aortic dilation is already present. Therefore, we measured the impact of drugs (the renin-angiotensin system inhibitors losartan and enalapril) on survival and thoracic aortic growth in a mouse model of Marfan syndrome when extensive aortic dilation was already present. METHODS/STUDY POPULATION: Male and female fibrillin-1 hypomorphic (FBN1 mgR/mgR) mice (n=10-12/group) were stratified into treatment groups by aortic diameter at 6 weeks of age to ensure an equivalent average aortic diameter in each group at the start of the study. Osmotic mini pumps filled with PBS (vehicle), enalapril (2 mg/kg/d), or losartan (20 mg/kg/d) were implanted subcutaneously into mice after stratification. Mini pumps infusing drug or vehicle were replaced every 4 weeks for a total duration of 12 weeks. Wild type littermates (n=10) were infused with PBS as a negative control to the Marfan mouse model. Ascending aortic diameters from male and female FBN1 mgR/mgR mice and their wild type littermates were assessed by ultrasound every 4 weeks from 6 to 18 weeks of age. Aortic diameters were measured luminal edge to luminal edge during diastole. RESULTS/ANTICIPATED RESULTS: 6 week old FBN1 mgR/mgR mice exhibited significantly dilated ascending thoracic aortas at study initiation compared to their wild type sex-matched littermates (in males: FBN1 mgR/mgR = 1.87 +/− 0.07mm, wild type = 1.23 +/− 0.07mm; p <0.001) (in females: FBN1 mgR/mgR = 1.56 +/− 0.07mm, wild type = 1.18 +/− 0.07mm; p <0.001). Baseline mortality of FBN1 mgR/mgR mice infused with PBS was 36% in male and 22% in female mice at the time of study termination. Within sex-matched mgR littermates, there was no significant difference in survival between groups treated with PBS, enalapril, or losartan after 12 weeks (p=0.224 for males, p=0.094 in females). In the same groups, no significant difference in maximum ascending aortic diameter was detected after treatment for 12 weeks (in males: PBS=2.69 +/− 0.19 mm, enalapril=2.04 +/− 0.27 mm, losartan=2.42 +/− 0.28 mm; p=0.24) (in females: PBS = 1.92 +/− 0.13, enalapril=1.89 +/− 0.31, losartan=1.98 +/− 0.17; p=0.86). Furthermore, aortic diameters in the FBN1 mgR/mgR mice were found to demonstrate sexual dimorphism. DISCUSSION/SIGNIFICANCE OF IMPACT: This research shows that losartan is not effective when administered after significant thoracic aortic dilation has already occurred in FBN1 mgR/mgR mice. This has important translational implications because losartan is usually not started in patients with Marfan syndrome until significant aortic dilation is already present. Therefore, more research needs to be done to determine the critical time period within which this medicine will be effective if given to patients. In addition, this research demonstrates that male FBN1mgR/mgR mice have a significantly larger aortic diameter than female FBN1mgR/mgR mice. This sexual dimorphism has recently been observed in patients with Marfan syndrome as well. Additional studies for understanding the mechanism underlying this sexual dimorphism have the potential to elucidate new therapeutic approaches for aortic disease.

3503

Restrictive feeding and excessive hunger in young children with obesity: A case series

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OBJECTIVES/SPECIFIC AIMS: The purpose of this case series is to show how helping parents instill a non-restrictive, structure-based (i.e., authoritative) approach to feeding is useful in addressing family food conflicts in a clinical child obesity treatment program. METHODS/STUDY POPULATION: Case reports are presented for 3 young children (two 8-year-old males and one 7-year-old female) with obesity (BMI ≥ 95th percentile for age and sex). Patients underwent family-based treatment at Brenner FIT® (Families In Training), an interdisciplinary tertiary weight management clinic. RESULTS/ANTICIPATED RESULTS: All patients experienced a period of rapid weight gain and/or severe onset obesity. Parents reported a combination of problematic eating behaviors (e.g., sneaking food, frequent complaints of hunger, vomiting from rapid consumption). Families implemented structure-based feeding with a meal-snack schedule and allowed children to eat until they were full from the food provided at meal-snack times. BMI z-score decreased from 2.19 to 2.07 in patient 1 and from 2.43 to 2.09 in patient 2 (follow-up weight was not available for patient 3). DISCUSSION/SIGNIFICANCE OF IMPACT: The improvements observed by our clinical program after families lifted restriction and instituted authoritative feeding is anecdotal evidence for the ecological validity of existing empirical work. Randomized controlled trials are needed to examine causality.

