstrated high levels of endotoxin (900 EU/mL) and fungal and aerobic bacterial contamination while UP LVM alginate was negative for endotoxin and microbial contaminants. This was corroborated by histological analysis of microcapsules made from Sigma alginate which demonstrated an intense inflammatory response and demonstrated macrophage infiltration in addition to dense fibroblast activation at both transplant sites. Microcapsules made with UP LVM alginate demonstrated a mild foreign body reaction with minimal peri-capsular fibroblast growth in the subcutaneous site while those transplanted in the peritoneal cavity did not show any cellular infiltrate.

Keywords: Cell Encapsulation; Type 1 Diabetes; Alginate; Islet Transplantation;

Poster #: 20

YOUNG PORCINE ISLETS CAN MATURED DURING IN VITRO CULTURE AND MAINTAIN PROLONGED EUGLYCEMIA AFTER TRANSPLANTATION INTO DIABETIC ATHYMIC NUDE MICE

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Islet transplantation is limited by a scarcity of quality donors, inconsistent islet yields and a need for chronic immunosuppression. The development of a viable biological alternative to human islets would address these key issues. We have developed a unique islet isolation method using gentle enzymatic digestion that avoids toxic purification gradients and relies on gradual islet maturation over a 7-14 day in vitro culture period. The aim of this study was to demonstrate the function of a marginal mass of porcine islet xenografts without immunosuppression after prolonged in vitro culture. Athymic nude mice (8 weeks old, N=10) were rendered diabetic with streptozotocin. Diabetes was confirmed after 3 days BG > 350 mg/dL, after which, mice were maintained on insulin pre-transplant. Pancreatic tissue from young pre-weaned Landrace pigs (22±0.5 days old) was cultured in vitro after partial enzymatic digestion. Porcine islets that were cultured for either 7 or 14 days in vitro were transplanted under the kidney capsule of diabetic mice at a dose of 1500 IEq per recipient. Mean non-fasted blood glucose levels, as measured from capillary tail prick samples, was 552±24mg/dL pre-transplant (mean±sem). All mice became euglycemic after xenotransplantation. Non-encapsulated islet xenografts under the kidney capsule in diabetic nude mice maintained euglycemia until nephrectomy (Day 60) for both culture duration groups. At two and four weeks post-transplant, recipient mice were responsive to an oral glucose challenge. Both transplant groups remained euglycemic at 30 (167±7 mg/dL, 7 day culture; 185±8 mg/dL, 12 day culture) and at 60 days (172±11 mg/dL, 7 day culture; 176±8 mg/dL, 12 day culture) post-transplant. Histology of islets within the explanted kidney stained positive for insulin and glucagon. Young pig islets can survive and function when transplanted in diabetic mice after prolonged in vitro culture. This data is critical to enhance our understanding of islet biol

Keywords: Porcine Islet Xenotransplantation; Type 1 Diabetes; Islet Transplantation;

Poster #: 21

Alginate Encapsulated Islets Allow For Adequate Tissue Oxygenation Even At Hypoxic Conditions

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Post-transplant graft failure and death is a serious setback negatively impacting human islet allotransplantation success. This has been postulated to result from hypoxia encountered immediately after transplantation due to poor implant-site vascularization. In order to survive and function adequately, transplanted islets must be able to withstand the transient hypoxic shock until they are adequately vascularized. In this study, we evaluated the effects of in vitro hypoxic culture on islet viability and function in alginate bioencapsulated islets at predetermined oxygen concentrations for a three day period. Groups of of islets isolated from young Yorkshire pigs were cultured for 7 days in vitro in UCI maturation media (n=3). Half of the islets (5000/group) were encapsulated in 2.5% UP LVM alginate to make alginate-encapsulated microcapsules (417±12µm). The other islets were left unencapsulated (control). The islets were then incubated in a hypoxia chamber (Biospherix Ltd, New York) at 0%, 2.5%, 10% and 20% O2 for 72 hours. At 24 and 72 hours after incubation, 200 IEq of islets were stained with fluorescent viability (Calcein Blue/Propidium Iodide) and apoptosis dyes (YoPro-1) and examined under a fluorescent microscope. Encapsulated and free islets maintained viability (92±1; free, 85±3; encapsulated) best at 20% O2. Encapsulated islets remain viable at anoxic conditions (0% O2), but this trend could not be seen in other low oxygen environments (4±1%; 2.5% O2, 14±2%; 10% O2). No significant additive detrimental impact on islet viability was noted in alginate encapsulated islets cultured at hypoxic conditions when compared with unencapsulated islets (12±2; free, 13±1; encapsulated), indicating no compromise in their oxygen permeability [$p=0.007$, ANOVA, $p<0.05$]. This study demonstrates that alginate encapsulated islets are able to allow for adequate tissue oxygenation even at hypoxic conditions and are ideal candidates for future studies.

Keywords: Islet Transplantation; Type 1 Diabetes; Tissue Hypoxia; Xenotransplantation; Cell Encapsulation;

Poster #: 22

iPS Modeling of VCP-Associated Disease: A Novel Platform for Drug Strategies

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Valosin Containing Protein (VCP) disease is an autosomal dominant disorder caused by mutations in the VCP gene and is associated with progressive muscle weakness and atrophy, primarily of the pelvic and shoulder girdle muscles. Affected individuals exhibit striking scapular winging due to shoulder girdle weakness. Currently, there are no treatments available and patients are dying early from cardiac and respiratory failure, typically in their 40s and 50s. The generation of disease-specific induced pluripotent stem cells (iPSC) offers a novel platform to investigate mechanisms of VCP disease and potential treatments similar to other neurodegenerative disease models including Amyotrophic Lateral Sclerosis (ALS), Duchenne muscular dystrophy (DMD), Parkinson's disease, Alzheimer's disease (AD), and Type I Juvenile Diabetes mellitus (T1DM). Herein, we report the generation and characterization of a human iPSC line into a myoblast lineage to examine the underlying mechanisms in VCP disease. We characterized the human iPSC line at days 0, 21, and 49 and assessed expression of pluripotency markers NANOG, OCT4, and desmin, a myogenic marker. We report that treatment with Rapamycin (mTOR inhibitor) and Dexamethasone demonstrated an ameliorative effect in the histopathology and autophagy cascade intermediates. Collectively, our results demonstrate that patient-specific iPSC technology for myogenic differentiation may represent a useful preclinical tool in the disease modeling and drug screening for understanding the complex cellular and molecular mechanisms in VCP disease and in the development of personalized regenerative cell therapies.

Keywords: Valosin Containing Protein; Induced Pluripotent Stem Cells; Rapamycin; Dexamethasone; Amyotrophic Lateral Sclerosis;

Poster #: 24

Electrophysiological evidence for connectivity of fetal retinal sheet transplant in a novel immunodeficient retinal degenerate rat model

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Retinal degenerative (RD) diseases cause a gradual loss of vision and have no effective treatment. Previously we have established a transplantation protocol for fetal retinal sheets in the S334ter line-3 RD rat model. The present study provides electrophysiological evidence that implanted fetal retinal sheets restore light response in a novel immunodeficient S334ter line-3 RD rat model (SD-Foxn1 Tg(S334ter)3Lav). Control, non-RD rats were compared to immunodeficient S334ter line 3 RD rats that were transplanted with intact fetal retinal sheets in the subretinal space. The size and location of the transplant was followed using OCT before electrophysiological testing. Prior to electrophysiological testing, rats were dark-adapted overnight. Transplanted rats were anesthetized, a craniotomy was performed, and the superficial layer of the superior colliculus (SC) was exposed. Single and multi-unit responses to a 40ms 6.5mcd/m2 light flash were recorded from locations in SC approximately 200µm apart. Responses were analyzed using a custom Matlab program. OCT scans indicated that the placement of the retinal sheet transplants remained constant and were located between the retinal pigment epithelium and the host retina. In control rats, visual responses were robust in all areas of the SC. However, in the immunodeficient S334ter rat the same stimulus was unable to elicit a response in the majority of the SC recording sites. Interestingly, robust responses were observed in a cluster of recording sites that were all within several hundred microns of each other. Fetal retinal sheet transplants were stable for several months in immunodeficient S334ter rats and did not display any signs of host-graph rejection. The location of responses to light in the SC corresponded to transplant location in the retina. These data suggest that retinal sheet transplants are not only capable of integrating and surviving in the retina of immunodeficient rats but can restore light response.

Keywords: Stem cell; Retinal degeneration; Electrophysiology;

Poster #: 25

Age-Related Changes in Emotional Memory and Forgetting: Gist Vs. Detail

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Changes in memory performance are one hallmark of cognitive dysfunction in healthy aging. However, it is unclear whether there are modulatory systems specific to emotion that may allow older adults to compensate for this. In our recent study of emotion and memory, we reported that older adults remember emotional information better after a 24-hour delay compared to young adults (Leal & Yassa, Behav Neurosci 2014). The Wechsler Memory Scale (WMS) Logical Memory Subset, a test in which subjects are read two stories and tested on their memory of the stories immediately and after a delay, does not assess or control for emotional content. To do so for this study, we developed an emotional version of the logical memory subset that included negative, neutral, and positive stories. Adults aged 60-85 were tested on their memory of the three stories after an immediate, 20-minute, and 1-week delay. Performance on gist and detail information was assessed. Subjects were split into aged impaired (AI) and aged unimpaired (AU) based on the Rey Auditory Verbal Learning Test (RAVLT; Rey, 1941). Overall, we found a negativity bias for both gist and detail information where the negative story was better remembered while overall memory performance declined over time. Impairment in recalling neutral gist information was shown in AI individuals over time, signifying selective forgetting of neutral information. Emotional gist information did not differ across AU and AI groups over time. These findings suggest that the modulatory influence of emotion can alter how experiences are remembered, and this modulation changes in the context of normal aging. This novel insight on age-related changes in emotional memory could lead to using emotional content as a mechanism of intervention in older adults who exhibit cognitive impairments.

Keywords: memory; aging; emotion; modulation; changes;

Poster #: 27

Cognitive Exercise to Preserve Memory and Functional Ability in Older Adults With Mild Cognitive Impairment

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Mild Cognitive Impairment (MCI) affects more than 20% of adults over 65 increasing their risk of progression towards Alzheimer's disease. Thus, it is of critical importance to develop effective interventions that may delay cognitive decline in this population. Effects of non-pharmacological cognitive interventions have shown promising, yet inconsistent results, and furthermore, little is known about longitudinal effects or whether alterations of peripheral biomarkers might moderate the outcome. The present multi-disciplinary team of researchers developed and implemented two cognitive interventions and compared their efficacy against an active control group. MCI patients recruited through the UCI Alzheimer's Disease Research Center donated blood and received cognitive testing and questionnaires at baseline (T1), after 6 weeks (T2), and after 12 weeks (T3). After T1, participants were randomly assigned to one of three groups. Group A (Cognitive Exercise, n=8) participated in weekly group sessions and completed homework focusing on cognitive enrichment strategies. Group B (Working Memory, n=8) completed daily exercises targeting working memory using a tablet at home. Group C (Active Control, n=4) participated in weekly group sessions and completed tablet-based homework targeting verbal skills. Our sample consists of 20 participants (7 women) currently in training or who have completed the intervention (mean age: 75.2, SD: 6.9). Data collection and analyses will be complete by May 2015. So far, we have observed promising effects with preservation of selected cognitive functions in the experimental groups, whereas the control group shows decline across the intervention period. Blood samples are currently undergoing analyses for changes (e.g. profiles of amyloid beta, Tau, BDNF, cytokines/chemokines). Upon completion, data will serve as groundwork for future studies investigating the efficacy of targeted cognitive interventions in populations at risk for dementia.

Keywords: Cognitive Training; Mild Cognitive Impairment; Non-Pharmacological Intervention; Peripheral Biomarkers;

Poster #: 28

Do parents of children undergoing surgery and of children with chronic illnesses hold different types of misconceptions towards analgesics?

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Introduction: Parents often under treat children's pain at home due to parental misconceptions about analgesics. The aim of the current study was to compare medication attitudes between parents of healthy children undergoing surgery and parents of children with chronic illnesses. Methods: Participants included approximately 800 parents of healthy children ages 2 to 15 years undergoing outpatient surgery and 300 parents of children ages 0 to 18 with chronic illnesses (e.g. cancer, hemophilia). All parents completed the Medication Attitudes Questionnaire (MAQ). Results: Independent samples t-tests showed that parents of chronically ill children reported more fears of side effects of analgesics compared to parents of healthy children, $t(1057) = -2.05$, $p = 0.040$. Chi-square analyses of specific items revealed that a greater percentage of parents of chronically ill children endorsed the belief that pain medication works the same no matter how often it is used, $X2$ (2, N=1108) = 9.50, $p = 0.01$. Independent sample t-tests showed no group differences in beliefs about avoiding analgesics, $t(1050) = -0.211$, $p = 0.833$. In regards to the appropriate use subscale, independent sample t-tests revealed that parents of chronically ill children endorsed significantly fewer adaptive attitudes compared to parents of healthy children, $t(1066) = 2.4$, $p = 0.016$. Item analysis showed that fewer parents in the chronic illness group endorsed the belief that it is unlikely a child will become addicted when analgesics are consumed for pain, $X2$ (2, N = 1109) = 9.21, $p = 0.016$. Conclusion: Results showed that parents of children with chronic illness may hold more misconceptions regarding analgesic use for children compared to parents of healthy children. Because misconceptions about analgesics have been linked to less administration of analgesics, children with chronic illness may be at increased risk for suboptimal pain management compared to healthy children undergoing surgery.

Keywords: pain management; analgesics;

Poster #: 29

Stakeholder and Government Actions to Reduce Critical Drug Shortages in the United States

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This study examined the roles of various stakeholders in the role of drug shortages. Drug Shortages Crisis The number of total drug shortages has almost tripled from 2010 to 2013. Government Response In 2012, the FDA received authority to expedite reviews and inspections. In 2013, the FDA issued another report aimed to mitigate current drug shortages and develop long-term prevention strategies . Stakeholders' Responses Pharmaceutical manufacturers, largely represented by the International Society of Pharmaceutical Engineering (ISPE), have found that the lack of a "quality system", defined as a system that complies with regulations enforced by the FDA as well as the presence of internal procedures and specifications, to be the most common cause of drug shortages. They recommended ten additional factors to mitigate drug shortages. Professional medical organizations are actively conducting research, lobbying Congress, and partnering with other stakeholders. The U.S. Government, through the FDA, has updated its drug shortage website and begun to track artificial drug price mark-ups. Health care providers are sharing information with websites and RSS feeds. Hospitals have begun to prioritize distribution of their medications and to appoint staff to manage drug shortages. Looking Ahead A US Government Act signed in November 2013 aimed to ensure a steady supply and high quality product to buyers.

