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The transcriptional activity of *Mycobacterium tuberculosis* in vivo and its influence on treatment outcome*

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OBJECTIVES/GOALS: The overall goal of this project is to determine bacterial transcriptional signatures from clinical sputum and assess their potential to monitor treatment response and predict the outcome of drug therapy in patients with tuberculosis (TB). METHODS/STUDY POPULATION: We are developing a novel transcript capture sequencing (TC-Seq) approach to sequence the mRNA of *Mycobacterium tuberculosis* (Mtb) and analyze transcriptomes from clinical samples containing minimal amounts of bacterial RNA. This protocol generates single-stranded biotinylated probes from Mtb DNA. Probes are hybridized to and allow enrichment of Mtb-specific mRNA within next-generation RNA sequencing libraries. We will apply TC-Seq to sputum samples collected throughout an 18-month Phase II clinical trial investigating response to TB treatment to compare the transcriptome of Mtb between patients whose treatment results in cure or relapse. RESULTS/ANTICIPATED RESULTS: We have refined a technique to generate biotinylated probes starting from DNA of lab grown Mtb. This protocol achieves robust and unbiased sampling of the Mtb transcriptome from mixed samples containing both human and Mtb RNA. Preliminary sequencing of clinical sputum collected pretreatment has generated 1–4 million Mtb-specific reads, a sequencing depth that allows examination of the entire bacterial transcriptome. We will measure differential gene expression before and during treatment as well as between cure and relapse cases. These results will allow us to characterize bacterial response to treatment and identify bacterial markers that correlate with relapse. DISCUSSION/SIGNIFICANCE OF IMPACT: Understanding Mtb activity during treatment will offer new ways to assess the efficacy of different treatment regimens. Crucially, identifying clear bacterial markers that demarcate a cure or relapse outcome will have a significant impact on determining patient eligibility for shorter drug therapy.

Contemporary Research Challenges

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Developing dynamic dialogue: Enhancing provider–patient communication for HPV vaccination in clinics serving rural communities

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OBJECTIVES/GOALS: This poster discusses key methodological and theoretical issues in translation and implementation for improving HPV vaccine recommendations in clinics serving rural communities. METHODS/STUDY POPULATION: Leveraging implementation science, the study of how to improve the uptake of evidence-based practices, this pilot study uses a mixed-methods effectiveness-implementation design to engage local experts in identifying a bundle of locally-tailored implementation strategies to facilitate uptake of evidence-based HPV vaccine recommendations. In partnership with the University of Arkansas for Medical Sciences Rural Research Network, we will follow an evidence-based quality improvement process to develop locally tailored implementation strategies, which we will then evaluate for acceptability, feasibility, and effectiveness. RESULTS/ANTICIPATED RESULTS: This study aims to generate actionable insights into the design and implementation of tailored, evidence-based communication strategies that can be scaled to improve HPV vaccine uptake in rural communities. Findings from this pilot study will be used to support a future full-scale Hybrid-Type 3 effectiveness-implementation trial to evaluate the bundle of tailored implementation strategies. DISCUSSION/SIGNIFICANCE OF IMPACT: By addressing the rural-specific determinants of evidence-based HPV vaccine recommendations, this research will contribute to a deeper understanding of how to support high-quality, evidence-based provider recommendations in rural, underserved communities, and will mitigate rural disparities in HPV-related cancers.

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Imaging and CSF biomarkers to optimize neurosurgical intervention for post-hemorrhagic hydrocephalus of prematurity

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OBJECTIVES/GOALS: The timing of neurosurgery is highly variable for post-hemorrhagic hydrocephalus (PHH) of prematurity. We sought to utilize microvascular imaging (MVI) in ultrasound (US) to identify biomarkers to discern the opportune time for intervention and to analyze the cerebrospinal fluid (CSF) characteristics as they pertain to neurosurgical outcome. METHODS/STUDY POPULATION: The inclusion criteria for the study are admission to the neonatal intensive care unit (NICU) with a diagnosis of Papile grade III or IV. Exclusion criteria are congenital hydrocephalus and hydrocephalus secondary to myelomeningocele/brain tumor/vascular malformation. We are a level IV tertiary referral center. Our current clinical care pathway utilizes brain US at admission and at weekly intervals. Patients who meet certain clinical and radiographic parameters undergo temporary or permanent CSF diversion. RESULTS/ANTICIPATED RESULTS: NEL was implemented at our institution for PHH of prematurity in fall 2022. To date, we have had 20 patients who were diagnosed with grade III or IV IVH, of which 12 qualified for NEL. Our preliminary safety and feasibility results as well as the innovative bedside technique pioneered at our institution are currently in revision stages for publication. Preliminary results of the MVI data have yielded that hyperemia may confer venous congestion in the germinal matrix, which should then alert the neurosurgeon to delay any intervention to avoid progression of intraventricular blood. With regard to CSF

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