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.

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

Muhammad A. Parvaz, Kristen Kim, Sean Froudist-Walsh, Jeffrey H. Newcorn and Iliyan Ivanov

Icahn School of Medicine at Mount Sinai

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.

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RNA-nanoparticles to enhance and track dendritic cell migration

Adam J. Grippin[1,2], Elias J. Sayour[1], Brandon Wummer[1], Adam Monsalve[2], Tyler Wildes[1], Kyle Dyson[1], Jon Dobson[2,3] and Duane A. Mitchell[1]
[1] Department of Neurosurgery, Preston A. Wells, Jr. Center for Brain Tumor Therapy, University of Florida, Gainesville, FL, USA; [2] J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, USA; [3] Department of Materials Science & Engineering, University of Florida, Gainesville, FL, USA; [4] Clinical and Translational Science Institute, University of Florida

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.

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Role of the antioxidant enzyme catalase in respiratory syncytial virus infection

Maria Ansar[1], Jeffrey M. Chambliss[2], Naryana Komaravelli[2], Teodora Ivanciuc[2], Antonella Casola[2] and Roberto P. Garofalo[2]
[1] University of Texas Medical Branch, Galveston, TX, USA;
[2] Department of Pediatrics, University of Texas Medical Branch, Galveston, TX, USA

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.

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

Bradley Bowles[1], Rosalie M. Sterner[2], Kimberly N. Kremer[3], Amel Dudakovic[4], Jennifer J. Westendorf[5], Andre J. Van Wijnen[5] and Karen E. Hedin[6]