with the development of MetS and identifiable endothelial dysfunction in a cohort of Hispanic pre-pubertal children. To do so we propose the following aims: (1) To measure expression of adiponectin and leptin levels in a Hispanic pre-pubertal cohort and determine their correlation with features of the MetS. (2) To perform proteomic analysis in a Hispanic pre-pubertal cohort. (3) Evaluate early onset of endothelial dysfunction and its correlation with expression of adiponectin and leptin levels in a Hispanic pre-pubertal cohort. METHODS/STUDY POPULATION: A cross-sectional pilot study will obtain a random representative sampling of children aged 6–12 years from all geographical areas of Puerto Rico. Children will be assessed regarding pre-pubertal status through Tanner staging and later divided into pre-MetS Versus MetS groups as well as controls. MetS will include children meeting 3 or more of the current International Diabetes Federation (IDF) criteria. Pre-MetS will include children with at least 1 criterion for MetS. Anthropometric data, blood pressure readings, ultrasound-based noninvasive testing for endothelial dysfunction, and laboratory assays will be performed to the study population and data analyzed for correlation. Total adiponectin and leptin levels will be measured using a commercially available quantitative sandwich enzyme-linked immunoassay test. The study will be submitted to the University of Puerto Rico Medical Sciences Campus' Institutional Review Board (IRB) for approval. Written consent and assent will be obtained from parents and children respectively to ensure patient anonymity. RESULTS/ANTICIPATED RESULTS: We hypothesize that low levels of adiponectin and high levels of leptin will correlate with features of the MetS as defined by the IDF consensus statement, as well as with clinical features of MetS in undiagnosed Hispanic pre-pubertal youth. We also hypothesize that non-invasive testing of endothelial function will correlate both with clinical features of the MetS and with low levels of adinopectin and high levels of leptin. DISCUSSION/SIGNIFICANCE OF IMPACT: The correlation of findings suggestive of endothelial dysfunction and biomarker expression (mainly adiponectin and leptin levels) in a pre-pubertal cohort has yet to be established and could also provide information regarding early atherogenesis in otherwise unidentified youth at risk. Therefore, by using a proteomic approach, this study aims to measure associations between clinical features of the MetS and expression of proteins associated with an adverse cardiometabolic profile in a Hispanic pre-pubertal population. We will concurrently measure the degree of endothelial dysfunction and evaluate whether a correlation exists between previously mentioned protein expression and early onset of dysfunction.

2121

Quantitative structural knee measurements improve classification of accelerated knee osteoarthritis: Data from the osteoarthritis initiative

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OBJECTIVES/SPECIFIC AIMS: The aim of this study is to determine whether quantitative measures of knee structures including effusion, bone marrow lesions, cartilage, and meniscal damage can improve upon an existing model of demographic and clinical characteristics to classify accelerated knee osteoarthritis (AKOA). METHODS/STUDY POPULATION: We conducted a case-control study using data from baseline and four annual follow-up visits from the osteoarthritis initiative. Participants had no radiographic knee osteoarthritis (KOA) at baseline. AKOA is defined as progressing from no KOA to advance-stage KOA in at least 1 knee within 48 months. AKOA knees were matched 1:1 based on sex to (1) participants who did not develop KOA within 48 months and (2) participants who developed KOA but not AKOA. Analyses were person based. Classification and regression tree analysis was used to determine the important variables and percent of variance explained. RESULTS/ANTICIPATED RESULTS: A previous classification and regression tree analysis found that age, BMI, serum glucose, and femorotibial angle explained 31% of the variability between those who did and did not develop AKOA. Including structural measurements as candidate variables yielded a model that included effusion, BMI, serum glucose, cruciate ligament degeneration and coronal slope and explained 39% of the variability. DISCUSSION/SIGNIFICANCE OF IMPACT: Knee structural measurements improve classification of participants who developed AKOA Versus those who did not. Further research is needed to better classify patients at risk for AKOA.

2267

Radiofrequency renal denervation attenuates kidney fibrosis in spontaneously hypertensive rats

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OBJECTIVES/SPECIFIC AIMS: The goal of this study was to investigate whether RF-RDN attenuates renal fibrosis and inflammation in SHR with established hypertension. METHODS/STUDY POPULATION: Twenty-two-week-old SHR received bilateral RF-RDN or Sham-RDN (Biosense Webster Stockert 70 generator and RF-probe). Four weeks later, SHR were sacrificed and paraffin sections of kidneys were stained for fibrosis by Masson's trichrome staining. Kidney tissue were homogenized for measurement of cytokines levels by ELISA. RESULTS/ANTICIPATED RESULTS: The results showed that Sham-RDN treated SHR had extensive fibrosis as demonstrated by moderate thickening of Bowman's capsule, collagen deposition in glomerulus, extensive tubulointerstitial fibrosis, and segmental glomerulosclerosis. In contrast, RF-RDN significantly reduced each of these pathological components of fibrosis in kidney cortex and medulla as compared with Sham-RDN treated kidneys. In other studies, RF-RDN decreased B cells, CD4+ T cells, and CD8+ T cells in the kidney of SHR as measured by flow cytometry. Meanwhile, kidney tissue levels of IL-17, INF-γ, MIP-3a, TNF-α, and TGF-β were decreased as compared with respective levels in Sham-RDN. DISCUSSION/SIGNIFICANCE OF IMPACT: Together, these findings demonstrate that removal of the influence of heightened renal sympathetic activity by RF-RDN decreases kidney inflammatory markers and attenuates renal fibrosis in hypertensive SHR.

