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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

https://doi.org/10.1017/cts.2024.782 Published online by Cambridge University Press

characteristics, we anticipate that protein, cell count, hemoglobin, iron, and ferritin will decrease with NEL. DISCUSSION/SIGNIFICANCE OF IMPACT: The timing of PHH of prematurity is highly variable. We expect that MVI will offer radiographic biomarkers to guide optimal timing of neurosurgical intervention. A better understanding of CSF characteristics could potentially educate the neurosurgeon with regard to optimal timing of permanent CSF diversion based on specific CSF parameters.

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## CEACAM6 molecules mediate cell adhesion and signaling by modifying integrins in human solid tumors

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OBJECTIVES/GOALS: To determine the role of carcinoembryonic antigen cell adhesion molecule 6 (CEACAM6) in signaling cascade and interaction with other cell surface proteins in human epithelial solid tumors such pancreatic adenocarcinoma and colon cancer METHODS/STUDY POPULATION: In this study, we employed three-dimensional (3D) tumor models to replicate the in vivo tumor microenvironment better, allowing for a more accurate assessment of cellular responses compared to traditional two-dimensional (2D) cultures. We used immunoprecipitate to pull down the CEACAM6 protein and investigate the integrins expression level. RESULTS/ANTICIPATED RESULTS: The expression and functional activity of CEACAM6 are susceptible to modulation by various surface proteins, leading to notable alterations in cellular behavior. Integrins, particularly Integrin B4, are one such protein whose expression is influenced by CEACAM6-mediated intracellular signaling cascades, suggesting a complex interplay that enhances CEACAM6 activation.The 3D models facilitate cell–cell interactions, enabling tumor cells to proliferate and undergo metabolic changes that reflect actual tumor biology. Thereby enhancing the relevance of crosstalk between CEACAM6 and integrins. These findings underscore the potential of CEACAM6 as a promising therapeutic target. They reveal a molecular mechanism that could inform the development of innovative therapeutic strategies in cancer. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings underscore the potential of CEACAM6 as a promising therapeutic target, revealing a novel molecular mechanism that could inform the development of innovative therapeutic strategies for pancreatic and colon cancer and potentially other malignancies.

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## Methods for determining the conclusiveness of systematic review results: A living scoping review

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OBJECTIVES/GOALS: Understanding systematic review results help prioritise more valuable studies. However, evaluating whether a systematic review has conclusively answered a question is difficult, and it is unclear which tools are available for such assessments. Thus, we mapped the extent of methods for determining the conclusiveness of systematic review results. METHODS/STUDY POPULATION: We searched Medline (Ovid), EMBASE (Ovid), and Web of Science to find papers with methods to determine whether systematic review results were conclusive or should be updated. The characteristics of primary references for included methods are presented. We classified and summarized available methods. RESULTS/ANTICIPATED RESULTS: A total of 58 unique methods were identified. Many have been published since 2010 and often did not include a worked example. We found 25 mathematical methods for the conclusiveness of meta-analyses, which included cumulative meta-analysis, fail-safe number, fragility index, prediction and machine learning model, simulation-based power, conditional power, and graphical approaches. There were 15 methods for the conclusiveness of cumulative meta-analyses, such as quality control approach, trial sequential analysis, sequential meta-analysis, and law of iterated logarithm. And, 18 methods assessed the conclusiveness of systematic reviews: GRADE framework, the strength of a body of evidence approach, methods for assessing the need to update a systematic review, and methods for specific clinical domains. DISCUSSION/SIGNIFICANCE OF IMPACT: We found a wide range of methods that can be used to determine the conclusiveness of systematic review results. End-users of systematic reviews can review our results to find the most appropriate methods for their contexts and decisions.

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## Collaborative method to improve investigator assistance for study planning

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OBJECTIVES/GOALS: Planning research studies can be daunting for early-career investigators. The UW Madison Institute for Clinical and Translational Research (ICTR) has many services to assist, but navigating them can be convoluted. Therefore, we developed a method to streamline services for investigators. METHODS/STUDY POPULATION: Investigators were reaching out to ICTR research support services for assistance in the wrong order, delaying their study progress. To streamline ICTR services and improve investigator support, we developed the ICTR COllaborative Network (ICON) that meets weekly to discuss investigator needs and how best ICTR services can assist them. This group consists of members from ICTR's Research and Protocol Development Program, the Recruitment and Retention Resource Center, and the Collaborative Center for Health Equity. After discussion and decision-making, a member of the group schedules a studio, bringing key services together at one time to help investigators more efficiently. RESULTS/ANTICIPATED RESULTS: The group has worked with 22 investigators, decreasing the time to study implementation. One investigator indicated ICON saved her team over four months of work. Other investigators indicated the assistance with finding community partners and collaborators was essential to their success. We expect ICON, with its goal to streamline regulatory submissions and study planning, will continue to help investigators improve organization during study start up and execution, while enhancing recruitment strategies. This will result in quicker study completion and the capability to move forward with future projects and grant submissions. DISCUSSION/SIGNIFICANCE OF IMPACT: ICON streamlined the consult process, improved

https://doi.org/10.1017/cts.2024.782 Published online by Cambridge University Press