syndrome (MetSyn) often occurs. Receptor for advanced glycation end products (RAGE) is highly expressed in the lung, is a strong predictor of FEV1, and is a key mediator of MetSyn. To determine if the loss of RAGE protects from the persistence of effects of particulate associated lung injury in a murine model. METHODS/STUDY POPULATION: Wild type (WT) and RAGE knockout (RKO) mice were exposed to 100 μg of PM (WTC-Aggregate, PM53) or PBS control by oropharyngeal aspiration. Lung function, methacholine challenge, and bronchoalveolar lavage (BAL) were quantified 28 days after PM exposure using flexiVent (Scireq Montreal, QC). BAL was obtained and cell differentials, cytokines and transcription factors were assayed. Bio-volume to airspace ratio and mean chord length were measured (Image J and Adobe Photoshop). RESULTS/ANTICIPATED RESULTS: WT mice were hyper-reactive to methacholine compared with their PBS controls 28 days after a single exposure to PM. They recovered from increased neutrophilia, loss of FEV, decreased compliance, and increased resistance, which were previously observed 24-hours after exposure. RKO were not hyper-reactive when compared with their own PBS controls. Lung histology shows persistence of loss of alveolar space in WT mice exposed to PM after 28 days. Area fraction was significantly higher in PM exposed WT mice after 28 days which was not significant after 24 hours. Mean chord length was significantly shorter for PM exposed at both time points for WT mice. The relative expression of phosphorylated to total CREB and ERK1/2 proteins was lower in RKO PM exposed mice compared with WT PM while STAT3 expression was lower in WT PM compared with WT PBS. PM induced a lower fold change of total proteins from the PBS controls in RKO for CREB, p38, ERK1/2, STAT3, and STAT5. JNK and p70S6k total proteins expressed a decreased fold change in WT PM exposed mice compared with WT PBS controls. DISCUSSION/SIGNIFICANCE OF IMPACT: A single dose of PM can produce persistent airway hyper-reactivity after 28 days of exposure. This PM induced injury is alleviated in the absence of RAGE, similar to what was seen at 24 hours. Inhibiting RAGE may be key to limiting the persistent inflammatory effects of high intensity PM exposure.

2350

The role of gut microbiota in the susceptibility of Parkinson disease development

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OBJECTIVES/SPECIFIC AIMS: Several clinical studies have established a correlation between changes in relative bacterial populations in the gut and Parkinson disease. However, few published experiments have been able to parse out whether these associations are causative or correlative. Our aim is to determine how bacteria in the gut may impact the health and resilience of dopaminergic signaling. Our experiment is designed to serve as a proof-of-principle that controlled alterations to the gut microbiome alters mechanisms in dopamine homeostasis in the midbrain. METHODS/STUDY POPULATION: Bacterial inoculation 8–10-week-old germ-free male mice (C57BL/6) were exclusively used in this experiment. Mice were orally gavaged every 3 days (D0, 3, 6, and 9) with 100 μL novel bacterial suspension (~108 CFU resuspended in PBS with 1.5% $NaHCO_3$) or vehicle and were sacrificed on D11. Tissue preparation—brains were quickly extracted and the striatum was isolated and homogenized in either RIPA buffer with protease inhibitors (for Western blot analysis) or in 0.1 N $HClO_4$ (for HPLC processing). The homogenates were processed through fractional centrifugation to remove cellular debris. Lysate samples were frozen at −80°C until ready for analysis. Protein expression quantification—expression of proteins were measured using intensity of bands from Western blots. Lysates were denatured prior to loading with LB with 10% β-mercaptoethanol and 30-minute incubation at 37°C. All immunoblots were normalized to immunoreactivity to α-tubulin. Immunoblot intensity was determined using the ImageJ software. Dopamine/dopamine metabolite quantification HPLC analysis was used to determine dopamine and dopamine metabolite concentration. Aliquots of the lysate were injected onto a C18 column using a mobile phase consisting of 50 mM $H_2NaO_4P{\cdot}H_2O$, 0.72 mM sodium octyl sulfate, 75 μM Na_2 EDTA, and 10% acetonitrile (pH 3.0). The mobile phase was pumped through the system at 0.3 mL/minute. RESULTS/ANTICIPATED RESULTS: Measured total dopamine concentration through HPLC analysis in the striatum showed no significant differences in the bacteria-treated group relative to the control group. The metabolites DOPAC and HVA had an elevated measured concentration in the bacteria-treated group relative to the control group. Western blot analysis showed decreased immunoreactivity for DAT and TH in the bacteria-treated group compared with the control group. There was no significance difference in the immunoreactivity for VMAT2. DISCUSSION/SIGNIFICANCE OF IMPACT: This study demonstrates that dopamine signaling dynamics in the midbrain can be altered by changes in the gut flora in mice. These results further substantiate the impact of the gut-brain axis and may even point to a potential avenue of bolstering the resilience of dopaminergic neurons in preventing the onset of PD. Further experiments must be performed to understand the mechanism of the observed changes and to determine if these changes have any salutary effect.