Keywords: Drug shortages; Pharmacy; Government; Anesthesiology;

Poster #: 30

Comparison and Trends of Inpatient and Outpatient Anesthesia Claims Reported to the National Practitioner Data Bank

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Introduction Malpractice suits are the main driver of medical quality in the US healthcare system and remain the primary focus by which providers are held accountable for providing care. Anesthesiologists are considered among the highest risk group. Objective To analyze and compare inpatient and outpatient anesthesia claims reported to the National Practitioner Data Bank. Methods Information was gathered from the National Practioner Data Bank which is a federal repository that collects and disseminates adverse information regarding healthcare practioners in the United States. During the 9-year period between 2005 and 2013, 2,408 medical malpractice claims were attributed to physician anesthesia providers and met criteria for inclusion in the study. Results Of the included claims, 1,841 (76.5%) occurred in the inpatient setting and 567 (23.5%) occurred in the outpatient setting. The median payment for all anesthesia-related claims is $245,000 (IQR = $457,589). Inpatient claims are significantly more expensive than outpatient claims ($p<0.001$). The median payments for inpatient and outpatient claims are $261,742 (IQR = $483,611) and $189,349 (IQR = $415,719), respectively. Over the 9-year period, the frequency of anesthesia-related claims decreased 41.4% (4.6%/year). Inpatient claims decreased a total of 45.5% (5.1%/year) and outpatient claims decreased 24.3% (2.7%/year) Conclusions The frequency of outpatient claims has remained stable over time compared to the decrease in inpatient claims. Outpatient claims represent an increasing proportion of spending for anesthesia malpractice.

Keywords: Anesthesiology; Malpractice; Ambulatory; Inpatient;

Poster #: 31

DIFFERENTIAL EXPRESSION OF AUTOPHAGY/MITOPHAGY MARKERS IN NORMAL AND AMD HUMAN TRANSMITOCHONDRIAL CYBRIDS

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Age-related macular degeneration (AMD), one of the leading causes of vision loss in older individuals of developed countries, is known to be associated with mitochondrial (mt) dysfunction. Mitochondrial damage, accumulation of lipofuschin in retinal pigment epithelium (RPE), and oxidative stress, are hallmarks of AMD. Autophagy is an intracellular degradation process that maintains cellular homeostasis by eliminating misfolded or unwanted protein aggregates, removing damaged organelles, such as mitochondria (mitophagy), endoplasmic reticulum, and peroxisomes, and clearing intracellular pathogens. It is speculated that elevated autophagy and the release of intracellular proteins via exosomes by the aged RPE may contribute to drusen formation. Therefore, the purpose of this study was to determine the role of autophagy in transmitochondrial AMD and normal cybrids. To create transmitochondrial cybrids, platelets isolated from normal and AMD human subjects were fused with a human retinal pigment epithelial cell line (ARPE-19) devoid of mitochondrial DNA (Rho0 cells). In this in vitro cybrid model, all of the cells carry the same nuclear genes but vary in mtDNA content. Normal (n = 4) and AMD (n = 4) cybrids were cultured for 24 hours and RNA was isolated. Gene expression profiles of autophagy/mitophagy markers, LC3B, Atg5, Atg12, and PARK2, were analyzed using quantitative RT-PCR. Age-matched normal cybrids served as controls. We observed significant up-regulation of autophagy/mitophagy markers: LC3B (??Ct=1.65 ± 0.61, Fold change= 3.13, P=0.01), Atg5 (??Ct=0.58 ± 0.25, Fold change= 1.50, P=0.026), Atg12 (??Ct=0.97 ± 0.31, Fold change= 1.95, P=0.0047), and PARK2 (??Ct=2.4 ± 0.53, Fold change= 5.20, P=0.0002) in AMD cybrids compared to normal cybrids. Since all nuclei in the cybrids are identical, altered expression of all of the genes can be attributed to mtDNA variations, and indicates that the AMD mtDNA can induce cells to enter into autophagy/mitophagy. Further stud

Keywords: AMD; RPE; MITOCHONDRIA; AUTOPHAGY; MITOPHAGY;

Poster #: 32

Efficacy and Safety of Diazoxide Choline Controlled-Release Tablet in Patients with Prader-Willi syndrome

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Prader-Willi syndrome (PWS) is a complex multi-system genetic disorder affecting approximately 1:12,000 individuals. Features include hypotonia leading to poor suck, difficulty feeding and failure to thrive in infancy. The central neurological defect causes patients to sense that they are starving and results in hyperphagia, morbid obesity, and an increased incidence of diabetes. Developmental delay/mild intellectual disability, growth hormone deficiency, behavioral problems, and neuroendocrine abnormalities are frequently observed. Diazoxide choline controlled-release tablets (DCCR) work by improving sensitivity to leptin and insulin in AgRP and POMC neurons in the hypothalamus, reducing deposition and increasing ß-oxidation of fat and resting energy expenditure, and normalized GABA responsiveness. We performed a 10 weeks of open label titration and a randomized double-blind, placebo controlled 4 week extension phase. This abstract summarizes data from the 13 subjects enrolled in the study including 5 females and 8 males. On average they were 16 years old (11-21 years), weighed 89kg (56.9 – 133.6 kg), had BMI of 38.1 (25 – 53.8) and 51.7% body fat (42.9 - 60.7%). The mean hyperphagia score was 38.1 (25 – 53.8). More than 90% of the subjects showed improvement in their hyperphagia scores (p=0.02) with an average reduction in hyperphagia of 33%. Additionally, we observed a 2.4% reduction in fat mass, 2% reduction in weight, 90 kcal increase in resting energy expenditure, 3.3% increase in lean body mass in growth hormone (GH) treated subjects and elimination of aggressive, violent and threatening behavior. The most common AE's included peripheral edema, often transient and related to the vasodilatory action of the drug; and hyperglycemia in a subset of patients which decreased at a lower dose and resolved with drug discontinuation. In conclusion the drug shows improvement in hyperphagia, body fat, lean body mass composition and behavior problems in PWS

Keywords: Prader Willi; hyperphagia; diazoxide; obesity; treatment trial;

Poster #: 33

Development of Student-Assisted LEGO Therapy for Autism

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Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by persistent difficulties in the social use of verbal and nonverbal communication. Recent estimates suggest that the prevalence rate of ASD is 1 in 68, which is a dramatic increase compared to previous years. Despite increased prevalence rates, only few evidence-based behavioral interventions are available for the treatment of ASD. LEGO is advantageous in attracting and motivating children with ASD because of its structured and predictable play, intrinsically enjoyable properties, and opportunities for originality. The purpose of this study was to develop a LEGO Therapy curriculum for children with Autism Spectrum Disorders (ASD) and document its effectiveness in improving ASD symptoms. More specifically, a LEGO curriculum was designed with the focus on increasing collaborative work, division of labor, sharing, turn-taking, eye contact, gaze following, and verbal communication. For the study, children diagnosed with ASD between the ages of 5-12 participated in LEGO Therapy for an hour, once per week, for five weeks. During each session, children would engage in one-on-one therapy with a student researcher, with both taking turns as either a 'builder' or an 'instructor'. To monitor progress over the five-week period, the Autism Impact Measure (AIM) questionnaire was administered to parents to monitor ASD symptoms. Results showed that after five sessions of LEGO Therapy, there was a decrease in ASD symptoms and an improvement in social use of verbal and nonverbal communication. Our student-assisted LEGO therapy allowed children with ASD to practice verbal and nonverbal communication with an emphasis on social support, social problem solving, and conflict resolution. The study findings suggest that behavioral interventions using LEGO may help children with ASD initiate and sustain higher quality interactions with peers.

Keywords: Autism Spectrum Disorders; Behavioral Intervention; Development; Behavioral Therapy;

Poster #: 34

Thyroid Stimulating Hormone (TSH) and Free Thyroxine (fT4) comparisons across Growth Hormone treatment and PWS subtypes.

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Background: Prader-Willi Syndrome (PWS) is a complex, multi-system syndrome that occurs at a frequency of approximately 1/10,000-1/30,000 and is equally distributed among males and females and all ethnic groups. PWS results from loss of expression of paternally-inherited genes on the chromosome 15 q11-q13 by a variety of mechanisms which include large deletions (70-75%), maternal UPD (20-30%), and imprinting defects (2-5%) or balanced translocations. The deletion subtype is further divided into type I and type II deletions depending on chromosome breakpoint assignments. PWS is the most common genetic syndrome with obesity and individuals have a characteristic behavior disorder often with mild intellectual disability, infantile hypotonia associated with poor sucking, short stature and obesity. PWS is characterized by hypothalamic-pituitary axis dysfunction with growth hormone deficiency, hypogonadism and several other hormonal deficiencies resulting in short stature, centrally-driven excessive appetite (hyperphagia), central obesity, cryptorchidism and decreased lean mass. There is very limited literature on the thyroid function in PWS. The aim of the current study is to determine thyroid function in common subtypes, deletion and uniparental disomy (UPD) of PWS and to evaluate the therapeutic effects of growth hormone treatment on thyroid profile in a large cohort of 64 subjects. Methods: Sixty-four subjects with genetically confirmed diagnosis of PWS were included in this study at University of California, Irvine and Case Western Reserve University. Informed consent was obtained from all eligible participants or their legally responsible caregivers. Sample analysis for genetic studies was performed. Individuals who were FISH negative had UPD studies if available as part of the research, and those who had negative FISH and UPD studies but were methylation abnormal was presumed to have imprinting center defects. There were 33 males and 31 females in the age range o

Keywords: Prader-Willi syndrome; Hypothyroidism; 15 q11-q13; imprinting;

Poster #: 35

Reduced IP3-mediated Ca2+ signaling in autism spectrum disorders in the context of fragile X and tuberous sclerosis syndromes.

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Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder affecting up to 2% of children and characterized by impaired social skills, delayed or disordered language and communication skills, and repetitive, stereotypic behavior. Growing evidence supports a role of Ca2+ signaling in the pathogenesis of ASD. Inositol trisphosphate (IP3)-mediated Ca2+ release from intracellular stores participates in a variety of functions, from synaptic plasticity and memory, to long-term gene transcription changes and immune response. IP3 is produced upon stimulation of G-protein coupled receptors (GPCR) and binds to IP3 receptor/channel (IP3R) in the membrane of the endoplasmic reticulum (ER), liberating Ca2+ sequestered in the ER lumen into the cytoplasm. Here, we report that human fibroblasts from three genetically distinct monogenic models of ASD – fragile X and tuberous sclerosis TSC1 and TSC2 – uniformly display depressed Ca2+ release through IP3 receptors. We observed defects in whole-cell Ca2+ signals evoked by G-protein-coupled cell surface receptors and by photoreleased IP3, and at the level of local elementary Ca2+ events, suggesting fundamental defects in IP3R channel activity in ASD. Given its ubiquitous functions in the body, malfunctioning of IP3-mediated signaling may account for the heterogeneity of non-neuronal symptoms seen in ASD, such as gastrointestinal tract problems and immunological complications.

Keywords: Autism spectrum disorder; fragile x syndrome; tuberous scelrosis; calcium signaling; IP3 receptor;

Poster #: 36

Correlation Between Adolescent Level of Denial for Alcohol Substance Abuse and Improved Drinking Habits

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Drinking under the age of 21 has become widespread despite being illegal and chronic misuse of alcohol can cause a variety of diseases and psychological problems. For adolescents under the age of 21 the brain is still developing leaving them vulnerable to develop alcohol dependence or abuse. Denial is considered a primitive defense mechanism in the development of a child, and can be a barrier to treatment. We hypothesize that CASI program is sufficient to help identify adolescent patients in the ED who have a lower level of denial regarding their drinking problem reported improved drinking habits compared to patients that report a higher level of denial regarding their drinking problem. In order to examine this, research associates will screen for patients entering the UCIMC ED who are between 12-17 years of age, are English speaking, and are coherent and able to provide written consent, along with their parent's written assent. The patient used a tablet containing the CASI program and the parent and/or legal guardian exited the room for privacy. All adolescent patients were asked to participate in a follow up survey after three months via computer. The survey consisted a mixture of questions from AUDIT-C, CRAFFT, and AAIDS pertaining to their use of alcohol. From the study there were 59 recruited cases and 30 patients completed follow up. The results revealed that Audit-C and CRAFFT questions had significant decreases at follow up, but denial of alcohol use did not predict change in AUDIT-C score. However, those who said alcohol had a high effect on their life had a significant decrease in AUDIT-C scores after follow-up. Even though these findings suggest that denial was not a predictor of AUDIT-C score, CASI was still an effective tool in suggesting healthier lifestyles for adolescents.

Keywords: Adolescent; Computerized; Alcohol; Denial; Intervention;

Poster #: 37

Are parental perceived stress and anxiety a predictor of postoperative recovery in children?

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Objective: High levels of preoperative anxiety in both parent and child are associated with negative postoperative behavioral changes in children. Parental anxiety has been found to be a predictor for higher levels of anxiety in children in the preoperative and postoperative setting. This study examined the effects of parental stress and anxiety on children's postoperative recovery at home following outpatient surgery. Methods: Participants included 434 children aged 2 to 15 years old undergoing outpatient tonsillectomy and adenoidectomy at Children's Hospital of Orange County. Parents completed the Perceived Stress Scale (PSS) and the State-Trait Anxiety Inventory (STAI-T) before the surgery, and the Recovery Inventory for their children on postoperative days one, two, three, seven, and fourteen at home. Results: Using Pearson product-moment correlation, parental trait anxiety was found to be negatively associated with children's recovery on day 1 ($p = .045$). Chi-square analyses also demonstrated that a lesser proportion of children with parents who reported high anxiety were categorized as having "good" recovery compared to children with low anxiety parents ($p = 0.04$). No significant associations were found between parental perceived stress and children's postoperative recovery. Conclusions: Results of this study suggest that children with high anxiety parents may exhibit poorer postoperative recovery compared to children of low anxiety parents. It is also possible that high anxiety impacts parental perceptions of children's postoperative recovery. Future research is needed in order to understand the relationship between parental anxiety and children's recover from surgery in order to identify best methods of targeting parental anxiety in interventions in the pediatric surgical setting.

Keywords: parental anxiety; parental stress; child recovery; postoperative recovery; behavioral changes;

Poster #: 38

Influence of teacher cognitions and institutional barriers on elementary school physical activity

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Research has shown that both social and structural environment influence child physical activity (PA). Based on Social Cognitive Theory, it was hypothesized that teachers' cognitions in regards to teaching physical education (PE) would predict elementary school students' activity during the school day after controlling for institutional context. Participants- Fourth and fifth grade students (n=108; age M=9.1, BMI M=19.6, 55% Male) from four classes in two elementary schools (two classes per school) and their respective teachers for each class (n=4, age M=44.5, 100% Female). Procedures-Students in each class wore a Fitbit Zip device to monitor physical activity throughout school day from 8 AM to approximately 2 PM for five days. Teachers completed surveys in regards to PE self-efficacy (sample item: I am not qualified to teach) and perceptions of institutional barriers to teaching PE (sample item: insufficient time in the school day). Results-Student activity, teachers' perceived self-efficacy, and teachers' perceived institutional barriers were all significantly different across the two participating schools ($p's < .001$). There was a significant correlation between perceived barriers and child activity in the expected direction ($r=-.32$, $p<. 001$) but no correlation between perceived self-efficacy and child activity. The association between child activity and perceived barriers was no longer significant after controlling for school. Conclusions-Institutional barriers to teaching PE emerged as a stronger influence on elementary school children's physical activity during the school day than teachers' self-efficacy for teaching PE. Decreasing these barriers and creating an environment more conducive to physical education may help promote students' physical activity levels.