3008

Role of Interferon-gamma in Natural Clearance of Chlamydia trachomatis Infection in Women

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OBJECTIVES/SPECIFIC AIMS: Chlamydia trachomatis (CT) infection can lead to reproductive morbidity in women. Animal models suggest that protection against CT is mediated through the cytokine interferon-gamma (IFN-γ), produced by CD4+ T-cells, which clears CT through intracellular tryptophan depletion. In humans, correlates of protection remain to be elucidated, which hinders chlamydia vaccine development. Natural clearance of CT infection (e.g., clearance before antibiotics) may be an immunological correlate of protection, evidenced by (1) CT clearance without antibiotics; and (2) a 4-fold reduced risk of CT reinfection within 6 months. We have identified women with and without natural clearance of CT infection. By comparing these two groups of women, the role of IFN-γ-mediated natural clearance of CT infection will be investigated. METHODS/STUDY POPULATION: Through collaboration with a cohort study of CT-infected women, we have access to stored specimens from women who naturally cleared CT or had persisting CT infection. Using peripheral blood mononuclear cell (PBMC), we will assess whether natural clearance of CT infection is associated with IFN-γ-producing CD4+ T-cells by stimulating PBMC ex vivo with CT antigens using intracellular cytokine staining. We will also use cervicovaginal lavage (CVL) and untargeted High-Performance Liquid Chromatography-Mass Spectrometry to assess for tryptophan-dependent and -independent metabolic pathways associated with natural clearance of CT infection. RESULTS/ANTICIPATED RESULTS:: To date, IFN-γ has been measured in 10 women who did not clear CT infection, demonstrating that <20% of these women produced significant levels of IFN-γ. Women who naturally cleared CT have yet to be studied. Untargeted HPLC-MS has been performed on 6 women (3 who cleared matched to 3 with persisting CT infection). To date, 11 pathways that are significantly associated with natural clearance have been identified. DISCUSSION/SIGNIFICANCE OF IMPACT: The outcome of natural clearance

of CT infection is distinct from women with persisting chlamydia. These studies may inform whether IFN-γ, produced by CD4+ T-cells, or tryptophan-dependent or -independent metabolic pathways are associated with natural clearance, which may advance chlamydia vaccine development.

3424

Serial Biomarker Monitoring Predicts Long Term Outcomes in Acute Graft Versus Host Disease