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Impacts of a long-term community-university partnership on investigator-initiated research at an Urban Research University

Emily Zimmerman, Chanel Bea, Alicia Aroche and Alex Krist

OBJECTIVES/SPECIFIC AIMS: Engaging Richmond is a community-university partnership, made up of local residents and university faculty and staff that was established in 2011 with an NIH supplement to a Clinical and Translational Science Research Award at Virginia Commonwealth University (VCU). The primary aims of the supplement were to (1) to conduct community-based participatory research (CBPR) on the leading causes of health disparities perceived by the Richmond community and (2) to thereby highlight community needs and assets and build capacity for future community-engaged research (CEnR). The goal was to prepare a community-focused, community-prioritized, health equity report while building capacity, strengthening relationships, and discovering local barriers to CEnR, and therefore to stimulate, facilitate, and inform future CEnR at VCU. METHODS/STUDY POPULATION: This is a case study exploring the impact of 1 community-university partnership on investigator-initiated research using historical and qualitative data. RESULTS/ANTICIPATED RESULTS: Although Engaging Richmond received only 12 months of support from the NIH supplement that provided its initial funding, the community-university partnership has worked continuously since its formation in 2011. This work has not only helped to build connections with the community and key stakeholders, it has also contributed substantially to the resources available to university faculty pursuing CEnR. Specifically, we find that Engaging Richmond has contributed to investigator initiated research in the following ways, either working as co-investigators or in a consultative capacity: consultation on proposal development (5 projects); assisted with instrument development (4 projects); participant recruitment (7 projects); data collection and analysis (6 projects); dissemination (5 projects). In addition to collaboration on projects, Engaging Richmond has increased institutional capacity for CEnR through its contributions to the Annual Community Engaged Institute at the university and the Center of Clinical and Translational Science's Community Review Board (CRB). The CRB helps researchers work successfully in a community setting, enhance the research design, help to improve study implementation and assist with translation and dissemination of findings. DISCUSSION/SIGNIFICANCE OF IMPACT: Although community-university partnerships have become much more common over the past several decades, there remains a gap in research evidence on the impact of these partnerships. In their 2004 review, Viswanathan *et al.* note that community-based participatory research studies infrequently document improved capacity of researchers and research organizations as an outcome, despite the expectation that such improvement will accrue through investment in CEnR. A more recent study assessing the range of community-university partnerships across a research university also noted the lack of processes in place to assess impacts (Holton *et al.*, 2015). While assessments of CEnR impact on communities have become increasingly common as demand for evidence about the effectiveness of community-engaged partnerships has mounted, there does not appear to be a similar trend in assessing the impact of these efforts on faculty research and institutional capacity. By focusing on the impact of 1 community-university partnership that has been sustained for over 5 years, we highlight the ways in which having ongoing partnerships in place can support and strengthen investigator-initiated research, reflecting the flexible, "2-way approach" (Weerts and Sandmann, 2010) at the heart of CEnR.

