($p < 0.05$). Mechanistically, MELK inhibition resulted in decrease of FOXM1 protein levels 3 hours post-treatment. DISCUSSION/SIGNIFICANCE OF IMPACT: MELK is highly expressed in ALL and represents a novel therapeutic target likely via modulating FOXM1 activity. Functional and mechanistic studies will complement and ensure the success of the undergoing Phase I/II clinical trial of OTS167 in patients with refractory or relapsed AML, ALL, and other advanced hematologic malignancies.

2210

Anatomical substrates of cognitive fatigue in aging and in Parkinson's disease

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OBJECTIVES/SPECIFIC AIMS: Identify objective neurological substrates of cognitive fatigue in Parkinson's disease and in aging. METHODS/STUDY POPULATION: Structural and diffusion MRI. Behavioral assessments for aged adults and Parkinson's disease. RESULTS/ANTICIPATED RESULTS: Gray and white matter deficits that correlate with deficits in the basal ganglia for fatigued Parkinson's disease patients Versus anterior cingulate cortex in healthy aged adults with fatigue. DISCUSSION/SIGNIFICANCE OF IMPACT: Over 50% of patients with Parkison's disease and 38% of healthy older adults suffer from cognitive fatigue. However, diagnostics are limited to subjective surveys and there are no treatments for either population. Therefore, objective measures are greatly needed for better diagnosis and development of treatment targets.

2218

Investigating the correlation between rheumatoid arthritis and *Prevotella copri*

Hannah Fehlner-Peach

OBJECTIVES/SPECIFIC AIMS: Rheumatoid arthritis (RA) is one of the most prevalent systemic autoimmune diseases. It is caused by a combination of genetic and environmental factors. In humans, the intestinal microbe *Prevotella copri* strongly correlates with RA in previously untreated new-onset rheumatoid arthritis (NORA) patients. Metagenomic assembly of *P. copri* from NORA patients and healthy controls suggests genetic differences between *P. copri* from each group. In order to test the hypothesis that genetic differences in *P. copri* from arthritis patients promote arthritis, I am performing genomic comparison of primary *P. copri* isolates from NORA patients and healthy controls, and analysis of the immune response to *P. copri* in mice. Mice colonized with *P. copri* have increased susceptibility to DSS-induced weight loss and death compared with uncolonized controls. Future experiments will assess the local and systemic immune response in *P. copri*-colonized, DSS-treated mice. If this work is successful, then it may be possible to exploit genetic variation in *P. copri*. This could lead to new biomarkers for human disease or even insight into drug metabolism. METHODS/STUDY POPULATION: To validate a strategy to screen for the presence of *P. copri* in feces, qPCR primers were designed to amplify 8 regions across the 3.5 Mb *P. copri* reference genome using NCBI PrimerBlast. Primers were validated with DNA from feces for which *P. copri* abundance was previously determined by 16S rDNA sequencing. *P. copri* genome-specific primers were used to screen bacterial isolates from NORA patients and healthy controls. The 16S V3-V4 region was sequenced and compared with the *P. copri* reference 16S sequence to confirm >97% similarity. Genomes of 2 NORA patient isolates were sequenced on Illumina MiSeq, and sequences were compared with the reference genome. A strategy was developed to colonize mice with *P. copri*: 3-week-old C57BL/6 mice were treated with antibiotics in drinking water for 2 weeks, then switched to water for 2 days before oral gavage with *P. copri*; 6–7 days after inoculation, *P. copri* colonization was assessed by plating feces from inoculated mice, and by qPCR of fecal DNA with *P. copri*-specific primers. A systemic immune response to *P. copri* was assessed by microbe-specific ELISA for IgG and IgA in the sera of colonized mice. RESULTS/ANTICIPATED RESULTS: *P. copri* was detected in the stool of 20% of healthy individuals and 50% of NORA patients. *P. copri* was isolated form 4 healthy individuals and 6 NORA patients. Whole genomes of 96 primary isolates from NORA patients and healthy controls will be sequenced on the Illumina HiSeq platform, and their genomes will be assembled and compared using Spades software. For 2 *P. copri* isolates for a NORA patient, 89% of 250 bp reads aligned >95% to the *P. copri* reference genome. Mice can be colonized with *P. copri* gavaged at >106 CFU. *P. copri*-specific IgG and IgA were detected in the sera of colonized mice. DISCUSSION/SIGNIFICANCE OF IMPACT: Several primary isolates of *P. copri* have been collected from healthy controls and NORA patients, which will enable whole genome comparison of these isolates. For the 2 *P. copri* isolates sequenced, 89% of 250 bp reads aligned >95% to the *P. copri* reference genome, indicating variability between NORA patient *P. copri* strains and the *P. copri* reference genome. The establishment of colonization of mice with *P. copri* will allow further characterization of the immune response to *P. copri* at steady state and under pro-inflammatory conditions. Further, the systemic immune response to *P. copri* indicates that this microbe may have potential to play a role in systemic disease.