2064

Regulation of retinal protein O-GlcNAcylation by angiotensin-(1-7) and cAMP

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OBJECTIVES/SPECIFIC AIMS: Increased retinal protein O-GlcNAcylation occurs in response to hyperglycemia and contributes to diabetic retinopathy. Renin-angiotensin system (RAS) blockers reduce the incidence of diabetic retinopathy. Beneficial effects of RAS blockers are often attributed to production of angiotensin-(1-7) (Ang1-7). The objective here is to determine the impact of Ang1-7 on retinal protein O-GlcNAcylation. METHODS/STUDY POPULATION: C57/BL6 mice were fed a high-fat diet for 8 weeks and then treated for 3 weeks with either a vehicle control, the RAS blocker captopril, or captopril and the Ang1-7 receptor antagonist A779. R28 cells were used to assess levels of O-GlcNAcylated proteins in response to Ang1-7, and the role of cAMP was investigated with addition of forskolin, 6-Bnz-cAMP-AM, and 8-pCPT-2-O-Me-cAMP-AM to cell culture medium. RESULTS/ANTICIPATED RESULTS: Captopril attenuated retinal protein O-GlcNAcylation in mice fed a high-fat diet. This effect was reversed by A779. Ang1-7 attenuated protein O-GlcNAcylation and increased cAMP levels. Forskolin and the EPAC selective cAMP analog 8-pCPT-2-O-Me-cAMP-AM, but not the PKA selective cAMP analog 6-Bnz-cAMP-AM, attenuated O-GlcNAcylation. Inhibiting EPAC blocked the effect of forskolin, whereas inhibiting PKA did not. DISCUSSION/SIGNIFICANCE OF IMPACT: This study demonstrates a novel role for Ang1-7 in the retina and identifies a potential EPAC-dependent mechanism that regulates protein O-GlcNAcylation. Thus, future therapeutics targeted at an Ang1-7/EPAC axis in retina may be used to address DR.

2023

Relationship power imbalance and history of male partner HIV testing among pregnant women in central Uganda

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OBJECTIVES/SPECIFIC AIMS: We investigated the association between relationship power imbalance (which can have a negative impact on HIV prevention) and male partner HIV testing, using baseline data from a HIV self-testing trial in 3 antenatal clinics in central Uganda. METHODS/STUDY POPULATION: Pregnant women with HIV-male partners were recruited and randomized by day into standard of care or intervention (HIV self-testing kits). Analyses were performed in SAS 9.4, with χ^2 tests and $p < 0.05$ for significance. RESULTS/ANTICIPATED RESULTS: In total, 1514 women were recruited (737 standard of care, 777 intervention). Overall, 39.6% of male partners had previously tested for HIV. Among women <26, contributions to expenses differed by partner testing (overall $p < 0.001$, 47.6% of women whose partners tested made no contribution vs. 63.2% of women whose partners did not test). Relationship status differed by partner testing (overall $p = 0.02$, 12.4% of women whose partners tested showed a sometimes difficult relationship vs. 5.7% of women whose partners did not test). Among women 26 +, decision making for family visits differed by partner testing (overall $p = 0.005$, 52.9% of women made joint decisions with partners who tested vs. 36.5% whose partners did not test). DISCUSSION/SIGNIFICANCE OF IMPACT: Higher relationship power balance was associated with higher HIV testing among male partners when measured by contribution to expenses and decision making for family visits, but not relationship status. Relationship power balance should be considered when counseling women and men to increase HIV testing.

2482

Reward-based learning as a function of the severity of substance abuse risk in drug-naïve youth

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OBJECTIVES/SPECIFIC AIMS: Deficits in reward-based learning have been shown in youth at risk for developing substance use disorders (SUD). Here, we investigated whether computational models can be used to more precisely delineate the additive effects of such risk loading (i.e., the comparison between youth with ADHD, and those with ADHD and familial SUD) on reward-based learning in youth. METHODS/STUDY POPULATION: In total, 41 drug-naïve youth, stratified into 3 groups based on ADHD diagnosis and parental SUD: healthy controls (HC, n = 13; neither ADHD nor parental SUD), low risk (LR, n = 13; ADHD only), and high risk (HR, n = 15; both ADHD and parental SUD), performed a reward task. Learning rates, prediction and congruence *t*-scores were computed using a reinforcement learning model and analyzed via a multivariate ANOVA. RESULTS/ANTICIPATED RESULTS: The analyses showed a significant linear effect in task accuracy, which decreased with increasing risk profiles. Analyses of the model-derived variables also showed similar significant linear effects in learning rates and the congruence *t*-score, but not in the prediction *t*-score. These effects were primarily driven by significantly higher learning rate and congruence *t*-score in HC compared with HR youth. DISCUSSION/SIGNIFICANCE OF IMPACT: These results show most profound deficits in reward-learning in HR youth. These findings also show that computational analyses can offer added value over conventional behavioral analyses by more precisely evaluating group differences in relation to SUD risk.