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Effects of cortical stimulation of the noninfarcted Versus peri-infarcted motor cortex

Serena-Kaye Kinley-Cooper and DeAnna Adkins

OBJECTIVES/SPECIFIC AIMS: The objectives of this study are to determine whether high-frequency ipsi-lesion or low-frequency contra-lesion ECS improves forelimb function following experimental stroke in aged animals with focal and large strokes. We also want to investigate whether ECS-induced improvements in motor function are related to an enhancement of neural structural plasticity (dendrites and synapses) and changes in growth promoting (BDNF) and growth inhibiting (NOGO-A) expression in the infarcted motor cortex in young and aged animals. METHODS/STUDY POPULATION: We will

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investigate whether excitatory ECS of the infarcted cortex or inhibition of the noninfarcted cortex combined with daily impaired-forelimb rehabilitative training (RT) results in greater motor functional recovery compared to RT alone. Immunohistochemical (IHC) analyses and unbiased stereological techniques will be performed to investigate changes in proteins associated with dendritic restructuring (MAP2), synaptic plasticity (PSD95 and synaptophysin), and alteration in the expression of BDNF and NOGO-A. RESULTS/ANTICIPATED RESULTS: We expect that inhibitory ECS of the noninfarcted motor cortex will improve behavioral outcomes in moderate to severe stroke animals compared with excitatory ECS or no stimulation (RT alone) animals. We predict that the ECS condition that improves motor performance most significantly compared with RT alone will have a corresponding greater increase in remaining ipsi-infarct motor cortical dendritic and synaptic plasticity (demonstrated by a greater density of MAP2, synaptophysin, and PSD-95 immunoreactivity), and greater expression of BDNF. It is unknown, but also expected that better behavioral recovery will coincide with a greater reduction in NOGO-A in the injured motor cortex. DISCUSSION/SIGNIFICANCE OF IMPACT: These studies will aid in creating a model that will allow for a better understanding of the relationship between brain stimulation, severity of injury and, in future studies, aging. These studies will also help clarify previous conflicting brain stimulation results.

2395

Self-assembling cartilage from equine mesenchymal stem cells: A comparison of bone marrow and cord blood-derived MSCs

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OBJECTIVES/SPECIFIC AIMS: Joint injury is a common cause of premature retirement for many equine athletes. Implantation of engineered cartilage offers the potential to increase the success rate of surgical intervention and hasten recovery times. Mesenchymal stem cells (MSCs) offer a particularly attractive cell source for cartilage engineering. Although bone marrow-derived MSCs (BM-MSCs) have been most extensively characterized for musculoskeletal tissue engineering, studies suggest cord blood MSCs (CB-MSCs) may elicit a more robust chondrogenic phenotype. The objective of this study was to determine superior equine MSC source for cartilage engineering via a self-assembling process (SAP). METHODS/STUDY POPULATION: MSCs derived from bone marrow or cord blood were stimulated to undergo chondrogenesis via 3D culture and then used to generate cartilage via SAP. The resulting neocartilage produced from either BM-MSCs or CB-MSCs was compared by measuring biochemical, mechanical, and histological properties. RESULTS/ANTICIPATED RESULTS: We found that while BM-MSCs possessed higher tensile properties and collagen content, CB-MSCs had superior compressive properties and GAG content. Moreover, CB-MSCs had lower alkaline phosphatase activity and higher collagen type II, suggesting a more hyaline cartilage-like phenotype. DISCUSSION/SIGNIFICANCE OF IMPACT: In conclusion, while both BM-MSCs and CB-MSCs were able to form neocartilage, CB-MSCs resulted in tissue more closely resembling native equine articular cartilage, and is therefore the superior MSC source for purposes of cartilage self-assembly.

2420

Loss of eptB decreases systemic inflammation during *Salmonella* infection and allows for evasion of the host immune response

