it with funnel plots. DISCUSSION/SIGNIFICANCE OF FINDINGS: Understanding the factors that influence the growth of asymptomatic thoracic aortic aneurysms (TAA) is paramount, as the size and growth rate of TAAs dictates the clinical course. Little is understood about the degree to which different characteristics influence growth. This meta-analysis will help elucidate factors that promote TAA growth.

Evaluation

85965

Biomechanical analysis of vertebral body polymethylmethacrylate cement augmentation performed using two different techniques

Kabir Torres[1], BA, Brandon B. Carlson[2], MD, MPH, Douglas C. Burton[1], MD, Jacob Birlingmair[1], MD, R. Sean Jackson[1], MD, Joshua T. Bunch[1], MD, Terrence McIff[1], PhD and Stephanie Robinson[1]
[1]University of Kansas - School of Medicine and [2]Department of Orthopedics - University of Kansas Medical Center

ABSTRACT IMPACT: This study will answer key questions that spine surgeons have regarding techniques used in cement augmentation of vertebral compression fractures and will ultimately advance patient care for such injuries. OBJECTIVES/GOALS: The objective of this study is to determine if a difference exists in load-bearing characteristics and load-to-fracture between injecting cement anteriorly prior to screw placement versus cement augmentation via fenestrated pedicle screws. We also expect differences in load-to-failure characteristics between different cement volumes. METHODS/STUDY POPULATION: This study will be performed in a bioengineering laboratory that has access to a Materials Testing System (MTS). Eight cadaveric specimens will be selected from our stock after pre-screening via CT for inclusion and exclusion criteria. The levels T8-L1 will be dissected from the vertebral column along with any soft tissue structures. The vertebral bodies will be potted in an epoxy mold. From each spine, there are 2 groups of three. One vertebral body from each spine will serve as an internal control, one will be augmented with cement via a cannula and then instrumented with a non-fenestrated screw and the third will be instrumented will a fenestrated screw and then augmented with cement. After appropriate curing time, repeat CT imaging will be completed. The specimens will then be loaded to failure and the results analyzed. RESULTS/ANTICIPATED RESULTS: We hypothesize that we will see a better anterior spread with the cannula/non-fenestrated screw method as compared to the fenestrated screw. The reason being is that we would expect the fenestrated screw to experience more cement extruding from the fenestration rather than being directed anteriorly. We believe a better anterior spread of the cement will lead to a greater load-bearing capacity for the vertebral body. We also believe that a difference will exist in load-to-failure testing with the two volumes being tested, though we cannot predict to what a degree this difference will be impactful as there have been few studies prior looking at this. DISCUSSION/SIGNIFICANCE OF FINDINGS: This study is significant because it will aid in determining the optimal technique to implement in the setting of vertebral compression fractures. This will lead to improved patient care as well as a greater understanding of the instrumentation used in such procedures. The results will lay the groundwork for future research on this procedure.

Precision Medicine

15564

Going with the Flow: Engineering Vascularized Urothelial Flaps for Female-to-Male Phalloplasty in Transgender Patients

Jason Harris[1], Xue Dong[1], Ryan Bender[2], Sarah Caughey[1], Nabih Berri[1] and Jason Spector[1]
[1]Weill Cornell Medicine and [2]Downstate Medical Center