Keywords: physical activity; children; school;

Poster #: 39

Clinic in the Park: Community-Based Outreach for Injury Prevention

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Purpose Clinic in the Park, a health collaborative co-located at a Farmers Market, is designed to connect, screen and educate. . This study is designed to assess if Clinic visitors would participate in infant safe sleep chats. Methods: Primary messages are 1) back to sleep, only infant in crib; 2) no after-market products; and 3) bed-sharing risks. Handouts, (English & Spanish) contain messages and displays of proper and improper sleep environment;. Qualitative and quantitative data are 1) manual counters of visitors; 2) Collaborator evaluation; 3) Visitor comments. Results Families came to the Farmers Market and received a bonus of unexpected education on child health. Of the total of 14,123 visitors, 9% (N=1261) chatted with a pediatrician & educator at the Safe Sleep Station. Qualitative results indicate that 1) most know the back to sleep message; 2) most do not know the standards of care for safe sleep – no toys, bumpers or items in crib; and 3) dangers of bed-sharing with adult. Discussions included potential hazards and/or ineffectiveness of after-market products and toddler sleep habits. Interaction between family members occurred in the context of the pediatric health chat allowing for more in-depth discussion. Conclusions Safe Sleep Environment needs clarification. Parents have questions, which may not be answered in the well child visit or prenatal period. The venue – public space – is unique for injury prevention messaging which allows for a longer discussion than can typically be accommodated in a well child visit and enhances what is offered in the pediatric visit. Additionally, those who do not attend child pediatric visits, i.e. grandparents, relatives and friends, or those who are expecting their first child can participate in the counseling. Teenagers, (potential babysitters), were provided information. This contributes to uniformity of messaging and more in-depth discussion than feasible in a well child visit.

Keywords: Infant; Safe Sleep; Injury Prevention; SIDS;

Poster #: 40

LENGTH OF STAY ANALYSIS OF PEDIATRIC PSYCHIATRIC VISITS AT TWO EMERGENCY DEPARTMENTS

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The objective of this study aims to analyze pediatric psychiatric patient length of stay between two hospital sites over a two-year period (2010-2012). This longitudinal, retrospective study also hopes to identify factors that correlate to a drastic increase in time of stay throughout the recent years. The rise in pediatric psychiatric patient length of stay affects hospital cost, resources, and crowding. With this study, we hope to expand our knowledge on pediatric psychiatric behavior and uncover factors to prevent this escalating trend. Length of stay (determined by the time patient enters triage to the time the patient is discharged), age, gender, race/ethnicity, chief complaint, medical history, previous psychiatric family history, alcohol and drug history, and insurance type were all analyzed for any correlations through secure patient medical record databases at both hospital sites. Results showed a clear increase in length of stay for pediatric psychiatric patients over the two-year period, with no significant time difference between the two hospital sites. Findings also suggested that the factor of chief complaint (suicidal ideation and suicide attempts) had a significant connection with increased hospital length of stay. With these outcomes, future research can be done to analyze the in-depth relationship between pediatric psychiatric patients with suicidal ideation and increasing hospital length of stay. In addition, these results and variables can be tested in future studies for significance and correlation with periods of ED overcrowding.

Keywords: Length of Stay; Pediatric Psychiatric; ED Crowding; Hospital Cost Resources;

Poster #: 41

The Efficacy of LEGO Therapy in Decreasing Autism Symptoms

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The purpose of this study was to determine the effectiveness of LEGO therapy in improving Autism Spectrum Disorder (ASD) symptoms, especially: collaborative work, division of labor, sharing, turn-taking, cue eye contact, gaze following, and verbal communication. Since children with ASD are naturally drawn to repetitive, predictable, and repeating patterns, LEGO is advantageous in attracting and motivating children with ASD because of its structured and predictable play, intrinsically enjoyable properties, and opportunities for originality. LEGO therapy allows the children to practice verbal and nonverbal communication with an emphasis on social support, social problem solving, and conflict resolution. Behavioral interventions using LEGO aim to help children with ASD initiate and sustain higher quality interactions with peers. During the study, five children diagnosed with ASD between the ages of 5-12 underwent five weeks, with an hour-long session each week, of LEGO Therapy. During each session, children would engage in one-on-one therapy with a student researcher, with both taking turns as either a 'builder' or an 'instructor'. Together, the student researcher and the child work to construct the LEGO set. To monitor progress over the five-week period, parents were given three Autism Impact Measure (AIM) questionnaires to monitor any reduction in ASD symptoms. After five sessions of LEGO Therapy, there was a general decrease in ASD symptoms and an improvement in social interactions between the children and their peers.

Keywords: Autism; LEGO; Therapy; children; social;

Poster #: 42

Genotype-phenotype study of patients possessing mutations in valosin-containing protein (VCP)

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Mutations in valosin-containing protein (VCP) lead to inclusion-body myopathy that is associated with Paget's disease of bone, frontotemporal dementia, and amyotropic lateral sclerosis (ALS). VCP disease is a progressive, fatal genetic disorder. VCP is a chaperone and a key player in the ubiquitin-proteasome system of protein degradation. Approximately 30 missense mutations in the gene have been qualitatively documented as leading to the clinical variation phenotype of VCP disease. We have now recruited the largest number of subjects with VCP disease and our aim is to quantify genotype-phenotype correlations for the clinical and biochemical features of VCP mutations. To accomplish this objective, >200 members of 46 families carrying the VCP mutation were grouped according to their specific mutation. For each group, clinical features such as age of onset of myopathy, Paget's disease, dementia, bone and muscle markers were recorded. The frequency of associated conditions (ALS, Parkinson's, Alzheimer's, cataracts, and cancer) were also recorded in order to determine whether VCP mutations may be implicated in the etiology of these associated diseases. We will present data on the genotype/phenotype correlations of 30 mutations and age of onset of the varied manifestations of VCP associated myopathy, Paget's disease of the bone and dementia. By understanding the association between the type of VCP mutation and its clinical presentation, clinicians will be better able to diagnose VCP disease earlier and manage patients more effectively.

Keywords: inclusion body myopathy; Paget's disease of bone; valosin containing protein; frontotemporal dementia; genotype-phenotype;

Poster #: 43

A Kinetic Model of GPCRs: Analysis of G protein Activity, Occupancy, Coupling and Receptor-State Affinity Constants

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G protein-coupled receptors (GPCRs) regulate nearly all known physiological processes and hence are central to the pathogenesis and pharmacological treatment of many disorders. GPCR output pathways are controlled by the balanced action of two proteins – G proteins and beta arrestins. Most therapeutic agonists activate both pathways simultaneously, triggering their beneficial effects primarily through one pathway and their unwanted effects through the other. Evidence now indicates that some drugs, termed biased agonists, can signal through one pathway selectively while causing little activation of the other. To facilitate the identification of biased agonists in screening assays, we developed a model for G protein signaling and used it to validate our method for quantifying biased agonism. Here we present a kinetic, quaternary complex model that describes activation of G proteins by GPCRs. Our model accounts for GTPase activity and the binding of 1) drug with receptor, 2) receptor with G protein, and 3) guanine nucleotide (GTP and GDP) with G protein. We solved the model numerically to predict the extents of G protein activation, receptor occupancy by ligand, and receptor coupling that result from varying the ligand concentration, the presence of guanine nucleotide, the ratio of G protein to receptor, and the equilibrium constants governing receptor pre-coupling and constitutive activity. We also simulated responses downstream from G protein activation using a transducer function. Our model provides an explanation for agonist-induced increases or decreases in receptor-G protein coupling coincident with G protein activation. In addition, we demonstrate that the affinity constants of a ligand for both the active and inactive states of the receptor can be derived to a close approximation from analysis of simulated responses downstream from receptor activation.

Keywords: GPCR; biased agonism; kinetic model; receptor states; G protein signaling;

Poster #: 45

Microbial community characterization of fecal samples from healthy premature infants compared with those that develop late onset sepsis

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OBJECTIVE: Extreme low birth weight (ELBW) infants are at very high risk for developing necrotizing enterocolitis (NEC), a common cause for morbidity and mortality among these infants. Premature birth and early feeding are both important risk factors. A majority of infants with NEC go on to develop severe late onset sepsis (LOS) requiring prolonged broad spectrum antibiotics and debilitating surgical intervention. We aim to characterize gut microbial communities from otherwise healthy premature infants in relation with previous antibiotic use and feeding patterns, and to compare them to those from ELBW infants who develop LOS (with or without NEC). This will help devise strategies to preserve a healthier microbiome and improve outcomes in ELBW infants. METHODS: Fecal samples have been collected from 37 ELBW infants, including 24 controls, 5 with NEC, and 7 septic non-NEC. Metagenomic DNA will be extracted, and barcoded sequencing libraries will be prepared with the NexteraXT kit followed by Illumina sequencing. Following QC with Prinseq and Deconseq, prophage regions will be identified with PhiSpy, metagenomic reads will be analyzed with Metaphlan for taxonomy, and Humann for pathway analysis. Clinical and demographic characteristics of these subjects will be captured. RESULTS: Recent studies suggest that intestinal microbial communities are involved in the development of NEC. We expect to find less diverse microbial communities dominated by Firmicutes, gram negative bacteria or Candida spp in the fecal microbial communities of babies with NEC, compared to the otherwise well ELBW infants. Preliminary findings from comparative metagenomic analysis will be reported. SIGNIFICANCE: A large number of ELBW infants develop NEC and LOS. Understanding the characteristics of normal gut microbial communities in ELBW infants will enable strategies to preserve or reconstitute healthy microbial community assembly after modification by diverse therapeutic interventions.

Keywords: Necrotizing Enterocolitis; Metabolomics; Microbiome;

Poster #: 47

Higher levels of secreted S100 A8/9 levels from peritumor perirenal adipose tissues are associated with renal cell carcinoma (RCC)

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Purpose: To define the relationship between obesity and RCC, we studied the interaction between perirenal adipose tissues (PAT) and RCC. Material and Methods: PAT directly over tumors, PAT away from tumors, subcutaneous adipose tissues (AT) and renal sinus AT were collected and conditioned medium (CM) was generated from 90 patients undergoing surgery for renal cortical neoplasms. We evaluated the CM for its effect on proliferation and migration of ccRCC cell line Caki-2 by MTT assay and Boyden chamber cell migration assay, respectively, and for secreted levels of S100 A8/9 by ELISA. Results: Compared to patients with benign histopathology, peritumor PAT CM from pT3 ccRCC patients significantly increased CaKi-2 cell migration ($P<0.05$), but did not affect the proliferation ($P>0.05$). Patients with ccRCC at stage pT2 and pT3 had higher levels of S100 A8/9 in peritumor PAT and sinus AT CM than those with benign pathology or ccRCC at stage pT1. Sinus AT exhibits the highest level of S100 A8/9 (9.13± 2.75ng/ml), followed by peritumor PAT (2.40±0.64ng/ml), Skin AT (0.71±0.22ng/ml) and PAT away from tumors (0.70±0.20ng/ml). The mean BMI values from ccRCC patients at stage pT1, pT2 and pT3 are not significantly different, which are 30.1±7.3, 28.9±4.6 and 28.9±4.0kg/m2, respectively ($P>0.05$). Conclusion: The higher S100 A8/9 levels in peritumor PAT and sinus AT CM associated with higher stage ccRCC may have potential prognostic value. Further studies are in progress to determine cellular mechanisms of S100 A8/9's action. Fat specific metrics will likely be superior to BMI for predicting tumor status and behavior.

Keywords: S100A8/A9; Perirenal Adipose Tissue; Renal Cell Carcinoma;

Poster #: 49

Evaluation of Quality of Upper Urinary Tract Biopsy Using Bigopsy Forceps: Preliminary Report and Proposal for Multi-Institutional Study

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Introduction: The use of ureteroscopic biopsy devices is critical to providing an accurate diagnosis for patients with upper tract urothelial carcinoma (UTUC). The BIGopsy biopsy device (Cook Medical, Bloomington, IN, USA) is a novel instrument developed to extract deeper and larger biopsy samples. Herein we performed a single-center retrospective comparison of endoscopic biopsy quality using the BIGopsy device and other contemporary biopsy devices. Methods: Between 2011–2014, 22 endoscopic biopsies were performed for suspected UTUC in 16 patients. Biopsies were performed with BIGopsy forceps, Piranha biopsy forceps (Boston Scientific, Newport Beach, CA, USA), or a standard 2.4F nitinol basket (Boston Scientific, Newport Beach, CA, USA). Lesion location, specimen size, and the presence of crush artifacts and intact urothelium were recorded. Histopathology was retrospectively reviewed by one pathologist, blinded to the type of biopsy device used, who graded the quality of each biopsy specimen on a scale from 1-10. Results: Sixteen endoscopic biopsies (72.7%) were obtained using BIGopsy forceps and 6 (27.3%) using other biopsy devices. The mean specimen size was 3.10mm (SD 2.22) for the BIGopsy forceps and 2.08mm (SD 1.20) ($p=0.186$) for other biopsy devices. Biopsy specimens obtained using BIGopsy forceps contained significantly more intact urothelium ($p=0.031$) and less crush artifacts ($p=0.007$). BIGopsy specimens received the highest scores in biopsy quality and ease of biopsy interpretation as graded by a pathologist. Conclusions: Upper tract biopsies obtained using BIGopsy forceps are of higher quality and contain more intact urothelium than biopsies obtained using other devices. When compared to other devices, BIGopsy enables pathologists to more easily reach definitive and accurate diagnoses. A larger multicenter study comparing different biopsy devices is proposed to validate these findings.

Keywords: BIGopsy; Urothelial Carcinoma; Biopsy; Ureteroscopy; Upper Tract;

Poster #: 51

Mapping the Autonomic Nerve Distribution of the Urinary Bladder Using Three-Dimensional Image Reconstruction

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Introduction and Objective: A virtual 3D map of the autonomic nerve distribution to the bladder could redefine our understanding of the relationship between neural tissue and bladder urothelium, and could have important ramifications for common diseases such as bladder overactivity and interstitial cystitis. Furthermore, it may help improve nerve-modulating therapies and prevent unwarranted nerve damage during invasive procedures. Thus, we developed a 3D image reconstruction of autonomic nerve tissue innervating the urinary bladder using male and female cadaver histopathology. Methods: We obtained bladder specimens from a male and female cadaver. Axial cross sections of the bladder neck were generated at 3-5mm intervals and stained for S100 protein. Nerves were manually demarcated using ImageScope software (Aperior, Vista, CA). Distances between autonomic nerves and bladder mucosa were recorded using AutoCAD software (Autodesk, Venice, CA). Blender computer graphics software (Amsterdam, Netherlands) was used to generate 3D reconstructions of autonomic nerve anatomy and nerve density. Results: Axial cross-sections and 3D image reconstructions showed that autonomic innervation was highly concentrated in the posterior aspect of the bladder neck in both male and female bladder specimens. Mean distances between autonomic nerve tissue and the bladder mucosa was 1.15mm posteriorly versus 4.0mm anteriorly in the male bladder (0.27-2.87 vs. 2.03-6.20, $p<0.001$) and 1.51mm posteriorly versus 1.83mm anteriorly in the female bladder (0.50-2.91 vs. 0.55-3.07, $p=0.027$). Conclusions: Novel 3D reconstruction of the bladder is feasible and may help redefine our understanding of human bladder innervation. Autonomic innervation of the bladder is highly focused in the posterior aspect of the bladder neck in both male and female bladders.