Lillian F. Zhang, Fabian Rivera-Chavez, Hirotaka Hiyoshi and Andreas J. Baumler

OBJECTIVES/SPECIFIC AIMS: Our long-term goal is to elucidate the molecular mechanisms and virulence factors that control the differential presentation of infection with Salmonella typhimurium and Salmonella typhi. The objectives of this study are to study the mechanisms that enable S. typhi to trigger a decreased inflammatory response in comparison with S. typhimurium and evade detection by the immune system, leading to the development of asymptomatic chronic carriage of S. typhi. METHODS/STUDY POPULATION: A loss of function eptB mutant S. typhimurium strain was generated. Lipopolysaccharide (LPS) was isolated from wild-type and eptB mutant S. typhimurium and wild-type S. typhi. Binding of LPS to recombinant intelectin was tested by dot blot and enzyme-linked immunosorbant assay (ELISA). C57BL/6 mice were infected with wild-type or eptB mutant S. typhimurium by oral gavage and inflammatory cytokines in the spleen, liver, and Peyer's patches were measured by qPCR. RESULTS/ANTICIPATED RESULTS: LPS isolated from wild-type S. typhimurium is not bound by intelectin, a protein that has been proposed to function in innate immunity and that is known to be able to bind certain moieties within LPS. Conversely, LPS isolated from eptB mutant S. typhimurium and wild-type S. typhi, which lacks a functional eptB, is bound by intelectin. Mice infected with an eptB mutant S. typhimurium exhibit decreased expression of inflammatory cytokines in the spleen compared to mice infected with the wild type S. typhimurium, suggesting that loss of eptB function allows a nontyphoidal Salmonella serovar to mimic the stealth phenotype of typhoidal serovars. Together, these results suggest that loss of eptB function allows intelectin to bind to and detoxify Salmonella LPS, leading to decreased systemic inflammation during infection. DISCUSSION/SIGNIFICANCE OF IMPACT: These results have broad implications for how pathogens such as S. typhimurium induce systemic shock during infection and may also help to explain a mechanism for how S. typhi is able to evade immune detection and enhance dissemination to systemic sites, leading to development of the asymptomatic chronic carrier state. Further investigation of this novel virulence mechanism will mark a decisive step forward in understanding the mechanisms underlying the differential pathogenesis of S. typhimurium-induced gastroenteritis and S. typhi-induced typhoid fever. Additionally, these results contribute to our understanding of the interactions between host and pathogen in affecting disease presentation, which will have wide appeal among researchers interested in microbial pathogenesis and the contribution of host-pathogen interactions to health and disease.

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Magnetic nanoparticles facilitate tracking of dendritic cells for treatment of malignant brain tumors

Adam Grippin, Elias Sayour, Jon Dobson and Duane A. Mitchell

OBJECTIVES/SPECIFIC AIMS: Immune-based therapies hold great promise for treatment of refractory tumors. However, development is limited by a lack of identified immune correlates to vaccination. We recently showed that dendritic cells (DCs) prolong progression-free survival (PFS) and overall survival (OS) in patients with glioblastoma, and that DC migration to site draining lymph nodes robustly correlates with both PFS and OS. While this appears to be a reliable immune correlate, the complexity of routine labeling for PET and SPECT prohibits validation in a large clinical study. We therefore seek to develop a safe, translatable reporter that can be imaged with a widely available imaging modality. METHODS/STUDY POPULATION: The cationic liposome 1,2-doleoyl-3-trimethylammonium-propane (DOTAP) was loaded with MRI-imageable iron oxide nanoparticles (IONPs) with or without the neutral molecules PEG and cholesterol. The resulting nanoparticles were loaded with RNA to form RNA-NPs that were characterized with transmission electron microscopy (TEM) and used to transfect DCs in vitro; 4.7 T MRI was then used to image particles or cells in agarose gel phantoms. RESULTS/ANTICIPATED RESULTS: TEM images of RNA-NPs indicate the presence of IONP-loaded liposomes. In vitro transfection experiments demonstrate that iron oxide does not reduce RNA-NP-mediated transfection of DCs. Additionally, small amounts of either PEG or cholesterol within RNA-NPs increased transfection of DC2.4s and enhanced T-cell priming by bone marrow-derived dendritic cells. A series of 4.7 T MRI images of particles in cells, spleens, and LNs demonstrated quantifiable differences in particle density between groups. DISCUSSION/SIGNIFICANCE OF IMPACT: This data suggests that IONP-loaded RNA-NPs can be imaged with MRI and manipulated to augment DC function. Future work will include in vivo imaging in mice and safety studies to facilitate translation into first-in-human studies. Successful completion of this project would provide a powerful clinical tool to improve and track patient responses to immune therapy.

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Metabo-therapy for RARRES1-depleted epithelial cells using repurposed mitochondrial metabolism inhibitor, metformin

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OBJECTIVES/SPECIFIC AIMS: The goal of this study is to examine bioenergetic phenotype of retinoic acid receptor responder 1 (RARRES1)-depleted epithelial cells and to facilitate the discovery of personalized metabo-therapeutics in the context of cancers characterized with loss of or low expression of RARRES1. METHODS/STUDY POPULATION: Anoikis assay and annexinV labeling were used to assess drug resistance and apoptotic phenotype in RARRES1-depleted epithelial cells. Metabolomics, AMP kinase activity, mito-tracker, and extracellular flux assays were used to examine the bioenergetic profile of

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