2173

RNA-nanoparticles to enhance and track dendritic cell migration

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OBJECTIVES/SPECIFIC AIMS: Despite aggressive chemotherapy, surgical resection, and radiation therapy, glioblastoma remains almost universally fatal. In a pilot, randomized, and blinded clinical trial, we recently demonstrated that administration of RNA-loaded DC vaccines was associated with significantly improved progression-free and overall survival in patients with glioblastoma (Mitchell *et al.*, *Nature*, 2015). Furthermore, clinical outcomes correlated with DC migration to vaccine-site draining lymph nodes measured by Indium-111 labeling of RNA-loaded DCs and SPECT/CT imaging. Although these studies demonstrated that tracking DC migration may be an important clinical biomarker for response to DC vaccination, the complexity and regulatory requirements associated with nuclear labelling to track DC migration limits widespread application of this technique. We have therefore developed RNA-loaded magnetic nanoparticles (RNA-NPs) to enhance DC migration to LNs and track that migration with a widely available imaging modality (i.e., MRI). METHODS/STUDY POPULATION: Cationic liposomes were loaded with iron oxide nanoparticles with or without cholesterol. The resulting nanoparticles were complexed with RNA and used to transfect DCs ex vivo. RNA-NP-loaded DsRed + DCs were then injected intradermally into mice and tracked noninvasively with T2-weighted 11T MRI before excision and quantification with flow cytometry. RESULTS/ANTICIPATED RESULTS: In vitro experiments demonstrate that iron oxide loading does not reduce RNA-NP-mediated transfection of DCs. Additionally, replacement of cationic lipids with cholesterol increased RNA-NP transfection of the DC2.4 cell line and enhanced the T cell stimulatory capacity of treated bone marrow-derived dendritic cells (BMDCs). Compared to electroporation, RNA-NPs enhanced DC migration to lymph nodes and reduced T2 MRI intensity in DC-bearing lymph nodes. DISCUSSION/SIGNIFICANCE OF IMPACT: This data suggests that iron oxide-loaded RNA-NPs enable noninvasive cell tracking with MRI and enhance DC migration to lymph nodes. We have further shown that inclusion of cholesterol in RNA-NPs augments the stimulatory capacity of transfected DCs. Future work will consider effects of RNA-NPs on antitumor immune responses and the utility of MRI-detected DC migration as a biomarker of vaccine efficacy.

2385

Role of the antioxidant enzyme catalase in respiratory syncytial virus infection

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OBJECTIVES/SPECIFIC AIMS: The goal of this study is to further evaluate underlying disease parameters in respiratory syncytial virus (RSV) infection, that is reduction in antioxidant potential, and determining if supplementation of the antioxidant enzyme catalase could be employed as a potential therapeutic. METHODS/STUDY POPULATION: Nasopharyngeal secretions were obtained from patients (<2 years old) verified for RSV infection, and assessed for catalase activity and correlated with disease parameters. In addition, the BALB/c animal model of RSV infection was utilized to directly study the effect of supplemental catalase on RSV-related disease parameters in vivo. The catalase formulation used in these studies is pegylated, and has been tested to provide long-term increased catalase activity in vivo. We are also currently working on designing an in vitro model of catalase supplementation in A549 bronchial epithelial cells. RESULTS/ANTICIPATED RESULTS: Our preliminary data shows that patients with more severe disease (based on hospitalization, oxygen supplementation) have significantly lower levels of catalase activity ($p < 0.02$). Additionally, when pegylated-Catalase (PG-CAT) treatment is utilized in RSV infection of mice, there is significant improvement in several disease parameters. PG-CAT-treated mice show an attenuated body weight loss ($p < 0.001$) and clinical disease ($p < 0.02$), and also have lower levels of key pro-inflammatory cytokines including CXCL1 and TNF-α. PG-CAT treatment also resulted in a minor decrease in viral titer, which is being further evaluated. In addition, PG-CAT treatment resulted in an improvement in airway hyperresponsiveness observed at baseline, we are further characterizing this improvement and also conducting methacholine challenges. Currently, we are working to determine the underlying mechanism through which PG-CAT results in these improvements, and whether it is through changes in immune cell populations, cellular signaling or apoptosis signaling pathways (i.e., caspases). DISCUSSION/SIGNIFICANCE OF IMPACT: RSV is the leading cause of viral pneumonia and bronchiolitis in infants, with no vaccines or effective therapeutics available currently. Our study indicates that catalase activity could be used as a potential correlate for disease severity and be used as an indicator of disease during patient treatment. Additionally, and more importantly supplementation of catalase could be used as a potential therapeutic for treatment of RSV.

2559

Role of tissue non-specific alkaline phosphatase (TNAP) in promoting the survival of acute myeloid leukemia (AML) cells within the bone marrow microenvironment

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