Keywords: Bladder; Autonomic Nerves; Histopathology; Three-dimensional; Reconstruction;

Poster #: 52

Deleterious and salutary effects of Nrf2 inducer, Bardoxolone methyl, on CKD progression are dose dependent

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Oxidative stress and inflammation play a major role in progression of CKD. Our earlier studies have shown impairment of Nrf2 system and its contribution to oxidative stress and inflammation in CKD. Administration of natural Nrf2-inducing phytochemicals ameliorates acute and chronic kidney disease in experimental animals. However due to adverse outcomes clinical trial of the synthetic Nrf2 activator, bardoxolone methyl (BARD), in CKD patients was terminated. Likewise treatment with BARD analog, dh404 at 5-20 mg/kg/day intensified inflammation and accelerated CKD progression in diabetic obese Zucker rats. BARD activates Nrf2 via covalent modification of reactive cysteine residues in Nrf2 repressor, Keap-1. In addition to Nrf2, Keap1 suppresses IKKB, the positive regulator of NFkB, therefore its modification can trigger inflammation. We hypothesized that deleterious effects of high doses of BARD analogues may be due to activation of NFkB. CKD rats were randomized to receive dh404 at 2 mg/kg/day, 10mg/kg/day, or vehicle for 12 weeks. Vehicle-treated group exhibited glomerulosclerosis, interstitial fibrosis and inflammation, NFkB activation, upregulation of oxidative, inflammatory and fibrotic pathways, and suppression of Nrf2 activity. Treatment with low dose dh404 restored Nrf2 activity, suppressed NFkB and fibrotic pathways, reduced glomerulosclerosis, interstitial fibrosis and inflammation. In contrast treatment with high dh404 dosage intensified proteinuria, renal dysfunction and histological abnormalities, amplified up-regulations of NFkB and fibrotic pathways, and suppression of Nrf2 system. These observation revealed dose-dependent dimorphic impact of BARD on CKD progression. The dimorphic dose response to BARD analog, observed in CKD animals is consistent with hormetic properties of natural plant-based Nrf2 inducers which serve as insecticides in parasites that consume large quantities of plant products relative to their body mass.

Keywords: Chronic kidney disease; Nrf2 activator; Oxidative stress; inflammatio; fibrosis;

Poster #: 53

High amylose resistant starch diet ameliorates oxidative stress, inflammation, and progression of chronic kidney disease

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High amylose resistant starch diet ameliorates oxidative stress, inflammation, and progression of chronic kidney disease (CKD) Background- Inflammation is a major mediator of CKD progression and is partly driven by altered gut microbiome and intestinal barrier disruption, events which are caused by: urea influx in the intestine resulting in dominance of urease-possessing bacteria; disruption of epithelial barrier by urea-derived ammonia leading to endotoxemia and bacterial translocation; and restriction of potassium-rich fruits and vegetables which are common sources of fermentable fiber. Restriction of these foods leads to depletion of bacteria that convert indigestible carbohydrates to short chain fatty acids which are important nutrients for colonocytes and regulatory T lymphocytes. We hypothesized that a high resistant starch diet attenuates CKD progression. Methods- Male Sprague Dawley rats were fed a chow containing 0.7% adenine for 2 weeks to induce CKD. Rats were then fed diets supplemented with amylopectin (low-fiber control) or high fermentable fiber (amylose maize resistant starch, HAM-RS2) for 3 weeks. Results- CKD rats consuming low fiber diet exhibited reduced creatinine clearance, interstitial fibrosis, inflammation, tubular damage, activation of NFkB, upregulation of pro-inflammatory, pro-oxidant, and pro-fibrotic molecules; impaired Nrf2 activity, down-regulation of antioxidant enzymes, and disruption of colonic epithelial tight junction. The high resistant starch diet significantly attenuated these abnormalities. Conclusions- High resistant starch diet retards CKD progression and attenuates oxidative stress and inflammation in rats. Future studies are needed to explore the impact of HAM-RS2 in CKD patients

Keywords: Chronic kidney disease; Inflammation; Oxidative stress; Nrf2-Keap1 pathway; NFkB;

Poster #: 54

Passive gut phosphate absorption is increased in mice with chronic kidney disease.

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Background: Phosphorus overload is prevalent in chronic kidney disease (CKD) and contributes to cardiovascular morbidity and death. Dietary phosphate absorption occurs by sodium-dependent active uptake (Npt-2b transporter) or passive diffusion (paracellular pathways). Chronic gut inflammation with breakdown of intercellular tight junctions is present in CKD and is a likely source of systemic inflammation. The potential impact of this gut inflammation on phosphate uptake has not been explored. We used an in situ gut loop assay to measure active and passive phosphate uptake in the ileum of CKD and control mice. Methods: CKD was induced in adult mice via adenine diet x18 days. Mice were then placed on normal 0.5% phosphate (NP) or high 1.5% phosphate (HP) diet for 6 weeks. Under isoflurane anesthesia, 2.5 cm ileum loops (with intact blood supply) were created and injected with sodium- or choline-phosphate buffer radiolabeled with P-33. Phosphonoformic acid (Npt-2b inhibitor) was added to the choline-phosphate buffer to ensure exclusion of Npt-2b active transport. Amount of absorbed phosphate, normalized to mg protein, was calculated after timed incubation. Adjacent ileum tissue was processed for histology and Western blot. Results: Passive phosphate uptake (measured with sodium-free buffer) in the ileum of control mice plateaued after 1-minute incubation. Active transport was less than passive uptake and sometimes measured out as a negative value, suggesting efflux transport into the gut lumen. CKD mice showed increased passive phosphate uptake compared to controls, regardless of NP or HP diet. Histology showed influx of macrophages in the CKD ileum wall, and expression of the tight junction protein claudin-2 was significantly decreased. Conclusions: Passive phosphate uptake is increased in the gut of CKD mice and likely contributes to systemic phosphorus overload and cardiovascular disease.

Keywords: chronic kidney disease; phosphate absorption; epithelial barrier; tight junction proteins;

Poster #: 55

Evaluation of Myocardial Mechanics in AL Amyloid patients

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Introduction: AL Cardiac amyloidosis is an adverse prognostic factor when fibrillar deposits concentrate in ventricular walls without clinical manifestation (median survival rate of 1-2 yrs; decreased to <6 months in symptomatic congestive heart failure patients). This makes early detection essential. 2-Dimensional speckle tracking echocardiography (2D-STE) has been proven to be a sensitive and accurate diagnostic tool that quantifies myocardial mechanics and detects cardiac deformation before left ventricular ejection fraction (LVEF) changes occur, and could be used for early detection of cardiac involvement in AL. The objectives were to assess global longitudinal strain (GLS) using 2D-STE TomTec software in AL patients and compare 2D-STE software:? Syngo Velocity Vector Imaging(VVI), EchoPAC(GE), and TomTec. Methodology: Subjects included 35 biopsy confirmed AL amyloidosis patients with normal LVEF, and increased wall thickness. All echocardiographic examinations were obtained at the Mayo Clinic using the American Society of Echocardiography guidelines. All images were exported (DICOM) from the central archival system and analyzed using 2D-STE by placing tracking points at mid or end-systole. Data generated from 16 segments was used to calculate average GLS using all software. Results: Population (n=35) mean age was 68±10yrs, 23(66%) were males. All patients had normal EF 65±5% with increased wall thickness 16±2mm (Normal <12mm). GLS was reduced across all systems despite normal EF (P<0.0001). GLS for TomTec (Fig 4), VVI, and GE were -11.9±3.1, -11.7±2.6, and -11.6±3.0 respectively. There was no clinical or statistical difference between software, only minimal mean differences not statistically significant (P>0.05 Paired t-test), with good intervendor agreement (Fig.1–3). Conclusion: In a group of AL amyloidosis patients with normal EF and increased wall thickness, GLS was reduced. Values across all software were similar, with good inter-vendor agreement.

Keywords: Amyloidosis; Myocardial; Mechanics; Speckle-tracking; Echocardiography;

Poster #: 56

CONTEMPORARY FIBEROPTIC AND DISTAL SENSOR ENDOSCOPIC DEVICES PRODUCE HEAT CAPABLE OF CAUSING THERMAL INJURY

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Introduction: Illumination during contemporary endoscopic procedures is produced from powerful light sources such as contemporary xenon, halogen, and light emitting diodes (LED). Light sources produce thermal energy, which have resulted in thermal injury and ignition of flammable materials when improperly used in the operating room. Hence we evaluate the ignition and burn risks associated with contemporary fiberoptic and distal sensor endoscopic technologies. Methods: New and used SCB Xenon 300 light sources were used to illuminate a 4.8 mm fiberoptic cable, 10 mm laparoscope, 5 mm laparoscope, rigid cystoscope, semi-rigid ureteroscope, flexible cystoscope, flexible fiberoptic ureteroscope and distal sensor cystoscope (Karl Storz, Inc., Germany). Peak temperatures were measured at the distal end of each endoscopic instrument, including a distal sensor ureteroscope equipped with a built-in LED light source. Ignition risk was evaluated by placing each device on a flat and folded surgical drape. Human cadaver skin covered with surgical drape was exposed to each device to investigate the risk of thermal injury. Results: The peak temperatures for each device ranged from 26.9°C (flexible fiberoptic ureteroscope) to 194.5°C (fiberoptic cable) using a used xenon bulb. Drape ignition was noted when the fiberoptic cable was placed against a fold of the drape. Underlying cadaver skin damage occurred when in contact with the fiberoptic cable, 10 mm laparoscope, 5 mm laparoscope, and distal sensor cystoscope; however, little to no visible damage was observed on the surgical drape used. Conclusion: Fiberoptic light cables and endoscopic devices have the potential to generate high temperatures with the ability to cause cutaneous thermal injury and drape ignition. Thermal injury may occur without visible damage to drapes. Surgeons should remain vigilant regarding the risks associated with these devices, and should take necessary safety precautions to prevent patient injury.

Keywords: fiberoptic cable; temperature; thermal injury; laparoscope; endoscope;

Poster #: 57

Effect of tourniquet and reperfusion on lower extremity oxygenation during total knee arthroplasty

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INTRODUCTION Tourniquet use during total knee arthroplasty (TKA) has had the reported benefits of reduced intraoperative blood loss, cleaner surgical fields and reductions in operative time; however, some studies have associated prolonged tourniquet use with longer post-operative recovery and decreased range-of-motion. The goal of this study is to describe the dynamics of oxygen saturation (StO2) during intraoperative tourniquet application utilizing diffuse optical spectroscopy (DOS). METHODS 14 patients undergoing TKA, 9 primary and 5 revision, had the DOS sensor placed distal to the tourniquet to record the patient's somatic oxygen saturation prior to tourniquet inflation to 250 mm Hg until the completion of the case. DOS is a non-invasive spectroscopy system that quantifies hemoglobin content and oxygenation in real time. The primary DOS outcomes analyzed were StO2 and its kinetics during onset and release of tourniquet pressure. RESULTS The mean tourniquet time was 85.5 ± 4.8 minutes, with longer times used in revisions. The average baseline StO2 prior to tourniquet inflation was 74.9 ± 2.5 %, and mean minimum ischemic StO2 was 12.9 ± 4.1%. Mean StO2 following reperfusion after tourniquet release was 81.0 ± 2.4, which was significantly higher than baseline StO2 ($p = 0.011$). Using a two-phase linear fit, the mean time from tourniquet onset until steady state was 25.4 ± 4.1 minutes. There were 3 subjects whose post-release peak StO2 was lower than baseline. DISCUSSION DOS is capable of monitoring tissue StO2 intra-operatively distal to the tourniquet, providing real-time information on hemoglobin content and StO2. This study showed significantly higher mean StO2 over baseline after tourniquet release, as well as kinematic parameters that might better characterize patient's physiologic response during ischemia. This data may also help establish the ideal tourniquet time limits for TKA in order to to achieve the best clinical outcomes.

Keywords: Tourniquet time; Total knee arthroplasty; Oxygen saturation; Diffuse optical spectroscopy;

Poster #: 58

Laparoscopic Right Hemicolectomy: Short and Long Term Outcomes of Intracorporeal Versus Extracorporeal Anastomosis

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Introduction: The use of laparoscopy in right hemicolectomy allows for the option of a totally intracorporeal anastomosis (IA) in the construction of an ileocolic anastomosis. This may alleviate some of the technical limitations a surgeon faces with a laparoscopic-assisted extracorporeal anastomosis (EA). Experience with IA in the literature has been limited. We present a large consecutive case series comparing the postoperative and oncologic outcomes of IA versus EA for laparoscopic right hemicolectomy (LRHC). Materials and Methods: A retrospective chart review of 195 consecutive LRHC patients from March 2005 to June 2014 was performed. Patient demographics were reported, and postoperative outcomes were compared using multivariate regression analysis. Patients with colon cancer had their oncologic outcomes analyzed and survival assessed with Kaplan-Meier survival curves. Results: Over the study period, a total of 195 patients underwent LRHC; 86 (44%) patients received IA and 109 (56%) patients received EA. Both groups were demographically similar with the majority of patients at an ASA Class of II or III. The median Charlson comorbidity index of 3 for the IA group was higher than the EA group's score of 2. The most common indication for surgery was cancer: 56 (65%) of IA cases and 57 (52%) of EA cases. There was no significant difference in length of stay, return of bowel function, or risk of anastomotic leak, intra-abdominal abscess or wound complications. A subset analysis of patients who underwent LRHC for cancer showed no significant difference in the median number of lymph nodes harvested. There was no difference in overall survival and disease-free survival at 5.7 years for the two groups. Conclusions: Our large series reveals IA in LRHC has similar postoperative and oncologic outcomes as EA suggesting IA represents a valid technical advantage for the experienced colorectal surgeon. Large prospective randomized trials are needed to validate these findings.

Keywords: Intracorporeal anastomosis; Laparoscopy; Right Hemicolectomy; outcomes;

Poster #: 59

COMPARISON OF FLOW CHARACTERISTICS BETWEEN A NOVEL THREE-DIMENSIONALLY PRINTED URETERAL STENT AND CONVENTIONAL URETERAL STENTS IN AN EX VIVO PORCINE MODEL

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Introduction: We evaluated the flow characteristics of novel three-dimensionally (3D) printed ureteral stent prototypes to four conventional double-pigtail stents (6Fr Universa® Soft, 7Fr Percuflex™, 7/10Fr Applied Endopyelotomy, and 8.5F Filiform Double Pigtail) in an ex vivo porcine model. Methods: We created a computer aided design for ureteral stents using Solidworks software. The stents were then printed using an EOSINT P395 3D printer. We evaluated five standard stents using 6 ex vivo porcine urinary systems with kidneys and ureters intact. We deployed a 5Fr occlusion catheter in the interpolar calyx for each renal unit. In each renal unit antegrade irrigation with a 0.9% saline bag was placed 35 cm above the renal pelvis. Total, extra-luminal, and intra-luminal flow rates were measured in ml/min for each stent (Table 1). Results: The mean total flow rates for the 9Fr stents were significantly higher compared to the 6Fr, 7Fr, and 7/10Fr stents ($p<0.05$). No significant difference was seen in total flow rate for the 3D printed stent compared to the 8.5F stent. The mean extra-luminal flow rates for the 9Fr stents were similar to the 7Fr stents, but significantly lower than the 6Fr stents ($p<0.001$) and 8.5F stents ($p<0.05$) and significantly higher than the 7/10Fr stents ($p<0.001$). The mean intra-luminal flow rates for the 9Fr stents were significantly higher than all stents tested ($p<0.05$). Conclusion: The 3D printed 9Fr stents demonstrated adequate upper urinary tract drainage in a porcine model and showed mean flow rates comparable to the flow rates of contemporary stents. Continued advances in 3D printing technology may permit clinically viable 3D printed ureteral stents in the future.

