that subjects with nonresolving SA-PARDS, defined as intubation and mechanical ventilation, will have a monocyte/macrophage transcriptome characterized by continued hyper-inflammation (M1-like phenotype) that does not transition over time to an anti-inflammatory and pro-repair phenotype (M2-like). Additionally, we expect to see that subjects with non-resolving SA-PARDS will have evidence of continued inflammation driven by hyper-inflammatory neutrophils. Finally, we expect that subjects with non-resolving SA-PARDS will have epithelial cells characterized by continued upregulation of canonical pathways of innate immunity including interferon signaling and the damage associated molecular pattern recognition pathway. DISCUSSION/SIGNIFICANCE OF IMPACT: The discovery of immuno-endotypes in SA-PARDS would represent a major step toward developing precision medicine therapies for this group of patients. It would simultaneously provide a strategy to reduce biological heterogeneity and identify novel pathways and targets for therapy.

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Effectiveness of the addition of yoga to a behavioral weight loss intervention on measures of glycemic control for adults with overweight or obesity (MOVE for Health Study): A methods description

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OBJECTIVES/GOALS: * Examination of the acute glucose-lowering response to physical activity within a comprehensive behavioral weight loss intervention in adults without T2DM. * Explore whether the acute response to yogadiffers from the acute response to brisk walking and to examine whether these responses vary across the intervention period. METHODS/STUDY POPULATION: Participants in the behavioral weight loss and aerobic exercise group will start with 100 minutes per week of moderate-intensity aerobic activity, increasing every four weeks to 250–300 minutes, spread over five days. Activities will be self-selected, such as walking. Participants in the combined aerobic exercise and yoga group will do aerobic exercise three days a week and yoga two days a week, also progressing from 100 to 250–300 minutes weekly. All participants will follow an energy-restricted diet (1200–1800 kcal/day) and participate in weekly education sessions to learn lifestyle modification skills for successful weight loss. The study will explore differences in acute responses to yoga versus walking and how these vary during the intervention, controlling for initial and changing weight status. RESULTS/ANTICIPATED RESULTS: Primary and secondary outcomes from the parent study will include body weight, BMI, body composition (via DXA), cardiorespiratory fitness, energy intake, and physical activity. Glucose and insulin levels will be measured pre- and post-exercise, with HOMA-IR computed. Continuous glucose monitoring (CGM) will be used to track glucose responses during each session, with the area under the curve (AUC) as the primary metric. The study will also explore advanced CGM analytics in collaboration with the KUMC Diabetes Institute that will include in-depth analyzation of peak and trough change velocity as well as novel correlations betwen glucose dynamics and physical activity patterns with an aim to uncover insights that transcend conventional CGM analyses. DISCUSSION/SIGNIFICANCE OF IMPACT: This study uses advanced CGM analytics to examine glucose control during physical activity, collaborating with experts to create comprehensive models for glucose fluctuations. It compares acute responses to walking and yoga, addressing a key gap in research, with potential clinical insights for managing glucose in obesity.

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Unraveling the pathogenicity of a novel variant in Diamond Blackfan anemia*

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OBJECTIVES/GOALS: Diamond Blackfan anemia (DBA) is caused by loss of ribosomal proteins leading to death of red blood cell progenitors. We identified a novel heterozygous variant (c.167 +769C>T) in RPL30 in a patient with DBA. We hypothesized that this variant, in a gene not previously studied in DBA, would demonstrate DBA phenotype and reveal early drivers of disease. METHODS/STUDY POPULATION: To study the role of our novel variant, we developed an induced pluripotent stem cell (iPSC) model, including wild type (WT) and CRISPR-edited RPL30 mutant clones. We differentiated the iPSC into hematopoietic stem cells, identified cell populations with flow cytometry, and applied single-cell RNA sequencing. We identified erythroid clusters for differential gene expression analysis, using R Studio DESeq followed by Gene Ontology (GO) enrichment analysis. We are differentiating cells into red blood cells for further comparison with flow cytometry, bulk RNA sequencing, protein analysis, and hemoglobin staining. Our approach has relied on multidisciplinary expertise in clinical hematology and genetics, basic science study of ribosomes, computational biology, stem cell, and hematopoietic biology. RESULTS/ANTICIPATED RESULTS: Compared to WT hematopoietic stem cells, RPL30mutant cells had significantly decreased expression of RPL30. Analysis of top differentially expressed genes revealed downregulation of HSPA1A which encodes heat shock protein 70 (HSP70), chaperone of a critical red blood cell transcription factor. Loss of HSP70 protein has been implicated in RPL-mutated red blood cells previously as a potential modulator of severe DBA phenotype. Upon GO enrichment analysis of downregulated genes, biologic process terms GO:0042254 ribosome biogenesis, GO:1903708 positive regulation of hemopoiesis, and GO:0045646 regulation of erythrocyte differentiation were all highlighted as driver terms. We expect further differentiation to reveal early death of RPL30mutant cells with associated downregulated HSP70. DISCUSSION/SIGNIFICANCE OF IMPACT: Our results support our hypothesis that the RPL30 variant downregulates erythropoiesis, with a potential early role of HSP70 protein. Upon completion of our study, we will demonstrate the role of RPL30in DBA pathogenesis as well as provide understanding of its drivers, which is critical for improved management of this disease.

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Foundations for prescribing song-based therapies: A quantitative analysis of laryngeal exercises*

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OBJECTIVES/GOALS: Explore and compare the functional mechanisms of song-based exercises compared to speech-language

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