2219

Amyotrophic lateral sclerosis, stem cells and TALENted technology

Shaheen Kurani, Nicolas Madigan, Karl Clark, Stephen Ekker, Nathan Staff and Anthony Windebank

OBJECTIVES/SPECIFIC AIMS: The current treatment for amyotrophic lateral sclerosis (ALS) includes systemic delivery of neurotrophic factors (NTFs). Although this approach may seem theoretically sound, NTF efficacy within the central nervous system (CNS) is largely limited by the blood-brain barrier. Thus, a cell-based approach, which allows for targeted delivery of molecular therapies locally from the CNS, could lead to a paradigm shift in the field. METHODS/STUDY POPULATION: The Windebank and Staff group at Mayo Clinic completed a Phase I dose-escalation safety trial of autologous, adipose-derived mesenchymal stem cells (adMSCs) in an effort to move toward personalized medical treatment of ALS. The adMSCs were injected into the intrathecal space by lumbar puncture in 27 patients and the results showed an excellent safety profile across a range of doses. The team is moving forward with this idea by using gene-editing technology to develop clinical-grade, genetically modified autologous MSCs. The patient-derived adMSCs are modified at defined "safe-harbor" regions of the human genome through transcription activator-like effector nuclease (TALEN) technology. RESULTS/ANTICIPATED RESULTS: Our results show that electroporating adMSCs with plasmid DNA leads to efficient GFP or TALEN transgene expression, but yields low cell survival and a low rate of genetic modification. DISCUSSION/SIGNIFICANCE OF IMPACT: It can be concluded that: (1) TALEN technology may be used to target safe harbor loci for gene integration to produce therapeutic adMSC for ALS. (2) Primary barriers to adMSC modification are inefficient TALEN and donor template uptake, low cutting efficiency, and poor cell survival after electroporation. Future directions include optimizing the protocol to obtain 48 base pairs in the homology arms and increasing transfection efficiency.

2249

Gene expression signatures of acute respiratory syncytial virus infection in pediatric patients reveals insight into clinical pathogenesis

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OBJECTIVES/SPECIFIC AIMS: Respiratory viruses cause enormous medical burden, yet many of the specific virus and host genetic factors that impact pathogenesis are still largely unknown or poorly understood. To better understand the drivers of both acute clinical pathogenesis and long-term impacts, such as the development of asthma, we investigated the host response to respiratory syncytial virus (RSV) infections in pediatric patients. METHODS/STUDY POPULATION: We collected nasopharyngeal swabs from 32 pediatric patients with acute RSV infection. The swabs represented a mixed cell population including epithelial and immune cells at the active site of infection. Unbiased RNA sequencing with ribosomal RNA depletion allowed the simultaneous detection of host gene expression and RSV infection. We sequenced samples 2 × 75 bp on an Illumina NextSeq 500. Sequences were mapped to the human genome using the TopHat 2 aligner and FPKM estimation of reference genes and transcripts and assembly of novel transcripts were conducted with Cufflinks 2. RESULTS/ANTICIPATED RESULTS: During acute RSV infection we identified 7343 genes that were significantly expressed. Pathway analysis using KEGG revealed significant upregulation of pathways involved in innate immune response infection, ribosome function, oxidative phosphorylation, spliceosome and autoimmune disorders. We found high levels of innate immune response genes including CXCL8, IFITM1, IFITM2, IFITM3, IL1RN, and ISG15. In comparing RSV subtype A to RSV B we found significant differential expression of multiple noncoding RNAs. DISCUSSION/SIGNIFICANCE OF IMPACT: Examination of the host gene response during acute RSV infections, yielded important insight into the mechanisms that cause clinical pathogenesis and may provide understanding of the mechanisms that lead to known long-term impacts, such as the development of asthma. Together, this data may be used to guide clinical treatment and management decisions for children with severe RSV infections.

https://doi.org/10.1017/cts.2017.211 Published online by Cambridge University Press