Keywords: urology; 3D printing; ureteral stents;

Poster #: 60

Low-cost, Quantitative 3D Structural Imaging of the Nose and Other Facial Features Using Open Source Software

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Objectives: In functional nasal airway surgery , quantitative 3D imaging is often used to create volumetric representations of human facial features. Quantitative 3D imaging can be used to rigorously track changes in nasal morphology and provide numerical outcome measures. However, commercial 3D imaging systems are expensive. This study describes how open-source software and consumer cameras can be used to perform this task inexpensively and efficiently. Study Design: Computer-based research study Methods: 123D Catch developed by Autodesk was used to generate the 3D representation of the 3D printed silicone nasal model derived from a CT scan. The 3D model provided a Lambertian reference standard to consumer digital cameras including the Samsung Galaxy S5, Canon Rebel XTS, and Canon Rebel T5i. Diffuse illumination was used. Total image number was varied along with imaging using surface registration landmarks. Point clouds were created and CloudCompare, an open source program, was used to compare each camera reconstruction with the CT data from which the model was derived. Next, imaging of a subject's nose were performed, and software measurements were compared with those directly measured using a micrometer. Results: Results have showed that 123D Catch accurately provided 3D nose and facial representations after mesh comparison with CloudCompare by merging and aligning point clouds of the 123D Catch and CT data. In addition, 123D Catch can clearly reconstruct both inanimate objects and facial attributes with excellent accuracy. Conclusion: 123D Catch can be used as an inexpensive, alternate method to 3D reconstruct the nose and facial features compared to commercial 3D programs.

Keywords: photogrammetry; surface scanning; 3D imaging;

Poster #: 61

Mobile health applications to improve self-management and adherence to anticoagulation therapy in older adults: A Pilot Study

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Background: Mobile health (mHealth) applications (apps) have been found to improve self-management in patients with chronic conditions, particularly children and adults. Older adults are a group that can potentially benefit from mHealth interventions. Purpose: The purpose of the study was to design and test the feasibility of Mobile Applications for Seniors to enhance Safe anticoagulation therapy (MASS). The MASS is a mobile-based health technology intervention, composed of several culturally appropriate and age-sensitive tools and components to promote independence and self-care in older adults on oral anticoagulant treatment. The specific aims were to assess changes from baseline to 3-months of adherence, attitude, quality of life, and satisfaction and to identify decrease in adverse outcomes (e.g., bleeding, thromboembolic events) and treatment efficacy. Methods: The study used a single-arm, experimental, pre-post design to assess the feasibility of a 12-week mHealth-based intervention using the MASS in older adults referred from UCIMC anticoagulation clinics. Results: The MASS app development (English and Spanish) was completed. The components of the MASS app include 1) education about anticoagulation therapies and safety tips, 2) medication self-monitoring and reminders, 3) vitamin K content of foods including common Hispanic foods, 4) monitoring of signs and symptoms of bleeding, 5) monitoring INR, 6) connecting with people whom older adults trust, and 7) resources. Currently 18 participants are enrolled and the recruitment has progressed. The results of this study including three month follow-ups will be presented at the conference. Conclusion: In light of the increasing incidence and prevalence of conditions requiring anticoagulation therapy, the results of the study may offer important information in the use of information technology alternatives to meet the rising need for self-management in increasing numbers of patients and patient care-givers.

Keywords: mobile health; health application; self-management; chronic diseases; anticoagulation therapy;

Poster #: 65

Risk of Contamination in Orthopaedic Surgical Instruments

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1) INTRODUCTION Wound infection following surgery is a devastating complication to both patients and society with adverse sequelae including worse clinical outcomes, prolonged pain, and higher costs. These infections can occur from a number of different sources of contamination, one being the surgical instruments used during the procedure. Because instruments are rarely designed to be completely disassembled prior to sterilization, the goal of this study is to compare the contamination level between disassembled and assembled surgical instruments. 2) METHODS Two spinal pedicle screwdrivers and two standard hip femoral component broach handles were modified so that they could be disassembled, and then contaminated with a tryptic soy broth (TSB) suspension containing on average 4.0 x 106 Geobacillus stearothermophilus organisms per milliliter. One instrument from each pair was then reassembled and the other instrument was kept in the disassembled state. The instruments were then steam sterilized, with five rounds of the experiment sterilized at 132°C for 40 minutes and the other five rounds sterilized at 132°C for 20 minutes. Following sterilization, the instruments were swabbed in five target locations for remaining bacteria or spores. The samples were then placed in 3.5 mL of TSB, incubated for seven days at 55°C and checked for growth by subculture on agar plates. 3) RESULTS Bacterial growth was detected from control samples of the TSB suspension during each round of the experiment. Eradication of vegetative bacteria and spore forms was achieved at all target locations in both the assembled and disassembled instruments following steam sterilization at 132°C for 40 minutes and at 132°C for 20 minutes. 4) DISCUSSION/CONCLUSION Our study demonstrates that adequate decontamination of the tested surgical instruments can be achieved following steam sterilization in either the disassembled or assembled state, and there is no increased rick of infection transmission.

Keywords: Surgical Instrumentation; Sterilization;

Poster #: 66

Using the Anatomical Axis as an Alternative to the Mechanical Axis to Assess Knee Alignment.

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The treatment of knee osteoarthritis, and the preparation for total knee arthroplasty requires repetitive imaging to guide preoperative planning and operative technique. Full-length standing AP images are the gold standard in assessing the alignment of the limb via the measurement of the mechanical axis of the knee. The anatomical axis can be obtained from a more limited image of the knee, and as such is less expensive, and exposes the patient to less ionizing radiation. The objective of this cross-sectional prospective study was to examine the extent to which the anatomical axis as measured on a fixed flexed PA (Rosenberg) view correlates with the mechanical axis. The data of 209 TKA radiographs were analyzed to compare the correlation between mechanical and anatomical axis pre-operatively. The anatomical axis correlated with the mechanical axis when it was measured from both the standing full-length AP film as well as from a fixed flexed PA film. Using an angle of offset found from linear regression, these correlations become closer. Body mass index and Kellgren-Lawrence grade were not found to have a significant effect. It is the conclusion of this study that the anatomical axis, as measured from a limited knee film, may serve as a plausible estimate of the mechanical axis when done with a neutral angle of offset, and that offset angle depends on gender and the imaging technique used to determine the anatomical axis.

Keywords: Total joint arthroplasty; Anatomical knee alignment; Mechanical knee alignment; Varus deformity; Valgus deformity;

Poster #: 67

The Affordable Care Act: Disparities in Emergency Department Use for Mental Health Diagnoses In Young Adults

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Importance: Young adults have high levels of mental health needs but often lack health insurance. Recent health reforms have increased coverage, but it is unclear how this has affected psychiatric emergency department(ED) visits for various racial subgroups. Objective: In 2010, the Affordable Care Act(ACA) required insurers to permit children to remain on parental policies until age 26 as dependents. This study investigated the association between the dependent coverage provision and changes in young adults' usage of (ED) services for psychiatric diagnoses. Methods: Quasi-Experimental analysis of ED use in California from 2009-2011 encompassing 280,798 visits with a psychiatric diagnosis for individuals aged 19 to 31-years old. Analyses used a difference-in-differences approach comparing those targeted by the ACA dependent provision(19 to 25-year-olds) and those who were not(27 to 31-year-olds), evaluating changes in ED visit rates per 1,000 in California. Primary outcome measures included the quarterly ED visit rates with any psychiatric diagnosis, with subgroup analysis examining the effects of race(White, Black, Hispanic, Native American, Asian/Pacific Islander, Mixed/Other) and gender on the primary outcome. Results: Following the young adult dependent provision, psychiatric ED visits for 19 to 25-year-olds were 0.05 per 1,000 people($p<0.001$) fewer than for 27 to 31-year-olds. However, this significant reduction in psychiatric ED visits was not seen in males, Hispanics, Asians or Pacific Islanders. Furthermore, Hispanics, Asians, and Pacific Islanders were the only racial subgroups that did not see significant gains in the proportion of psychiatric ED visits covered by private insurance. Conclusions: The young adult dependent provision was associated with a modest reduction in ED use for psychiatric purposes, however racial disparities in the affect of this provision appear to exist for Hispanics, Asians and Pacific Islanders.

Keywords: Affordable Care Act; Young Adults; Emergency Department; Racial Disparities; Mental Health;

Poster #: 68

Discussing barriers to diabetes management behaviors with the doctor is associated with improved outcomes for patients with type 2 diabetes: analysis of audio recordings of medical visits

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BACKGROUND: Successful diabetes management requires consistent adherence to a set of behaviors including taking medications, blood sugar monitoring, exercise and healthy eating. Socioeconomically disadvantaged patients experience worse outcomes than more affluent patients because challenges in daily life often act as "contextual" barriers to these behaviors. OBJECTIVE: The current study examined whether discussing contextual barriers with the doctor leads to improved control of blood sugar (A1c), cholesterol (LDL) and systolic blood pressure (SBP). METHODS: Medical records and audio recordings of visits were obtained for a predominantly low-income sample of patients treated for type 2 diabetes at UC Irvine outpatient clinics between 2007-2013 (N=234) who consented to the Reducing Racial Disparities in Diabetes Coached Care study (R2D2C2). Medical records were examined to identify patients with a "red flag" outcome (RF; A1c>8%, LDL>100 mg/dl or SBP>140) that would indicate to the physician that the patient might be struggling to manage their diabetes. For patients with at least one RF, audio recordings of the medical visit were analyzed using a validated coding method to determine whether a specific contextual barrier was discussed and addressed with a "contextualized" plan of care (CPOC), tailored to help the patient overcome the barrier. The association between obtaining a CPOC and improvement in the RF outcome by the next regularly scheduled visit was assessed using Fisher's exact test. RESULTS: Of the 139 visits with at least one of the three RFs, a CPOC tied to a specific health behavior was discussed in 33 (24%) of them. 85% of patients who received a CPOC, compared to 62% of patients whose plan of care did not address a contextual barrier, showed improvement in the RF outcome (p= 0.019). CONCLUSION: Addressing contextual barriers to specific disease management behaviors during the medical visit may contribute to improved diabetes outcomes.

Keywords: medication adherence; diabetes; health behavior; doctor-patient communication; social determinants of health;

Poster #: 69

A Review of Transitional Care Programs for Vulnerable Populations

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Background: Transitioning from the hospital to the community is an anticipated yet stressful process. Ethnic minorities and socioeconomically disadvantaged individuals are especially vulnerable to poor health outcomes during transitions, placing them at higher risk of readmission. While there are many interventions in place to improve outcomes, these programs primarily target chronically ill older adults and are not specific to minorities or low socioeconomic status groups. In addition, hospitals serving low-income patients are about twice as likely to be penalized by the Centers for Medicare and Medicaid Services (CMS) for high hospital readmission rates compared with hospitals serving the fewest low-income patients. Purpose: Determine effective interventions to enhance care transitions in ethnic minorities and/or vulnerable populations with low socioeconomic status (low SES) in order to ultimately reduce health care costs, improve care quality, and increase patient satisfaction. Methods: A systematic literature search was conducted using the electronic databases PubMed, CINAHL, and Cochrane Library with key words 'transitional care,' 'minority,' 'continuity of care,' and 'Hispanics.' Results: Overall, the studies reviewed did not show statistically significant changes in hospital readmissions rates or emergency room usage after hospital discharge. However, the studies revealed an increase in primary care engagement, with one study showing an increase of patient engagement in their care plan. Conclusions/Implications: Many transitional care programs have been implemented to improve outcomes in older adults, however these programs have shown marginal effectiveness to reduce hospital readmission rates and improve health disparities in minorities and low-income groups. Further research should be considered to develop culturally tailored and patient-specific transitional care interventions, with a multi-faceted approach to evaluate the effectiveness of such programs.

Keywords: transitional care; minority; continuity of care; Hispanics;

Poster #: 70

Child and Parental Factors in Complementary and Alternative Medicine Use

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BACKGROUND There has been a growing focus on parental factors associated with Complementary and Alternative Medicine (CAM) use in children; the present study examined both child and parent factors, including parental perceptions of children's pain and child temperament, associated with frequency of CAM use in children with chronic illness. METHODS Parents of children ages 2 – 18 with chronic illness (N = 149) from CHOC Children's Hospital completed the Parental Pain Expression Perceptions (PPEP), Emotionality, Activity, and Sociability Temperament Survey (EAS-TS), and frequency of use from a list of 27 CAM therapies. RESULTS Negative binomial regression was used to examine the effect of pain perception (PPEP) and temperament (EAS-TS) on number of CAM therapies used. Results showed that parental misconceptions about active or loud pain expression in children (b = -.039, t(1) = 9.149, p = .002,) predicted the number of CAM therapies used, such that parents who reported more misconceptions about children's pain expression (e.g., that children always express pain through whining or crying) used more CAM therapies than parents who reported fewer misconceptions. Child temperament, including emotionality (b = .033, t(1) = 0.179, p = .672), and shyness (b = -.024, t(1) = 0.127, p = .721) did not predict CAM use, nor did parental misconceptions about quiet pain expressions (e.g., quiet children are not in pain) (b = .0.042, t(1) = 1.158, p = 0.282). CONCLUSION Results of the current investigation suggest parents who endorse more misconceptions about loud or active pain expressions may be more likely to use CAM therapies for children than parents with fewer misconceptions about pain expressions. Parental misconceptions of children's pain expression have been associated with giving fewer analgesics to children; therefore, it may be that parents who report these misconceptions are more likely to seek out non-pharmacological means of treating children's pain.

Keywords: Complementary and Alternative Medicine (CAM); Parental Pain Expression Perception; Child Temperament; Chronic Illness;

Poster #: 71

Differences in Personal Safety as a Concern and Policy Priority among Ethnically Diverse Older Adults

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Elder abuse is both an under-recognized and under-reported crime. To assess concern about elder abuse and neglect, the Orange County Aging Services Collaborative conducted a paper and online survey of senior living needs, using crime and personal safety as a proxy for elder abuse and neglect. Participants were asked to rate nine living needs and the importance of related policy priorities on a 5-point scale, ranging from 1 (very low) to 5 (very high). A total of 631 older adults, 60-plus, responded, including 372 English-speaking, 99 Spanish-speaking, and 116 Vietnamese-speaking individuals. Analyses examined differences in living needs and policy priorities by language of respondents, age (60-74, 75-84, and 85+), and gender using analyses of variance with multiple factors. Spanish speakers were significantly more concerned about safety (Mean + SD: 3.9 +1.3) than either English (3.1 + 1.3) or Vietnamese (3.3 + 1.2) speakers, who were comparably neutral. Along with Spanish speakers, English speakers rated the importance of personal safety as a policy priority significantly higher than their Vietnamese peers. Interestingly, those 85+ rated safety as a concern and policy priority as significantly less important than younger participants. No gender differences occurred in safety concerns; however, women rated all policy priorities as significantly more important than men. Additionally, Spanish speakers were generally more concerned about other living needs than any of their peers and, along with English speakers, wanted elected officials to do significantly more for them as they age than Vietnamese speakers. While it remains unclear whether any low personal safety ratings were due to a lack of knowledge about senior crime, results clearly indicate that service providers and policy makers ought to address the significant concerns about safety expressed by Spanish-speaking older adults participating in this survey.

