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-1 deficient T cells exhibited reduced cGVHD clinical scores compared with littermate wild-type controls. Donor-grafts containing fli-1 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-1 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-1 represents a promising therapeutic strategy for the goal of preventing cGVHD after allo-HCT while also directly targeting cancers which aberrantly express Fli-1.

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 if 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 anti-oxidant 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

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responses are affected by FOLFOX, we utilized a model antigen expressing murine colon cancer cell line syngeneic to C57BL/6 (MC38-CEA). Treatment was initiated when tumor size reached 50 mm^2. Mice were treated with either vehicle (PBS), 5-Fluorouracil (5-FU), Oxaliplatin, or combination (FOLFOX). Antigen-specific cytotoxic T cell (tet + Tc) were detected using Db-CEA-tetramer obtained from the NIH-tetramer core facility. Flow cytometry was performed for phenotypic analysis and tetramer positivity. Tumor growth was measured using standard caliper measurements. Statistical analysis was performed using *t*-test for continuous variables and ANOVA was used when comparing multiple groups. Statistical analysis was performed using SPSS. All arms were completed with n = 3–7. RESULTS/ANTICIPATED RESULTS: To determine how systemic treatment with chemotherapy affects cytotoxic T cell development (Tc), we established that we could detect antigen-specific Tc (tet + Tc) in the spleen, tumor, and draining lymph nodes of tumor-bearing mice. After establishing that the system worked appropriately, tumor-bearing mice were treated with different chemotherapy regimens and tumor growth was monitored. As expected, the combination of FOLFOX was significantly better than either drug individually (2-way ANOVA, $p < 0.01$). FOLFOX therapy also showed a significant ($p < 0.05$) increase in the number of tumor-associated tet + Tc, and tet + Tc expressing phenotypic markers of effector (Te) and resident memory (Trm) subsets. Tumor-associated tet + Tc highly expressed PD-1 (>50%); however, this was not significantly different between treatment or vehicle arms. Since 5-FU, one component of FOLFOX has previously shown a selective reduction of myeloid-derived suppressor cells, we also investigated the myeloid compartment. There were no significant differences in conventional or plasmacytoid dendritic cells, myeloid-derived suppressor cells, or tumor-associated macrophages. DISCUSSION/SIGNIFICANCE OF IMPACT: The future of cancer care involves multi-modality care tailored to patients. To more effectively combine therapy it is critical that we understand how currently utilized therapy works. In this study, we show that the primary chemotherapy regimen utilized in colorectal cancer increases tumor-associated antigen-specific cytotoxic T cells and the majority of these cells are PD-1 positive. This suggests that FOLFOX may work in concert with immune-based therapy when selected appropriately. Further study is warranted to determine optimal combination therapy and ways to maximize anti-tumor immunity in order to improve the treatment of patients with this deadly disease.

2044

Investigation of patient-reported outcomes following ACL reconstruction using Rasch analysis

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OBJECTIVES/SPECIFIC AIMS: The knee injury osteoarthritis and outcomes survey (KOOS) is a commonly used instrument to measure patient-reported quality of life (QOL) post-ACLR. The purpose is to evaluate the psychometric properties of the QOL subscale of the KOOS. METHODS/STUDY POPULATION: Rasch analysis of KOOS QOL subscale from 39 individuals 1–2 years post ACLR was conducted. Measurement properties and model fit of the rating scale, items, and persons were evaluated. Relationship of item difficulties and person measures was evaluated using probability curves and item maps. Reliability indicators were also examined. RESULTS/ANTICIPATED RESULTS: All items demonstrated infit and outfit mean squares and standard *z*-scores. The majority of persons (n = 38, 97.4%) demonstrated fit to the Rasch model. However, ceiling effects were noted (n = 4, 10.26%), indicating some participants report higher QOL than is measurable. The mean person measure was 1.73 logits higher than the mean item measure: this sample is skewed toward higher QOL. Person reliability was adequate (0.67) and person separation was 1.42. Calculation of person strata revealed that the KOOS QOL separated participants into 2 strata. DISCUSSION/SIGNIFICANCE OF IMPACT: Although all items of the KOOS QOL fit the model, not all categories of the rating scale were used. Overall, this sample reported high QOL, which is to be expected given the time since ACLR. If participants with a broader range of time since ACLR were included, that the KOOS QOL could identify additional person strata.