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OBJECTIVES/SPECIFIC AIMS: The first aim of the study is to evaluate the accuracy of serum biomarkers of acute GVHD measured after four weeks of corticosteroid therapy to predict 6 month NRM. The second aim of this study is to compare the accuracy of the biomarker algorithm to that of clinical response to corticosteroids after four weeks. The third aim of the study is to develop a novel regression model that uses weekly biomarker measurements over the first month of corticosteroid therapy to predict 6 month NRM. METHODS/STUDY POPULATION:. Patients who received HCT at one of 22 IRB-approved centers and provided blood samples to the Mount Sinai Acute GVHD International Consortium (MAGIC) biorepository and developed GVHD between January 2008 to May 2018 are included in this study. Patients were divided by time into a training set (Jan 2008-Dec 2015, n=233) for model development and a validation set (Jan 2015-May 2018, n=357) to evaluate the predictive performance of the model. The later time of the validation set was chosen deliberately to model contemporaneous GVHD treatment practices. The size of each group was designed so that there would be roughly equal numbers of deaths in both groups. RESULTS/ANTICIPATED RESULTS:. Serum concentrations of GVHD biomarkers after one month of corticosteroid therapy were measured in the validation set, and the predicted probability of NRM ($\hat{p}$) was computed according to the previously published algorithm: $\log[-\log(1 - \hat{p})] = -11.263 + 1.844(\log ST2) + 0.577(\log REG3\alpha)$. The performance of the biomarker algorithm was evaluated by creating receiver operating characteristic (ROC) curves and calculating the area under the curve (AUC) in the validation set. The AUC of the biomarker algorithm was a significantly better predictor of 6 month NRM than clinical response to treatment after four weeks of corticosteroids (0.84 vs. 0.64, $p<0.001$), which is a clinically relevant improvement in accuracy. To evaluate serial biomarker monitoring, serum biomarker concentrations will be measured weekly at five time points from treatment initiation to one month after corticosteroid therapy. We will use these values in the training set to develop a regression model for 6 month NRM that accounts for repeated biomarker measurements. The performance of this model will be tested in the validation set and the accuracy of the serial biomarker measurements will be compared to the accuracy of measuring biomarkers at the single time point after four weeks of corticosteroid therapy. An AUC improvement of 0.05 would be considered clinically significant. DISCUSSION/SIGNIFICANCE OF IMPACT: Clinical response to treatment after four weeks has been the standard endpoint in GVHD interventional trials for decades. If biomarkers measured at the same time more accurately predict long term mortality, this study would provide the basis for a novel endpoint in GVHD trials and enable more accurate determination of effect size of experimental interventions. An accurate biomarker algorithm will prove useful in guiding immunosuppressive treatment decisions for patients with GVHD. Patients identified by the algorithm as low-risk may benefit from reduced-dose corticosteroid therapy, potentially reducing lethal opportunistic infections. Patients identified as high-risk will be candidates for more intensive immunosuppression or investigational therapies. This precision medicine approach tailors therapy to the individual patient's biology.

3158

Sunitinib-Induced Cardiotoxicity in an Engineered Cardiac Microtissue Model

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OBJECTIVES/SPECIFIC AIMS: The aims of this study are threefold. Firstly, we are examining the effects of increased in vitro afterload (a proxy for hypertension) on human induced pluripotent stem cell cardiomyocyte (hiPSC-CM) response to sunitinib in a durable and dynamic cardiac microtissue culture system. Secondly, we are exploring effects of repeat exposure and recovery of both sunitinib and afterload throughout the lifetime of the hiPSC-CM microtissue. Finally, we are assessing methods to prevent and treat sunitinib induced cardiotoxicity. Primary outcomes for this study are commonly utilized metrics of cardiotoxicity: degree of caspase activation, electrophysiology benchmarks for minimum voltage threshold and maximum capture rate, and microtissue force generation. METHODS/STUDY POPULATION: HiPSC-CMs are cultured and matured as 3D cardiac microtissues (CMTs) on a microtissue array. After maturation, cells are exposed to sunitinib doses of 0μM, 0.5μM, 1μM or 5μM for 12 hours. Concurrently with sunitinib dosing, increases in microtissue array stiffness are created with application of an external magnetic field. Afterload spring constants are fixed at pre-determined physiologic values ranging from 0.5μN/μm, to 5μN/μm. For Aim 1: Half of the CMTs are harvested at 8 hours after sunitinib dosing to conduct the caspase 3/7 assay, and the remainder are examined for 3 days following drug exposure to track temporal changes in electrophysiology and force generation. For Aim 2: After CMT maturation, 12-hour exposures to sunitinib are repeated three times at a fixed dose, with doses separated by one week. Concurrently with sunitinib dosing, increases or decreases in microtissue stiffness are created by changing the strength of an applied external magnetic field to create "ramp up" or "ramp down" stiffness conditions. Caspase assay and contractility metrics are measured at each timepoint. For Aim 3: Experimental conditions are conducted as described in Aim 1. Prior to the introduction of sunitinib, either carvedilol or an AMP-kinase activator is added to the CMT culture media at physiologic concentrations. Primary outcomes are examined as in Aim 1. RESULTS/ANTICIPATED RESULTS: Aim 1: We hypothesize that increases in microtissue afterload, synchronized with sunitinib exposure will augment sunitinib toxicity in cardiomyocytes resulting in elevations of caspase 3/7 activity and minimum voltage capture as well as decreases in maximum capture rate and maximum force generation. Aim 2: We hypothesize that repeat