Keywords: Personal safety; Elder abuse; Language; Living needs; Policy priorities;

Poster #: 72

Investigating Cost Variation within Spinal Fusion Payment Groups

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INTRODUCTION: Medicare reimbursement to hospitals is provided as a fixed payment for each admission based on Diagnosis Related Group (DRG). In 2005, a study of total joint arthroplasty (TJA) showed that variation within DRGs can cause differences between hospital costs and Medicare reimbursement, resulting in predictable financial losses to hospitals and hindering access to care for some patients. Following this study, Medicare separated DRG 209 (which previously included all TJA procedures) into primary and revision TJA DRGs to reduce cost variation, establishing an effective "benchmark" for excessive variation. This study investigates the cost variation within spinal fusion DRGs. METHODS: Data were obtained from the Nationwide Inpatient Sample (2011). We analyzed all hospital costs for patients in spinal fusion DRGs (453-460) and TJA DRGs (466-470). Our primary outcome was the coefficient of variation (CV), defined as the ratio of the standard deviation (SD) to the mean (CV=SD/mean x 100), for all costs within a given DRG. CVs were compared to the established “benchmark” of TJA “DRG 209” (aggregate of primary and revision DRGs [466-470]) to determine if cost variation within current spinal fusion DRGs is “acceptable.” RESULTS: In 2011, mean costs for spinal fusions ranged from $27,153 (SD = $11,992) for DRG 460 to $77,965 (SD = $41,044) for DRG 456. CV in spinal fusion costs ranged from 44.2 (DRG 460) to 52.6 (DRG 456). In contrast, the mean cost for the TJA benchmark “DRG 209” was $15,903 (SD = $6,077) with a CV of 38.2. CONCLUSION: In this study, variations in cost within each spinal fusion DRG were found to be higher than in the established TJA benchmark. As in TJA, this variation may be leading to differences between costs and reimbursement that compromise access to care. Future studies should seek to identify drivers of cost variation to determine if changes can be made to further homogenize current payment groups and ensure equal access for all patients.

Keywords: Cost; Diagnosis-Related Groups; Spine;

Poster #: 73

Access to the Internet and Mobile Applications in a Mixed Population Emergency Department

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With society’s growing use and access to the internet and technological resources, physicians should work towards utilizing these valuable resources to advance patient education. Particularly in time sensitive areas like the emergency department (ED), patients are limited in the amount of care and information they receive. Although prior studies have measured the patients’ accessibility to the internet in other areas, it would be more accurate and relevant to sample our patient population at the UCI Medical Center ED to carry out changes that would most benefit our patient population. In order to better educate our patients and the community through these electronic resources, we must examine what percentage of our ED population has access to the internet and mobile devices. By surveying 241 of our patients who came into the ED at the UCI Medical Center, we were able to quantify that majority of both English and Spanish speaking patients had access to the internet and mobile devices. Although the patients varied in how comfortable they felt in utilizing the internet as another means of communication and obtaining education, this knowledge is certainly a starting point in our steps towards incorporating and advancing patient education within the ED.

Keywords: None

Poster #: 74

The EMPATHy Toolkit: Feasibility of a computer-based intervention to help patients with type 2 diabetes identify and articulate high-priority barriers to medication adherence to discuss with the doctor

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BACKGROUND: The full benefit of medication therapies is not realized in disadvantaged patients who exhibit high rates of medication nonadherence, but often have difficulty communicating concerns about their medications to the doctor. This project pilot tests a prototype software toolkit called “EMPATHy” to help patients identify the most important barriers to adherence that they face, and formulate a specific question about these high-priority barriers to discuss with the doctor. METHODS: EMPATHy was piloted in an ongoing intervention (Coached Care) in which lay community health workers meet with patients before a medical visit, and help them prepare a list of important questions for the doctor. A total of 46 low-income, Latino patients with poorly controlled type 2 diabetes were recruited and randomly assigned to complete either a single Coached Care visit incorporating the EMPATHy software (EMPATHy), or a Coached Care intervention visit with no software tools (comparison group). Prior to the visit, participants were asked to select the highest priority barrier (“biggest problem”) to taking medications from a list of commonly reported barriers. After the visit, they completed a short questionnaire about their experience with the intervention. RESULTS: Of the patients who used EMPATHy (N=23), 52% identified a different “highest priority” barrier using the software compared to what they selected in the pre-visit survey. 83%, compared to only 70% in the comparison group (N=23), strongly agreed that the coaching session focused on “very important issues”. 83% found the coaching session helpful, but only 71% found the activity on the iPad “easy to do”. CONCLUSIONS: The EMPATHy toolkit is feasible and acceptable to patients in a vulnerable population, and encourages discussion of a different array of high priority barriers compared to what patients raise without using the toolkit. Further efforts to improve ease-of-use of the toolkit are warranted.

Keywords: computer-based intervention; medication adherence; social determinants of health; doctor-patient communication;

Poster #: 75

Clinic in the Park: Using Public Space for Health

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BACKGROUND: Clinic in the Park is an innovative model to connect, screen, and educate families using public space for Health at a Farmers Market. The Collaborative is 40 nonprofit, academic, public and private organizations. METHODS: Tools to evaluate include passports tracking services rendered; counts of visitors (total per service station); and visitor and collaborator satisfaction/needs surveys. Measurable outcomes include: 1) number of families connected to health care and other services; 2) number of safety net screenings (e.g. vision, hearing, dental, BMI/dietitian consults, proper child safety seat); 3) health promotion tools provided (including booster seats, bicycle helmet fittings, developmental activities); 4) visitor and collaborator satisfaction. A pilot impact study was initiated. RESULTS: Over 2 years (2012-2014), 14,645 visitors received 26,438 services. Service examples include 3,705 connections to health insurance and public benefit programs; 803 dental services; 473 hearing screenings; 2,200 healthy eating chats/BMI; 3,151 early literacy and free books; 3,850 child safety tools/strategies; and many who simply wanted to “chat” with our doctors/health professionals. The Farm Adventure tour with fresh produce and physical activities are new and popular features. Pilot impact study revealed that 97% (n=30) found the Clinic useful and relevant, yet 90% of children had health insurance. CONCLUSIONS: Using public space for health connects families to resources. Families also chat with doctors and other health professionals in a relaxed environment without the time constraints of a medical office. The Clinic is component of a family-centered medical home (www.medicalhomeinfo.org).

Keywords: medical home; public space for health;

Poster #: 76

Improved Glycemic Control Using Telemedicine Interface

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Annually, 1.7 million people are newly diagnosed with diabetes in the U.S. and expenditure is on the rise to the tune of $245 million in 2012. Inefficient health systems and poor diabetic management will hasten neuropathic disease progression in patients. Health care providers can electronically communicate with patients using telemedicine to improve access of care, exchange information, reduce cost, and increase empowerment and patient satisfaction. Telemedicine is health information technology that uses text, audio, and/or video functionality to allow patients to upload physiologic data, access disease education, and communicate with health care providers. A systematic review was conducted to analyze telemedicine-based diabetic self-management programs to improve diabetic related outcomes. Methods: PubMed and CINAHL were searched using the terms including self-management, chronic, disease, diabetes, telemedicine, and information technology. Search was filtered for adults, publication date in the last 10 years, and randomized controlled trials that evaluated glycemic control measured by hemoglobin A1C. Results: The telemedicine-based programs for diabetes care showed significant reductions in hemoglobin A1C in 6 months and also improvement in frequency of access to healthcare providers, self-management environment, and changes of the standard of diabetic care. Study participants demonstrated tighter glucose control when treatment and counseling fits their lifestyle and are at their discretion. Limitations of the studies are costs of intervention and patient satisfaction were not consistently evaluated. Conclusion: In the growing field of telemedicine, strategies to enhance self-management in patients with chronic diseases such as diabetes can be shifted to primary care using telemedicine components. Healthcare providers should understand which group of diabetes patients could get the potential benefits from the telemedicine approach.

Keywords: telemedicine; diabetes; healthcare; treatment; information technology;

Poster #: 79

Paraventricular Nucleus in Acupuncture's Inhibition of the Von Bezold Jarsich Reflex

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Electroacupuncture (EA) stimulates specific somatic sensory nerves underlying P5-6 acupoints and modulates parasympathoexcitatory reflex responses through actions in the brainstem. Although Bezold Jarisch-induced decreases in blood pressure and heart rate reflex responses are modulated by acupuncture through actions in nucleus tractus solitarius (NTS) and nucleus ambiguus, in the role of the hypothalamus is unclear. The paraventricular nucleus (PVN) projects to NTS and regulates sympathetic outflow and blood pressure. Vagal afferent stimulation activates neurons in the PVN but little is known about cardiopulmonary physiological actions in this nucleus. We therefore hypothesized that the PVN projecting to NTS participates in the Bezold Jarisch responses and EA modulation of parasympathoexcitatory cardiovascular responses through opioids. Endorphinergic fibers were juxtaposed to NTS projecting glutamatergic PVN neurons. The PVN-NTS glutamatergic neurons activated by PBG expressed c-Fos. Rats were anesthetized, ventilated, and heart rate and mean blood pressures were monitored. Application of phenylbiguanide (PBG) every 10 min close to the right atrium induced consistent depressor and bradycardia reflex responses. Unilateral microinjection of kainic acid or kynurenic acid in the PVN reduced the reflex responses. Thirty min of bilateral EA at P5-6 acupoints, overlying the median nerves, reduced the depressor and bradycardia responses for >60 min. Unilateral inhibition of the PVN with 50 nl of naloxone reversed EA-inhibition during repeated PBG-induced responses. Thus, cardiopulmonary PVN responses are important in processing acupuncture modulation of inhibitory cardiopulmonary reflexes.

Keywords: vasovagal syncope; hypothalamus-brainstem; acupuncture; opioids; sympathetic;

Poster #: 80

Towards a Scalable Biomimetic Antibacterial Coating

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INTRODUCTION The nanopillars on cicada wings are inherently antibacterial, irrespective of surface chemistry. Applying such antibacterial nanostructured coatings to medical devices could obviate chemical antibiotics. The hurdles we seek to overcome include fabrication in FDA-approved polymers and scale-up difficulties. FABRICATION We applied industrial nanostructuring techniques to generate cicada-wing like nanostructures on the surfaces of poly(methylmethacrylate) (PMMA). We replicated the nanopillars of a cicada wing utilizing a double imprinting process. Negative molds were cast in hard polydimethylsiloxane (hPDMS) to produce elastomeric stamps presenting large areas (diameter 15 mm) of nanoholes. Next, we utilized dropcasting and thermal imprinting to generate fields of PMMA pillars. Films were characterized using scanning electron microscopy (SEM) and atomic force microscopy (AFM). To make the nanopatterning technique more industrially viable and generate larger patterned areas, we utilized nanoimprint lithography. A commercially available antireflective stamp (Holotools, Germany) with a nanopillared pattern similar to that of the cicada's wing was used to imprint large, flat, nanostructured polymer thin films. BACTERIA EXPERIMENTS Bacteria incubated on pillared films were deflated, as observed under SEM and atomic force microscopy (AFM). In contaminated aqueous environments, nanopillared surfaces 1) killed surface-adherent E. coli, as determined by a standard fluorescence based viability assay (Baclight, Invitrogen); and 2) decreased bacterial load in the aqueous environment, as evidenced by a decrease in colony forming units in suspension over time (up to 24 hours) when compared with flat controls. Our surfaces could be used for a wide variety of environmental and medical applications, including surgical trays / instruments and implantable medical devices or catheter tubes.

Keywords: Biomimetic; Antibacterial; Biocompatibility; Micro / Nanofabrication; Polymers;

Poster #: 81

Controlling Cell Adhesion on Device Surfaces by Nanotopography

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The ability to control cell adhesion on material surfaces is critical for biointegration of implants. Of particular interest to our research is developing an understanding of what the role surface topography plays in cell adhesion. This could lead to simple, durable ways to engineer surfaces without having to chemically modify the surface of materials used for implants. Hu et al. showed that nanopillars of varying aspect ratios and surface energies had strong effects on cell morphology, discouraging cell spreading. Our group discovered that human embryonic stem cells grown on nanopillar structures had a significantly reduced number of focal adhesions per cell and concordantly exhibit increased cell motility on the nanopillars (Kong et al. 2013). Based on these findings, we hypothesized that the pillar nanostructures would prevent cells from adhering. We created a library of nanopillars of different spacing on polymethylmethacrylate (PMMA) films by nanoimprint lithography using commercially available silicon and nickel molds. Nanopillars were characterized with scanning electron microscopy. To evaluate cell adhesion, we counted the number of fibroblasts adhering to flat PMMA, nanolines and the nanopillars and examined cell morphology on each pattern. We also examined the focal adhesion sites using fibroblasts transfected with GFP-tagged paxillin, a major protein the focal adhesion complex. After 24 hours, we observed that the cells adopted different cell morphologies, possibly indicating changes in adhesion dynamics. Fibroblasts showed a spread, spindle morphology on the flat film while the cells on pillars were smaller and more equiaxed. Preliminary results show cells on pillars had smaller focal adhesions than cells on flat PMMA. Our study has shown that nanopatterns in the 100-500 nm range do affect adhesion dynamics and modulate cell adhesion. This may provide researchers a useful means of controlling how cells adhere on implant surfaces.

Keywords: biomaterials; adhesion; nanotopography;

Poster #: 82

Evaluating Quality Of Life in Meniere's Disease Treated as Migraine

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Objective: To evaluate quality of life in patients with Meniere's disease (MD) and measure outcomes of quality of life (QOL) after medical treatment. Methods: A retrospective review of prospectively obtained surveys was performed on patients with definite MD who presented from January 2013 to August 2013 to our tertiary care neurotology practice. Standardized questionnaires on quality of life were given to consecutive MD patients who were prescribed migraine prophylactic medications (mostly verapamil and/or nortriptyline). The Meniere's disease Outcomes Questionnaire (MDOQ) was used to determine QOL in 3 domains: physical, emotional and social aspects. The pre-treatment quality of life score (total score for pre-treatment items) was compared with the post-treatment quality of life scores. The main outcome measure was the change in quality of life score. Results: The MDOQ was given to patients with at least a 3 month follow up and 26 questionnaires were obtained. Overall the mean change in quality of life score was 25.13 (range, -3 to 55). There was a statistically significant difference between score before treatment and score after treatment (P-value = 0.02). Quality of life was improved in 92% of respondents, unchanged in 4% and poorer in 4% patients after medical treatment. Conclusions: Majority of MD patients responded to medications used for migraine and quality of life was improved in a vast majority of these patients. This study further supports the notion that there is significant overlap of MD and migraines. It is possible that symptoms of MD may be caused by a migraine etiology.

Keywords: Vestibular migraine; Meniere's disease; Quality of life;

Poster #: 83

Transcanal micro-osteotome technique for excision of exostoses

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Objectives. To evaluate the outcomes and complications of transcanal excision of exostoses using micro-osteotomes, without a post-auricular incision or the use of the drill. Study Design. A retrospective chart review of patients undergoing exostoses excision Setting. Tertiary Care Medical Center Subjects and Methods. All of the patients underwent surgical removal of the exostoses using only a 1 or 2 mm micro-osteotomes. Patients were followed postoperatively and associated complications were evaluated. Results. One-hundred-thirty-eight ears in 106 patients were treated for obstructive exostosis. The average age of patients was 43 ± 16 years. Of these, 99 were male (93%) and 7 were female (7%). A majority of the patients (84%, n= 89) had 90 to 100% obstruction of the ear canal. Complete ear canal healing was seen in 80% of patients by 3 weeks. All but one patient had healed by 6 weeks post-operatively. There were 9 (6.5%) slit tympanic membrane perforations that healed with intraoperative gelfoam or fascia myringoplasty. One patient had an anterior canal mobilization which required Xeroform packing for 3 weeks for stabilization. There were no postoperative vertigo, facial paresis, conductive/sensorineural hearing loss, soft tissue stenoses, and no skin grafting required. Conclusions. This is the first study to report a series of cases where solely a transcanal approach using micro-osteotomes for removing exostoses was performed. Results indicate that it is a safe procedure with low complication rate and expeditious healing. Patients with 100% obstruction can have this procedure performed with no significant increase in morbidity.

