decreased significantly (-9.7 [3.82] Δ/SD; p = 0.044). Other bio-markers, RDW% (-0.2 [0.05] Δ/SD; p = 0.009) and MCV (-2.3 [0.33] Δ/SD; p = 0004), were significantly reduced. All other safety parameters were not altered. Six participants reported mild to moderate adverse events (acid indigestion) and were lost to follow-up. Depression scores significantly increased (+4.0 [0.75] Δ/SD; p = 0.002)). Results were similar with and without intent to treat analysis. DISCUSSION/SIGNIFICANCE OF IMPACT: Decreased FSH, but not IR, was observed following six months of GLYLO in postmenopausal women with obesity. Significant alterations in HDL, depression, RDW%, and MCV warrant further investigation. Findings are limited by the small sample size and loss to follow-up. Randomized, controlled trials are needed to confirm these results.

518
Modeling of cancer mutations found in pediatric DICER1 syndrome informs novel therapeutic targeting strategies

David Jee[1], Seungjae Lee[2], Dapeng Yang[2], Robert Rickert[2], Renfu Shang[2], Danwei Huangfu[2] and Eric C. Lai[2]
[1]Weill Cornell Medical College and [2]Memorial Sloan Kettering Cancer Center

OBJECTIVES/GOALS: Large-scale tumor sequencing efforts have led to annotations of novel cancer hotspot mutations that may underlie driver or cooperative function. We have sought to define the molecular consequences of such hotspots associated with pediatric DICER1 syndrome cancers, with the ultimate goal of revealing novel targets that may inform new standards of care. METHODS/STUDY POPULATION: We have performed genomic analysis to identify tumor types (in TCGA and MSK-IMPACT patient data) for which mutations in the Dicer1 gene (encoding Dicer protein) emerge as the dominant signature of driver function. As Dicer is a critical RNA processing factor responsible for the generation of microRNAs, which are posttranscriptional gene regulatory molecules, we have modeled these mutations in human embryonic stem cells in order to study the direct effects on miRNAs and their target genes in an isogenic background. In addition to providing the required setting for unambiguous attribution of function to specific mutations, clonal human ES cells offer an opportunity for modeling of both developmental and cancer requirements associated with altered Dicer function. RESULTS/ANTICIPATED RESULTS: Through generation of genomics and functional datasets from matched genotypes in Dicer mutated human ES cells, we have identified specific alterations in miRNAs and their effects on target genes. Unexpectedly, we found direct evidence for both loss of function and gain of function attributable to Dicer mutations. In addition, through integrated analysis of genomic data from tumor sequencing datasets and our human ES cell models, we have identified potential miRNA and target gene alterations that underlie tumorigenic potential, nominating gene candidates for targeted therapy in DICER1 syndrome. Direct mouse modeling of such candidate gene targets has revealed evidence for driver function of identified miRNA and their targets. DISCUSSION/SIGNIFICANCE OF IMPACT: DICER1 syndrome cancers comprise a wide variety of rare pediatric tumor types. Presently, we still lack an effective standard of care. Furthermore, the previous lack of molecular profiling precluded targeted therapy opportunities. Our precise knock-in modeling of Dicer hotspots and deep profiling of relevant tumors now provide candidate targets.

519
Staphylococcus colonization drives IFN-mediated monocyte recruitment and skin barrier disruption in cutaneous lupus erythematosus lesions

Lisa Abernathy-Close, Joseph Mears, Allison C. Billi, Sirisha Sirobhushanam, Annie Lu, Zeran Zhang, Amy Hurst and J Michelle Kahlenberg
University of Michigan

OBJECTIVES/GOALS: Cutaneous lupus erythematosus (CLE) is an inflammatory skin manifestation of lupus. CLE lesions are frequently colonized by Staphylococcus aureus, a microbe known to promote IFN production and inflammation. Here, we investigate whether type I IFN and inflammatory gene signatures in CLE lesions can be modulated with a topical antibiotic treatment. METHODS/STUDY POPULATION: SLE patients with active CLE lesions (n = 12) were recruited and randomized into a week of topical treatment with either 2% mupirocin or petroleum jelly vehicle. Paired samples were collected before and after 7 days of treatment to assess microbial lesional skin responses. Microbial samples from nares and lesional skin were used to determine baseline and posttreatment Staphylococcus abundance and microbial community profiles by 16S rRNA gene sequencing. Inflammatory responses were evaluated by bulk RNA sequencing of lesional skin biopsies. Immunophenotyping of CLE lesions was performed using CIBERSORTx to deconvolute the RNA-seq data into predicted cell populations impacted by treatment. RESULTS/ANTICIPATED RESULTS: We identified 173 differentially expressed genes in CLE lesions after topical mupirocin treatment. Mupirocin treatment decreased the abundance of Staphylococcus associated with CLE lesions without altering the overall diversity of the skin microbiota relative to vehicle. Decreased lesional Staphylococcus burden correlated with decreased IFN pathway signaling and inflammatory gene expression and increased barrier dysfunction. Interestingly, mupirocin treatment lowered skin monocyte levels, and this mupirocin-associated depletion of monocytes correlated with decreased inflammatory gene expression. DISCUSSION/SIGNIFICANCE OF IMPACT: Mupirocin treatment decreased lesional Staphylococcus burden and this correlated with decreased IFN signaling and inflammatory gene expression. This study suggests a topical antibiotic could be employed to decrease lupus skin inflammation and type I IFN responses by reducing Staphylococcus colonization.

520
Investigating the impact of hematopoietic cell transplant on morbidity and mortality of children with sickle cell disease*

Sadie Mason, Elizabeth O. Stenger, Marianne M. Yee and Kirsten M. Williams
Emory University and Aflac Cancer and Blood Disorders Center at Children's Healthcare of Atlanta

OBJECTIVES/GOALS: Our main objective was to compare 5-year survival and organ function between patients with sickle cell disease (SCD) who underwent hematopoietic cell transplant (HCT) and those who did not undergo HCT. We hypothesized that organ function would be improved in those with SCD who underwent HCT when compared to those who remained on standard therapy.