ABSTRACT IMPACT: This project uses rapid prototyping, 3D printing, and cell seeding to solve the most common post-operative complications that arise from the current methods of urethral elongation during phalloplasty. OBJECTIVES/GOALS: Post-op fistula and stricture formation occur in up to 50% of phalloplasty patients. These complications arise from the mismatch between skin and uroepithelium, or from scarring secondary to ischemia. Here we describe the fabrication of a novel vascularized urothelial flap for phalloplasty that contains discrete urothelial and vascular channels. METHODS/STUDY POPULATION: A custom designed 3D negative mold, with a urethral channel and a vascular inlet and outlet channel was prototyped in Adobe Fusion 360 and printed on a Prusa i3 MK3S printer in PLA. A 2mm diameter pluronic sacrificial macrofiber was used to connect the channels to form a vascular loop, and 1% type-I collagen was extruded over the mold. After solidifying, the scaffold was demolded and seeded with grade I urothelial carcinoma (SW780 cells, at 5-10 x 106 cells/mL) in the urethral channel, and adenovirus-infected E4 endothelial cells (at 3x106 cells/mL) in the vascular channel. The scaffolds were cultured up to 14 days and then fixed for histologic analysis. RESULTS/ANTICIPATED RESULTS: Collagen scaffolds were fabricated reliably using the custom 3D negative molds. After both seven and fourteen days of culture, the urothelial channel contained a robust, stable urothelial monolayer lining throughout the channel. By 14 days urothelial multilayer formation was seen, providing definitive evidence of a more mature urothelial layer. Grooves within the collagen allowed for nests of urothelial cells to develop, leading to increased multilayer formation. In addition, the vascular channels supported a healthy endothelial lining at both seven and fourteen days. There were no significant histological differences between constructs seeded with 5x106 urothelial cells/mL and 107 cells/mL. We anticipate that multilayer formation will increase with time, and that constructs will survive beyond 28 days. DISCUSSION/SIGNIFICANCE OF FINDINGS: We have developed a novel strategy to engineer vascularized urethral tissue. These constructs can be kept for at least 14 days and form stable monolayers and multilayers consistent with native urothelial architecture. Using 3D printing and autologous cell seeding promises to create patient-specific vascularized urethral flaps for phalloplasty.

22732

Impact of Type-I Interferon Manipulation During Embryo Implantation and Placentation

Michael K. Simoni, Sydnie Swanson, Monica Mainigi and Kellie Jurado
University of Pennsylvania

ABSTRACT IMPACT: This research will promote understanding the role of the Type-I Interferon signaling pathway during embryo

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implantation, potentially leading to a new diagnostic or treatment target in early pregnancy failure. OBJECTIVES/GOALS: Studies suggest interferon signaling regulation is tightly balanced between physiologic and pathophysiologic growth in early pregnancy. We propose to determine the impact of interferon-mediated inflammation on embryo implantation and early pregnancy failure in normal conditions and chronic inflammatory diseases in a novel mixed-mouse model. METHODS/STUDY POPULATION: To probe the role of type-I interferons (IFNs) in implantation, we will utilize a mouse model and non-surgically transfer both Ifnar1-/- and Ifnar1-/+ embryos into an immune-competent pseudopregnant wild-type female recipient. This will allow analysis of a litter with distinct genotypes within the same, immune-competent, uterine environment. Type-I IFN stimulation will be systemically induced with Poly-(I:C) at various time points around implantation. A similar approach will be used in mouse models of chronic inflammatory disease states associated with early pregnancy loss (e.g. systemic lupous erythematous). With this model, we will be able to control for deficiencies in maternal immune response to specifically determine the embryonic response to inflammation during implantation and development. RESULTS/ANTICIPATED RESULTS: We anticipate the Ifnar1-/+ embryos - those able to respond to Type-I IFN - and their surrounding implantation sites will exhibit more maternal-fetal barrier dysfunction in the form of impaired trophoblast fusion, improper formation of the microvascular architecture, and increased permeability of the maternal-fetal barrier, compared to embryos unable to respond to IFN. We will also conduct similar analyses in mouse models of chronic inflammatory diseases. We hypothesize these mice to have baseline endometrial inflammation that stimulated the IFN-pathway in IFN-capable embryos, producing breakdown of the maternal-fetal barrier. In these mice, we predict Ifnar1-/- embryos will show improved molecular outcomes when compared to Ifnar1-/+ embryos, and thus improved associated pregnancy outcomes. DISCUSSION/SIGNIFICANCE OF FINDINGS: This work can insight into the immunological mechanisms that govern embryo implantation and early placentation. This could provide more pointed means for management and intervention of early pregnancy failure and/or disease states that are commonly associated with poor reproductive outcomes.

