

monitored using a clinical scoring system, and changes in activation status of hematopoietic cell populations were quantified using flow cytometry. RESULTS/ANTICIPATED RESULTS: Recipients transplanted with fli-I deficient T cells exhibited reduced cGVHD clinical scores compared with littermate wild-type controls. Donor-grafts containing fli-I deficient T cells were associated with restrained T-cell responses including reduced Interferon- γ cytokine production, PD-1 expression, and differentiation into follicular helper T cells. fli-I T-cell deficient donor-grafts also improved donor B-cell reconstitution and reduced plasma cells in allo-HCT recipients relative to littermate wild-type control donor-graft recipients. DISCUSSION/SIGNIFICANCE OF IMPACT: Thus, inhibiting Fli-I represents a promising therapeutic strategy for the goal of preventing cGVHD after allo-HCT while also directly targeting cancers which aberrantly express Fli-I.

2333

Impact of spoken sentence predictability on cognitive spare capacity in elderly adults with hearing loss

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OBJECTIVES/SPECIFIC AIMS: Listening effort is needed to understand speech that is degraded by hearing loss and/or a noisy environment. Effortful listening reduces cognitive spare capacity (CSC). Predictive contexts aid speech perception accuracy, but it is not known whether the use of context reduces or preserves CSC. Here, we compare the impact of predictive context and cognitive load on behavioral indices of CSC in elderly, hearing-impaired adults. METHODS/STUDY POPULATION: Elderly, hearing-impaired adults listened in a noisy background to spoken sentences in which sentence-final words were either predictable or not predictable based on the sentence context. Cognitive load was manipulated by asking participants to remember either short or long sequences of visually presented digits. Participants were divided into low or high cognitive capacity groups based on a pretest of working memory. Accuracy and response times were examined for report of both sentence-final words and digit sequences. RESULTS/ANTICIPATED RESULTS: Preliminary results indicate that accuracy and response times for both words and digits were facilitated by sentence predictability, suggesting that the use of predictive sentence context preserves CSC. Response times for both words and digits and accuracy for digits were impaired under cognitive load. Trends were similar across high and low cognitive capacity groups. The preliminary results support the idea that habilitation strategies involving context use could potentially support CSC in elderly, hearing-impaired adults. DISCUSSION/SIGNIFICANCE OF IMPACT: These preliminary results support the concept that habilitation strategies involving context use could potentially support CSC in elderly, hearing-impaired adults.

2302

Impacts of postnatal nest change on early development

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OBJECTIVES/SPECIFIC AIMS: It has been reported that birth mode affects development, with cesarean section born mice gaining more body weight during development. Since mice C-sections involve fostering and nest change, we sought to determine whether changing only the nest and cage would have an effect on development. METHODS/STUDY POPULATION: A total of 53 mice were born to 9 dams, and 21 babies (4 litters) were exchanged in pairs to foreign cages and nests. Litters were followed for body weight and mothers were observed during periods for maternal and nonmaternal behaviors. RESULTS/ANTICIPATED RESULTS: The results show that average body weight was significantly higher in

the experimental group in both genders, with 20% higher body weights at weaning. The mothers from the litters that were changed to a new nest showed significantly more non-maternal behavior in the first 2 days of life, than the controls. DISCUSSION/SIGNIFICANCE OF IMPACT: The results suggest that changes in maternal behavior may be linked to the increased weight gain in their babies.

2461

Increasing butyrate levels by microbial manipulation or drug administration to delay Parkinson's disease progression

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OBJECTIVES/SPECIFIC AIMS: Determine if synthetic or endogenously produced butyrate can delay Parkinson's disease (PD) progression, attenuate PD associated GI dysfunction, and impact the gut-microbiota in mice expressing human mutant aSyn. METHODS/STUDY POPULATION: Two transgenic mouse models expressing human mutant alpha-synuclein (aSyn) will be used. Transgenic mice expressing aSyn A53T display GI dysfunction before motor deficit onset and will be used to investigate treatment impact on PD associated GI dysfunction. Mice expressing aSyn Y39C more accurately recapitulate age-related neuropathology and behavioral deficits and will be used to assess treatment impact on PD-associated neuropathology, motor, and cognitive function. Mice will receive a synthetic sodium butyrate, sodium phenylbutyrate, or a synbiotic treatment regimen for 3 months. Disease progression will be assessed by aSyn brain and gut neuropathology, brain and gut inflammatory status, behavioral deficits, and gastrointestinal function. In addition, fecal and gut-microbiota composition and neuroprotective gene expression in the brain will be investigated. RESULTS/ANTICIPATED RESULTS: Our preliminary data shows that both sodium butyrate and sodium phenylbutyrate delay disease progression in aSyn Y39C mice. Butyrate-treated mice have reduced aSyn oligomerization, reduced Lewy body formation, and improved motor and cognitive function compared to placebo-treated mice. 16S rRNA sequencing did not reveal fecal-microbiota shifts between treatment groups or with age progression. Further analysis assessing expression levels for genes with antioxidant and protein degradation roles will be performed to determine if sodium butyrate and sodium phenylbutyrate similarly impact cellular mechanisms to delay neurodegeneration. Our future experiments will focus on comparing sodium butyrate and synbiotic treatment outcomes in aSyn A53T mice. DISCUSSION/SIGNIFICANCE OF IMPACT: Our lab developed a Tg mouse model that more accurately recapitulate age-related symptoms, pathology, and mechanisms observed in PD patients compared with animal models onset by neurotoxins. Our use of an age-dependent model of a severe form of Parkinsonism, DLB, will better predict clinical outcomes in PD populations. We will be the first to assess if elevating select microbial product production enhances neuroprotective brain activity in a PD model. Results obtained will further characterize gut-brain axis communication mechanisms. These proposed experiments will be the first to determine if elevating microbial products improves GI deficits associated with PD and may lead to insight on the gut-brain axis role in PD. Overall, this proposal will be the first to investigate a novel, highly accessible treatment with the potential to delay PD progression and target motor, cognitive, and GI deficits associated with PD. Due to the current FDA approval of probiotics and prebiotics that enhance butyrate production, results obtained may be quickly translated for clinical use.

2363

Inducing anti-tumor immunity in colorectal cancer

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OBJECTIVES/SPECIFIC AIMS: Despite significant advances in screening and treatment, colorectal cancer is the second leading cancer killer in the United States today. Some of the most promising recent developments in cancer therapy have come from immune-based therapy. Immune-based therapy, however, has shown limited utility in patients with colorectal cancer. Studies have previously shown that certain chemotherapy regimens may be more effective in combination with immune-based therapy due to induction of inflammation in the tumor microenvironment. In this study, we sought to determine how standard chemotherapy (FOLFOX) affects the generation of antigen-specific anti-tumor immunity in colorectal cancer. METHODS/STUDY POPULATION: To determine the how antigen-specific immunity and T cell