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

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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.

2422

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

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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.

2427

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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