Keywords: External ear canal; Exostosis; surgical removal;

Poster #: 84

Loudness and Acoustic Parameters of Popular Children's Toys

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Purpose: This project was conducted to evaluate the loudness and acoustic parameters of toys designed for children. In addition, we investigated whether occluding the toys' speaker with tape would result in a significant loudness reduction; thereby potentially reducing the risk of noise induced hearing loss. Methods: Twenty-six toys were selected after an initial screening at two national retailers. Noise amplitudes at 0.25, 0.5, 1, 2, 4, and 8 kHz were measured using a digital sound level meter at a distance of 0 and 30 cm. The toys' speakers were then occluded using adhesive tape and the same acoustic parameters were re-measured. Results: Mean maximum noise amplitude of the toys at 0cm and 30cm was 1043. 9 dBA (range, 97 – 125 dBA) and 76.3 dBA (range 67-86 dBA), respectively. Mean maximum noise amplitude after occlusion at 0 cm and 30 cm distance was 87.988 dBA (range, 73-110dBA) and 66.0 dBA (range, 55-82 dBA), respectively, with a p-value <0.001. Conclusions: Proper use of most loudthe loudest toys with at a distant of 30cm between the speaker and the child's ear will likely not pose a risk of noise-induced hearing loss. However, since most toys are used at closer distances, use of adhesive tape is recommended as an effective modification to decrease the risk of hearing loss.

Keywords: Toys; Hearing loss; Noise induced hearing loss;

Poster #: 85

Phenotype and functional attributes of Herpes Simplex Virus specific CD8+ T cells in HSV-1 seropositive asymptomatic individuals

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A staggering number of individuals carry herpes simplex virus type 1 and/or type 2 (HSV-1/HSV-2). The majority of HSV infected individuals are asymptomatic (ASYMP), without any recurrent disease (cold sore, ocular and genital herpes), even though spontaneously reactivated virus shed in the body fluids (saliva, tears and vaginal secretions). However, small proportions of HSV-seropositive individuals are symptomatic (SYMP) and experience endless recurrences of herpes disease and often require continuous antiviral therapy. Objective of our study was to address why ASYMP individuals do not show any symptoms in spite of similar virus shedding among ASYMP and SYMP individuals. We used HSV-1 specific gB tetramers to determine the nature and frequency of memory CD8+ T cell subsets in the peripheral blood of HSV-seropositive ASYMP and SYMP individuals. Signs of recurrent disease in SYMP patients were defined as herpetic lid lesions, herpetic conjunctivitis, dendritic or geographic keratitis and stromal keratitis with one or more episodes per year for the past 2 years. We analyzed phenotype and functions of gB-specific CD8+ T cells from HLA-A*02:01 positive, HSV-1 seropositive individuals. We did not observe any difference in the frequency of gB-specific CD8+ T cells. However, ASYMP individuals maintained a significantly higher frequency of gB-specific effector memory CD8+ T cells (TEM) with multifunctional effector phenotype in terms of IFN-?, CD107a/b, granzyme B, granzyme K and perforin production as compared to SYMP individuals. We observed increased proliferation of gB-specific CD8+ T cells in ASYMP individuals. SYMP individuals had higher expression of PD-1 and Tim-3 than ASYMP individuals, which indicates an exhaustion phenotype of CD8+ T cells. Our findings provide an insight into the role of effector memory CD8+ T cells in mounting protection against reactivating herpes virus

Keywords: Herpes Simplex Virus; Effector Memory CD8+ T Cells; Symptomatic Herpes;

Poster #: 86

Effect of Plaque Removal Mechanism and Duration on Oral Biofilm

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Effect of Plaque Removal Mechanism and Duration on Oral Biofilm Objectives: Dental plaque contributes to oral and systemic health concerns, providing impetus for more effective approaches to oral hygiene. Goal of study was to identify the effects of plaque removal and re-accumulation of 1 min. vs. 2 min. brushing durations, and 2 different toothpaste formulations. Livionex Dental Gel (Livionex, Los Gatos, CA) is a novel formulation that eschews traditional abrasives, detergents, and anti-microbials. Colgate Total® (Colgate-Palmolive, New York, NY) was used as the control toothpaste. Methods: Ten subjects participated in this double-blinded, randomized, cross-over study. Volunteers brushed with a washout toothpaste (Tom's of Maine Whole Care Toothpaste, Kennebunk, ME) twice daily for 7 days. On the evening of Day 7 subjects used the assigned study dentifrice, either the treatment product or the control. Subjects then abstained from oral hygiene and food until their appointment the next morning. The next morning, subjects rinsed with GUM®Red-Cote®(Sunstar Americas,Inc., Chicago, IL) plaque disclosing solution, and intra-oral photographs were recorded. Subjects brushed with the same toothpaste as the previous night for 1 or 2 minutes and measurements and photographs were repeated. All subjects used both toothpastes and both cleaning durations with a 1-week washout between each of the 4 legs of the study. Photographs were analyzed using Image-J software to determine the new plaque surface area coverage. Results: Plaque accumulation and biofilm removal effects differed between the 2 dental gels that were tested. Moreover, 2 minutes of brushing duration removed more biofilm than 1 minute brushing regimen. Plaque levels differed significantly ($p<0.05$) between each brushing duration and each dentifrice used. Conclusion: Metal chelation may discourage plaque accumulation and support biofilm removal. Future studies are needed to expand on this pilot project.

Keywords: Biofilm; Gingivitis; Plaque; Metal Chelation; Dentifrice;

Poster #: 88

Rapamycin and Chloroquine: The In Vitro and In Vivo Effects of Autophagy-Modifying Drugs Show Unexpected Results in Valosin Containing Protein Multisystem Proteinopathy

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Mutations in the valosin containing protein (VCP) gene cause hereditary Inclusion body myopathy (hIBM) associated with Paget disease of bone (PDB), frontotemporal dementia (FTD), more recently termed multisystem proteinopathy (MSP). Affected individuals exhibit scapular winging and die from progressive muscle weakness, and cardiac and respiratory failure, typically in their 40s to 50s. Histologically, patients show the presence of rimmed vacuoles and TAR DNA-binding protein 43 (TDP-43)-positive large ubiquitinated inclusion bodies in the muscles. We have generated a VCPR155H/+ mouse model which recapitulates the disease phenotype and impaired autophagy typically observed in patients with VCP disease. Autophagy-modifying agents, such as rapamycin and chloroquine, at pharmacological doses have previously shown to alter the autophagic flux. Herein, we report results of administration of rapamycin, a specific inhibitor of the mechanistic target of rapamycin (mTOR) signaling pathway, and chloroquine, a lysosomal inhibitor which reverses autophagy by accumulating in lysosomes, responsible for blocking autophagy in 20-month old VCPR155H/+ mice. Rapamycin-treated mice demonstrated significant improvement in muscle performance, quadriceps histological analysis, and rescue of ubiquitin, and TDP-43 pathology and defective autophagy as indicated by decreased protein expression levels of LC3-I/II, p62/SQSTM1, optineurin and inhibiting the mTORC1 substrates. Conversely, chloroquine-treated VCPR155H/+ mice revealed progressive muscle weakness, cytoplasmic accumulation of TDP-43, ubiquitin-positive inclusion bodies and increased LC3-I/II, p62/SQSTM1, and optineurin expression levels. Our in vitro patient myoblasts studies treated with rapamycin demonstrated an overall improvement in the autophagy markers. Targeting the mTOR pathway ameliorates an increasing list of disorders, and these findings suggest that VCP disease may potentially be ameliorated by rapalogs.

Keywords: Rapamycin; Chloroquine; Autophagy; Valosin Containing Protein; Multisystem Proteinopathy;

Poster #: 89

Spectral domain optical coherence tomography analysis of the retina in a rat model: a comparison of transgenic immunodeficient retinal degenerate rat (SD-Foxn1 Tg(S334ter)3Lav) and rats with normal retina

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Retinal degeneration (RD) affects millions of people worldwide, and in vivo monitoring of the progression of this disorder is needed to aid the development of treatments for it, such as retinal sheet transplants. This study aims to show that RD worsens with age, and to demonstrate that Spectral Domain Optical Coherence Tomography (SD-OCT) can track the degeneration in a new immunodeficient RD rat model. Retinal cross-section SD-OCT scans (Bioptigen Envisu R2200 SDOIS) were obtained from rats (n=40) between P17-P77, using transgenic SD-Foxn1 Tg(S334ter)3Lav rats (=RD rats) as a model for retinal degeneration, and rats expressing human placental alkaline phosphatase (hPAP) as a normal retinal control group. Analysis was done using the Bioptigen analysis software InVivoVue Diver Release 2.0 (Bioptigen, Research Triangle Park, NC). Changes in the thickness of the total retina (TR), the outer retina (OR), and the inner nuclear layer (INL) were determined with respect to age. Using SigmaPlot 11.0 (Systat Software, Inc., San Jose, CA; Fisher-corrected multiple comparison tests), layer thicknesses were compared with age group and rat strain. P17 was the earliest age which retinas could be imaged. At P17, there was already a noticeable difference in TR and OR thickness between hPAP rats and RD rats. In hPAP rats, TR decreased with eye growth between P17-P77 by 10.4% (260µm to 233µm) whereas TR of RD rats decreased by 32.6% (133µm to 95µm). hPAP OR decreased with eye growth between P17-P77 by 6.5% (141µm to 132µm) whereas RD rat OR decreased by 28.8% (26µm to 20µm). hPAP INL decreased with eye growth between the ages of P17-P77 by 32.6% (38µm to 25µm) whereas RD rat INL decreased by 38.8% (34µm to 21µm). This study demonstrated that SD-OCT is a viable method of detecting and analyzing RD; and consequently, the status of the retina and any occurring changes can be monitored and analyzed over time in vivo. SD-OCT may be useful in the evaluation of treatments for RD.

Keywords: retinal degeneration; imaging methods; retina; optical coherence tomography;

Poster #: 90

Effect of Cyclic Loading due to Eye Blinking on the Permanent Elongation of Frontalis Suspension Slings

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Background: Frontalis suspension is a commonly performed surgical procedure to address severe blepharoptosis (droopy eyelid). It creates a linkage between the frontalis muscle and the tarsus of the upper eyelid allowing for a better eyelid position in primary gaze. Several surgical techniques and sling materials may be used in this procedure. However, one main common complication raised with frontalis suspension surgery is the reoccurrence of blepharoptosis that may be related to the choice of sling material. Noting that an average person blinks tens of thousands of times per day suggests that plastic (permanent) elongation may occur in the sling due to the cyclic loading effects caused by eye blinking. Objectives: To study the effect of cyclic loading on the most common slings used in frontalis suspension. Here, we are presenting the results of our preliminary studies on the sling materials—tissue (fascia lata) and alloplastic (silicone). Methods: A novel setup for evaluating the effect of cyclic loading was developed. Autogenous and banked fascia lata, and silicone rod (BD Visitec) slings were tested by this setup. Results: Under the conditions used in this study, 0.25 mm of plastic elongation occurred in silicone, banked fascia lata, and autogenous fascia lata respectively after 150K (±30K), 1.2M (±300K), and 1.9M (±350K) cycles. Discussion: Autogenous fascia lata is the most resistant to plastic elongation, followed by banked fascia lata, and silicone. In this study, 0.25 mm plastic elongation was used as a criterion for a proof of concept study and if the tests were run for more cycles—as in the new phase of our testing—elongation with more clinical relevance (~0.5mm) would have eventually occurred. Currently, an ongoing investigation is underway to evaluate the significance of these findings in clinical settings. The data collected in these studies are also being used to develop a novel sling that is resistant to plastic elongation.

Keywords: blepharoptosis; frontalis suspension; eye blinking; cyclic loading;

Poster #: 91

Multiple Linear Regression Model of Quantitative Volumetrics Reveal Abnormalities in the Inferior Lateral Ventricles, Amygdala, and Pallidum of Brain Injury Patients Compared to Normal Controls

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Until recently, imaging techniques did not have the ability to reliably delineate structural abnormalities in patients showing signs and symptoms of brain injury adding to the complication of differentiating between normal controls (NC) and brain injury patients (BI). However, advances in technology allow MRI-based brain volumetrics to suggest potential structural abnormalities that can be coupled with other clinical correlates resulting in a diagnosis. Using a multiple regression model controlling for age and gender, we looked to find any trends in the quantitative volumetrics of NC and BI. The study included 51 NC (31=males, 20=females, average age=49, standard deviation =14.5) and 55 BI (35=males, 20=females, average age=36.74, standard deviation=15.33). The prediction model along with the volumetric software program, NeuroQuant, isolated the specific brain regions in which the actual volume represented a statistically significant structural abnormality. We then looked at each brain region to see which ones are indicative of brain injury when statistically abnormal. The Left Inferior Lateral Ventricles showed the highest difference in percent of patients who show an abnormality 38.18% (BI) to 5.88% (NC), while the Left Amygdala and the Left Pallidum showed a difference of 10.91% (BI) to 1.96% (NC) and 10.91% (BI) to 3.92% respectively. The right side showed similar structural abnormalities: Inferior Lateral Ventricle 20.00% (BI) to 3.92% (NV), Amygdala 12.73% (BI) to 1.96% (NC), and the Pallidum 16.36% to 1.96%. The data also showed that abnormalities in cortical grey matter and Left Lateral Ventricles tend to lead to false positives. This study revealed that the three brain structures that seemed to show the most differentiation using this methodology were the Inferior Lateral Ventricles, Amygdala, and Pallidum. Future data collection and modeling can lead to structural models for specific brain injuries assisting the diagnostic physician to help BI.

Keywords: Brain Volumetrics; Quantitative Volumetrics; Brain Injury; Inferior Lateral Ventricles, Amygdala, and Pallidum;

Poster #: 92

Brain Anatomical Correlates of Child and Adult Symptoms in Attention-Deficit/Hyperactivity Disorder

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Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most frequently diagnosed neurodevelopmental disorders with a prevalence rate of approximately 5% in children and 2.5% in adults. Estimates suggest that 65% of children with ADHD continue to have problems in adulthood. The pathophysiology of ADHD includes a dysregulated modulation of cortical plasticity during brain development, resulting in an abnormal cortico-cortical connectivity that may persist into adulthood. Although some research supported this notion by showing abnormalities in the prefrontal cortex by being associated with ADHD symptoms in both children and adults with ADHD there are some changes in the association between brain circuitry and symptoms during adulthood. Most notably, many adults with ADHD show symptom improvements, but little is known if symptom improvements are associated with changes in structural brain anatomy. The purpose of the study was to address this gap in knowledge by analyzing structural and diffusion-weighted Magnetic Resonance Imaging data in 72 young adults (31 with ADHD and 41 controls) in relation to the diagnostic group and the number of self-reported childhood and adult symptoms. Voxel-wise linear regression models revealed significant associations between ADHD diagnosis and wide-spread changes to the maturation of white matter fiber bundles in the brain, leading to structural shape changes in secondary association areas of the middle and superior temporal gyrus, and fronto-basal portions of both frontal lobes. Structural MRI data and diffusion weighted data showed the strongest association with childhood ADHD symptoms. In adulthood, however, these associations weaken, most likely as a result of coping mechanisms. The findings suggest that ADHD diagnosis and symptoms are associated with structural brain abnormalities at an early age, which could aid in the development of brain imaging biomarkers for ADHD.