38766

Massively Parallel Reporter Assay Reveals Functional Impact of 3'-UTR SNPs Associated with Neurological and Psychiatric Disorders*

Andy B. Chen, Kriti Thapa, Hongyu Gao, Jill L. Reiter, Junjie Zhang, Xiaoling Xuei, Hongmei Gu, Yue Wang, Howard J. Edenberg and Yunlong Liu
Indiana University School of Medicine

ABSTRACT IMPACT: Screening the effect of thousands of non-coding genetic variants will help identify variants important in the etiology of diseases OBJECTIVES/GOALS: Massively parallel reporter assays (MPRAs) can experimentally evaluate the impact of genetic variants on gene expression. In this study, our objective was to systematically evaluate the functional activity of 3'-UTR SNPs associated with neurological disorders and use those results to help understand their contributions to disease etiology. METHODS/STUDY POPULATION: To choose variants to evaluate with the MPRA, we first gathered SNPs from the GWAS Catalog that were associated with any neurological disorder trait with p-value < 10-5. For each SNP, we identified the region that was in linkage disequilibrium ($r2 > 0.8$) and retrieved all the common 3'-UTR SNPs (allele-frequency > 0.05) within that region. We used an MPRA to measure the impact of these 3'-UTR variants in SH-SY5Y neuroblastoma cells and a microglial cell line. These results were then used to train a deep-learning model to predict the impact of variants and identify features that contribute to the predictions. RESULTS/ANTICIPATED RESULTS: Of the 13,515 3'-UTR SNPs tested, 400 and 657 significantly impacted gene expression in SH-SY5Y and microglia, respectively. Of the 84 SNPs significantly impacted in both cells, the direction of impact was the same in 81. The direction of eQTL in GTEx tissues agreed with the assay SNP effect in SH-SY5Y cells but not microglial cells. The deep-learning model predicted sequence activity level correlated with the experimental activity level (Spearman's corr = 0.45). The deep-learning model identified several predictive motifs similar to motifs of RNA-binding proteins. DISCUSSION/SIGNIFICANCE OF FINDINGS: This study demonstrates that MPRAs can be used to evaluate the effect of non-coding variants, and the results can be used to train a machine learning model and interpret its predictions. Together, these can help identify causal variants and further understand the etiology of diseases.

49193

The Association Between Specialized Pro-resolving Lipid Mediators and Markers of Neuroinflammation and Disease Severity in Acute Traumatic Brain Injury: A Prospective, Observational Cohort Study

Roy Poblete
University of Southern California, Keck School of Medicine

ABSTRACT IMPACT: Characterizing specialized pro-resolving lipid mediators (SPMs) of inflammation in a cohort of adult patients with traumatic brain injury (TBI) will potentially identify novel biomarkers of disease and would generate hypotheses regarding the role of SPMs in the pathophysiology and recovery after brain injury OBJECTIVES/GOALS: Primary aim: evaluate the association between plasma and cerebrospinal fluid (CSF) SPM levels with inflammatory markers known to mediate blood brain barrier (BBB) disruption. Secondary aim: evaluate the association between SPM levels and disease severity, 14-day Glasgow Coma Scale score (GCS) and survival. METHODS/STUDY POPULATION: This is a single-center, prospective, observational cohort study (target N=50). Adult participants with moderate-to-severe non-penetrating TBI will have blood and CSF sampled serially for laboratory measures of SPMs (resolvins, protectins, lipoxins, maresins) and inflammatory peptides (TNF-α, IL-1β, IL-6, MMP-9, TIMP-1) by liquid chromatography‟ mass spectrometry and RT-PCR & ELISA, respectively. Baseline patient characteristics, admission GCS, and 14-day GCS and mortality will be prospectively collected. To evaluate the association between SPMs and other continuous variables, Pearson's and Spearman's correlation will be used. Cox regression will be used to evaluate the association between SPM lipidomes and 14-day survival. RESULTS/ANTICIPATED RESULTS: As the primary outcome measure, the association between SPM levels with assayed inflammatory markers will be determined at 24 and 72 hours post-TBI. We hypothesize that SPMs will be negatively correlated with TNF-α, IL-1β, IL-6, MMP-9 and positively correlated with

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