2057

L1 expression analysis in adipose-derived stem cells

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OBJECTIVES/SPECIFIC AIMS: Long interspersed element-1s (L1s) are autonomous, mobile elements that are able to copy and insert themselves throughout the genome with their own reverse transcriptase and endonuclease.
These elements make up 17% of the human genome with over 500,000 copies, though the vast majority of L1s are defective with only a few dozen potentially responsible for L1 activity. Full-length L1s have the potential to contribute to mutagenesis through random insertion and increased genetic instability. Here we set out to study L1 expression at the specific loci level in bone marrow-derived stem cells (bmSCs) and adipose-derived stem cells (ASCs) and compare the levels of expression from ASCs from donor patients who are young and lean, obese, and old. Our hypothesis is that L1-related damage may contribute to mutation and inflammation that alters the function of these stem cells throughout the life of an individual. METHODS/STUDY POPULATION: ASCs and bmSCs were isolated from patient donors. The following samples were collected: ASCs from 3 young (under the age of 59) and lean (BMI < 30) patients, ASCs from 3 older patients (over the age of 59), ASCs from 3 patients with BMI > 30, and bmSCs from 4 young and lean patients. Cytoplasmic RNA from the cell populations was isolated and sequenced by RNA-Seq from the cell populations. Using our recently developed bioinformatics pipeline, we set out to quantify L1 expression and identify the few culprit L1s at specific loci that are actively transcribing to RNA in the ASC and bmSC samples. RESULTS/ANTICIPATED RESULTS: Here we provide proof of concept with the application of this novel method in characterizing full-length expressed L1s at the specific loci level in ASCs and bmSCs. We identified L1 loci that are commonly expressed in these cell types and observed an increase in L1 expression in the obese and old ASC cells compared with the young, lean ASCs and bmSCs. DISCUSSION/SIGNIFICANCE OF IMPACT: ASCs hold the promise of broad application in the biomedical field including regenerative treatment. There are reports that ASCs cultivated from older and obese donors are less effective in regenerative treatments. By demonstrating an increased expression of the mutagenic L1 element in ASCs from obese and old donors, this study provides further evidence suggesting the preferable use of ASCs from young and lean donors for regenerative therapies. These studies will also help us to understand the potential contribution of L1 expression to loss of stem cell function during the aging process.

2348

Lafora disease premature termination codons (PTCs) are likely candidates for suppression by aminoglycosides

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OBJECTIVES/SPECIFIC AIMS: A small molecule therapy is within reach to treat a molecular mechanism known to result in thousands of fatal diseases. For 10% of patients with a genetic disease, a nonsense/STOP mutation/premature termination codon (PTC) is the underlying cause of their malady. PTCs prematurely stop protein synthesis and yield truncated proteins. Truncated proteins typically provide little to no proper function or activity and are rapidly degraded; thus, disease is imminent. Recent work has demonstrated that small molecules including aminoglycosides can cause the ribosome to readthrough these PTCs. Thus, PTC readthrough with small molecules is a very attractive approach for treating diseases caused by PTCs. Small molecules that promote readthrough act on the ribosome and induce a ribosomal conformational change. In this conformation, the PTC is not recognized by the translational machinery and an amino acid is incorporated into the growing peptide chain, thus protein synthesis continues and does not stop. The use of a single small molecule to readthrough various PTC mutations has been repeatedly effective for in vitro studies and some of these have progressed to clinical trials. Although there has been success in defining these small molecules, the field has discovered that every PTC is unique and likely requires a different small molecule. Thus, developing a cell culture model to test read-through of Lafora PTCs and the functionality of the protein product is the first step to developing a readthrough therapy for a LD. METHODS/STUDY POPULATION: Method for in vitro quantification of

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