Keywords: White Matter; Diffusion Tensor Imaging; ADHD symptoms; Childhood; Adulthood;

Poster #: 94

The Effects of Nicotine on Incentive Motivation and Executive Function

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Nicotine may hijack the motivational system, which plays an important part in executive function. The present study was designed to examine the effects of cigarette smoking on incentive motivation and executive function in young adults with and without ADHD. A 2 group (ADHD versus no-ADHD) by 2 nicotine (smoking versus non-smoking) by 2 incentive motivation (monetary incentive versus no-incentive) crossover research design was used to measure performance on the Stroop Test, Stop Signal Reaction Task (SSRT), and the Wisconsin Card Sorting Test (WCST). These tests measure different aspects of executive function. It was hypothesized that smoking combined with monetary incentives improves performance on the Stroop Test, SSRT, and the WCST in smokers with ADHD but not in smokers without ADHD. Sixteen young adult smokers with ADHD (n=8) and without ADHD (n=8) participated in the study. All participants abstained from medication and drugs of abuse 12 hours prior to participation in the study. Results showed significant improvements on the Stroop Test in the incentive conditions compared to no-incentive conditions in smokers with ADHD ($t = 2.478$ $p = 0.042$). In contrast, smokers without ADHD showed a significant decline in Stroop performance between the non-smoking incentive and smoking no-incentive conditions ($t = -2.562$, $p = 0.037$). For the SSRT, smokers with ADHD showed a significant improvement between non-smoking incentive and smoking incentive conditions ($t = 2.836$, $p = 0.025$). Lastly, the WCST yielded no significant differences. These findings corroborate that nicotine highjacks the motivational system in individuals with executive function deficits, such as those with ADHD. Smoking cessation programs for individuals with ADHD need to focus on motivational strategies to replace the reinforcing effects of nicotine.

Keywords: Motivational System; Neuropsychological Functioning; Nicotine; ADHD;

Poster #: 95

The neurobehavioral effects of cigarette smoking in individuals with and without Attention-Deficit/Hyperactivity Disorder

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Previous research has shown that individuals with ADHD may self-medicate with nicotine, the main psychoactive and carcinogenic ingredient of tobacco smoke, to improve ADHD symptoms and cognitive performance. However, the underlying brain circuitry associated with nicotine-induced behavioral performance is unknown. The present study was designed to close this knowledge gap by analyzing the effects of smoking on brain activity during a cognitive challenge in smokers with and without ADHD using functional Magnetic Resonance Imaging (fMRI). Nonsmokers with and without ADHD were included to examine the effects of math on brain activity. Thirteen smokers with ADHD, 19 control smokers, 14 nonsmokers with ADHD, and 20 control nonsmokers were recruited for the study. All participants abstained from smoking, drugs, and alcohol use for 12 hours prior to the fMRI scan, which was verified with urinary and breath drug screens. Smokers had two separate scans – one after overnight abstinence from smoking (abstinence condition) and one immediately after the first cigarette of the day (smoking condition). Nonsmokers had one scan. Participants were instructed to solve mental arithmetic while in the scanner. Images were processed, analyzed, and FDR corrected with SPM8. Scanning was performed on a 3T scanner. The fMRI results showed activation in the superior frontal gyrus, lingual gyrus, and cingulate gyrus during the arithmetic task for all of the groups. In addition, math during the smoking condition activated the middle frontal gyrus in smokers with ADHD compared to control smokers. The findings support the notion of unique neurobehavioral effect of smoking in individuals with ADHD that is not present in individuals without ADHD. Such neurobehavioral effect may be a biomarker for susceptibility to nicotine and increased cancer risk in individuals with ADHD.

Keywords: drug abuse; brain circuitry; executive function; fMRI;

Poster #: 96

Antitumor effects of the novel proteasome inhibitor, Marizomib (NPI-0052), in malignant gliomas: ability to cross the blood brain barrier in animal models

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Background: Previous studies have shown that proteasome inhibition can be used as a strategy for treating malignant gliomas. Marizomib is a second generation irreversible proteasome inhibitor which has a more lipophilic structure, suggestive of potential for penetration of the blood brain barrier (BBB), and has a broader and more prolonged inhibition proteasome inhibition profile than bortezomib and carfilzomib, the two proteasome inhibitors approved for treatment of multiple myeloma. While bortezomib and carfilzomib have little-no activity against malignant gliomas, marizomib could be a novel therapeutic strategy for primary brain tumors. Marizomib is presently in clinical trial for multiple myeloma. Methods: The in vitro antitumor activity of marizomib was studied in human glioma lines U251 and D54. The ability of marizomib to cross the BBB and regulate proteasome activities was evaluated in cynomolgus monkeys and rats. The anti-tumor effect of marizomib in vivo was tested in an orthotopic xenograft model of human GBM. Results: Marizomib inhibited survival of U251 and D54 by ~90% at 60nM and markedly decreased GBM cell migration and invasion. While marizomib induced increased free radical production and apoptosis, the reactive oxygen species quenching agent NAC blocked these effects. In rats, marizomib distributed into the brain at 30% of blood levels, and the monkey studies revealed robust baseline chymotrypsin-like (CT-L) proteasome activity in brain tissue that was significantly inhibited (>30%) in animals treated with marizomib. Similar effects were seen against the caspase-like activity. Encouragingly, mice treated with marizomib survived significantly longer than the control animals ($p<0.05$). Conclusion: These preclinical studies demonstrate that marizomib can cross the BBB and inhibit proteasome activity in primate brain, and elicit a significant anti-tumor effect in a rodent intracranial model of malignant gliomas.

Keywords: malignant glioma; marizomib; proteasome inhibition; blood brain barrier; chymotrypsin-like;

Poster #: 97

Microvascular Function in Related to Short-term Exposure to Ambient Air Pollution and Particle Components in an Elderly Cohort Study

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Rationale: Positive associations between exposure to traffic-related air pollutants (TRAP) and cardiovascular morbidity may be mediated by adverse vascular responses characterized by reduced endothelium-mediated vasodilation and vasoconstriction. Methods: We conducted a cohort panel study with repeated measures in 93 non-smoking elderly subjects living in the Los Angeles air basin, who were monitored with =12 weekly follow-ups from 2012 to 2014. Daily ambient (regional) exposures including PM2.5, black carbon (BC), CO, NOX, and O3 were measured at regional air monitoring stations on the preceding 7 days of clinic follow-ups. Seven-day average personal exposures to NOX and 5-day average particle components in ultrafine, accumulation and coarse modes were measured. Microvascular function was measured with forearm blood flow dilatation response to brachial artery occlusion using a noninvasive plethysmograph (EndoPAT 2000) yielding the reactive hyperemia index (RHI). A linear mixed-effects model was used to analyze relations of air pollutants to RHI, adjusted for heat index and other potential confounders. Potential effect modification by personal NOX concentrations was explored. Results: We found that ambient TRAP (BC, CO, and NOX) have stronger inverse associations with RHI than PM2.5 and O3. An interquartile range change in 5-day average BC was associated with an RHI decrease of -0.15 (95% CI:-0.22, -0.07). For PM components, the most significant inverse associations were found for accumulation mode element carbon and reactive oxygen species. No significant effect modification at a nominal $p < 0.1$ by personal NOX was observed except for 3-day moving average CO exposure. However, the results suggested that subjects may be more susceptible to ambient TRAP exposure when personal NOX exposure concentration is higher. Conclusion: Exposure to TRAP are associated with microvascular dysfunction in elderly cohort and personal NOX concentrations may modify associations.

Keywords: Microvascular function; Air pollution; Personal exposure; Short-term; Cardiovascular disease;

Poster #: 98

Changes in the orexinergic pathway are linked to post-cardiac arrest coma recovery

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Cardiac arrest (CA) affects over half a million people annually, with 80-90% of survivors suffering from a comatose state. The mechanisms of coma and consciousness are nebulous and undefined. Orexin, a hypothalamic stimulatory neuropeptide, has recently been linked to arousal in a variety of brain injury states associated with coma. We have previously shown that administration of orexin to rats improves post-CA coma arousal. Here, we investigated the spatiotemporal dynamics of the orexinergic system during the post-CA recovery period in a rodent model. After implantation of electrodes to record electroencephalography (EEG), rats underwent controlled asphyxial CA, followed by cardiopulmonary resuscitation (CPR) until return of spontaneous circulation (ROSC). After ROSC, rats gradually recovered from their comatose state while serial EEG recordings and behavioral coma assessments (Neurologic Deficit Scores; NDS) were conducted to track coma recovery. Rats were euthanized at 2, 4, 24, 72 hrs and 13 days post-ROSC. Brain samples were collected at these time points and subjected to immunohistochemical (IHC) analysis to investigate the orexinergic pathway. EEG and NDS demonstrated significant coma levels at 2hrs post-ROSC, gradually recovering thereafter. IHC analysis displayed significant dynamics in the orexinergic pathway at the various coma levels. The number of hypothalamic neurons expressing orexin-A peptide in the lateral hypothalamus declined at the deepest coma levels (2 and 4hrs) but increased significantly at 24hrs when compared to a control peptide (melanin-concentrating hormone). Significant reductions in the intensity of neuronal orexin-A expression suggest ties between neuronal expression of orexin-A and post-CA arousal level. Finally, compensatory upregulation of orexin-1 and 2 receptor expression was found in cortical neuron cell bodies during the deepest coma levels.These results show a close link between the orexinergic pathway and post-CA coma recovery. Along with our prior data showing that orexin-A administration improves post-CA coma recovery, these findings support an important role for orexin in coma recovery. Further investigation is needed to elucidate whether the orexinergic pathway may be a potential therapeutic target for humans suffering from coma.

Keywords: Coma, Cardiac Arrest, Orexin, EEG

Poster #: 99

ROBOTIC-ASSISTED COLORECTAL SURGERY IN THE UNITED STATES: AN UPDATED ANALYSIS OF NATIONWIDE TRENDS AND OUTCOMES

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Importance: Robotic-assisted colorectal surgery (RACS) is becoming increasingly popular, yet data comparing its outcomes remains limited. Objective: Identify trends and outcomes of RACS nationwide and then compare them to the more established technique of Laparoscopic-assisted colorectal surgery (LACS). Design, Setting and Participants: Nationwide Inpatient Sample (NIS) database was used to retrospectively identify all patients that underwent RACS and LACS for cancer, benign and diverticular disease over the period of 2009-2012. Trends in different hospital settings and indications were analyzed. Multivariate logistic regression was used to compare postoperative outcomes. Main Outcome Measures: Trends and postoperative outcomes of RACS vs. LACS. Results: An estimated 281,877 colorectal procedures were preformed through 2009-2012 using minimally invasive techniques, with RACS accounting for 5% of cases. RACS progressively increased in frequency in all hospital settings with the majority of cases being done in large, urban and teaching hospitals. Diverticulitis was the most common indication for RACS by 2012. On multivariate analysis RACS was associated with shorter LOS (Rectal:-0.72, 95%CI -1.04to-0.40, Colonic: -0.36, CI95% -0.56to-0.16); lower anastomotic leak (Rectal: AOR=0.6, P=0.0078, Colonic: AOR=0.65, P=0.0078); lower conversion (Rectal: AOR=0.07, P<0.00001, Colonic: AOR=0.36, P<0.00001); lower ileus/bowel obstruction (Rectal: AOR=0.74, P=0.0082, Colonic: AOR=0.86, P=0.0082); higher hospital charges (Rectal: $10623.47, 95%CI 6562.04-14684.90, Colonic: $12114.34, 95%CI 9667.60-14561.09) compared to LACS. No significant differences were found in overall mortality, morbidity and post-operative bleeding.?? Conclusions: Use of RACS is limited but increasing nationwide. RACS is associated with higher hospital charges but lower anastomotic leak, conversion rate, LOS and postop ileus/bowel obstruction compared to LACS.

Keywords: Robotic; Laparoscopic; colorectal; surgery; NIS;

Poster #: 100

A Novel Method for 3D Reconstruction on Airway Using Endoscopic Images

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Intro Airway obstruction is a common pathological condition that can be found in all age groups. With its ease of accessibility, endoscopy is a standardized yet subjective method that aids physicians in diagnosing airway obstruction. While programs that allow 3D reconstruction of outer geometry are wildly available on the market, building 3D models from within is less developed. Objectives The objective of this study is to describe a method that reconstructs endoscopic airway footage in 3D to objectively measure quantitative information. Methods The combination of three software packages—MATLAB, VisualSFM, and MeshLab—enables 3D reconstruction of an object from video of endoscopic images of a structure. The recorded video was segmented into images using MATLAB. The image set was imported into VIsualSFM, which computed a sparse reconstruction using structure from motion algorithm and then a dense reconstruction via clustering views for multi-view stereo algorithm. With the reconstructed output, a point cloud, MeshLab was used to generate a mesh by Poisson reconstruction and applied texture to the final model. To validate the accuracy of the 3D model, a clay model of the oral cavity was constructed and video recorded using a 2-megapixels endoscope (DBpower, TD HD) at 30 fps and 720p. The volumes from the physical and computed models were compared. Results For the clay model, the distance between the maxillary central incisor and the mandibular central incisor was 93.0mm, and the volume was 347.0ml. For the computed 3D model, Netfabb was used to analyze the distance (5.17 unit) and the volume (59.2203 unit3). The scaled volume from the computed 3D model was 344.6ml, which yielded 0.692% error. Conclusion The result showed less than 0.7% difference between physically measured and computed volumes. The proposed method has the potential to provide a low-cost, minimally invasive, and accurate means to reconstruct airway anatomy from endoscopic video footage.

Keywords: Airway; 3D Reconstruction; Structure from Motion; Endoscopy; Multi-View Stereo;

Poster #: 102

Phenotypical Analysis of Stromal Vascular Fraction After Various Mechanical Stress: Seeking the Optimal Regenerative Mix

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Introduction: Fat grafting is a commonly used plastic surgery technique and its optimization is gaining attention in the field of regenerative medicine. “Nanofat grafting,” This technique implements mechanical emulsification and injection of standard lipoaspirate (LA) for cosmetic purposes (1). Despite good clinical results and the ability to produce adipose-derived stem cells (ADSCs) from nanofat, the regenerative components of the stromal vascular fraction (SVF) generated from this technique have yet to be defined. Methods: LA was obtained from patients undergoing routine procedures. Samples were divided into 50 ml aliquots and mechanically processed using a blender (n=2), nanofat technique (n=6), or left unprocessed (control n=6). Each group was then subjected to collagenase, red blood cell lysis and the resulting SVF pellets were evaluated with a fluorescence antibody panel. The SVF and subsequent cultured cells were analyzed for viability (absolute cell count) and surface markers at Time 0, Passages 0 (P0) and 1 (P1). Results: Compared to standard LA, nanofat-processed SVF yielded a significantly higher proportion of CD34+ cells (5.09% vs 14.3%, p=0.003) as well as mesenchymal markers CD13 (2.58% vs 8.81%, p=0.002), CD73 (4.14% vs 10.0%, p=0.043) and CD146 (5.33% vs 10.5%, p=0.040). CD34+ abundance persisted for two passages (P0 - 40.0% ± 36.6 vs 49.1% ± 15.0, P1 - 2.14% ± 1.24 vs 4.87% ± 2.85). Nanofat processing of LA resulted in a significantly reduced proportion of viable cells (48%) compared to blender (81.55%) and control (82%) groups (p=0.004). Blender-treated LA demonstrated severely retarded growth and was therefore not evaluated at subsequent passages. Conclusions: Nanofat results in fewer viable cells, but increased progenitor/stem cell activity when compared to blender-processed and control LA. Further research is needed to elucidate the underlying pathways of this apparent mechanically induced transdifferentiation.

Keywords: Nanofat; CD34; Regenerative Mix; Lipoaspirate; SVF;