Precision Medicine/Health

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Genetic optimization of low-compute techniques for peritoneal lesion detection during staging laparoscopy†*

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OBJECTIVES/GOALS: Accurate detection of peritoneal metastases during staging laparoscopy is critical for treatment planning, yet even skilled surgeons miss lesions. Thus, an optimized low-compute image-processing pipeline that maximizes recall while filtering non-lesion tissue can assist with this task. METHODS/STUDY POPULATION: The study population consists of 1414 images containing 5943 annotated lesions from 163 subjects undergoing staging laparoscopy for GI-origin cancer. All images were obtained during staging laparoscopy by the senior author (TS). From the original images, five binary masks were produced using red, green, blue, Canny, and Gabor filters. These were combined into a composite image, thresholded, and binarized after smoothing into a final prediction. Given the complex 16-dimensional space, a genetic fitness algorithm was used to optimize the final set of parameters to maximize recall while also penalizing coverage. RESULTS/ANTICIPATED RESULTS: Preliminary data show that the algorithm has a mean recall of 0.90 ± 0.18 and a mean predicted positive rate of 0.48 ± 0.20. Thus, the algorithm is able to exclude 52% of the image area while capturing 90% of lesion pixels. We plan to further validate these results and maximize this pipeline to demonstrate that simple tools can yield useful results. DISCUSSION/SIGNIFICANCE OF IMPACT: This project aims to develop a computationally simple image-processing pipeline that can achieve high recall while minimizing predicted positive coverage. This will be useful to highlight where lesions are most likely to exist and may be combined in the future with classification models.

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Early childhood mental health risk calculators as a decision tool in routine care: From generation to implementation†

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OBJECTIVES/GOALS: To advance the clinical utility of a risk calculator for identifying young children's mental health risk, we: 1) replicate an established mental health risk algorithm in two toddler-preschool samples; 2) determine added predictive value of child and parenting assets, advancing a strengths-based approach; and 3) discuss next steps for implementation. METHODS/STUDY POPULATION: Data were from two studies: A population-based Cohort 1 (N=2,763) and an independent risk-enriched Cohort 2 (N=323). In Cohort 1, children (48% girls) were 51.9% Black, 21.4% White, and 2.7% Other Race; 23.8% were Hispanic. In Cohort 2, children (44% girls) were 49.2% White, 38.1% Black, and 8.4% Other Race; 11.1% were Hispanic. Risks and assets were assessed in toddlerhood/early-preschool, and psychopathology was measured later in preschool. Epidemiologic risk prediction methods were applied to: 1) replicate the published risk model that includes demographics, irritability, and adverse childhood experiences (ACEs); 2) examine added predictive utility of child and parenting assets. Predictive utility was based on area under the curve (AUC) and/or the integrated discrimination improvement (IDI). RESULTS/ANTICIPATED RESULTS: The previously published risk algorithm that includes demographics, child irritability, and child ACEs was replicated in both cohorts (AUC=.70 for both; IDI=.07 in Cohort 1 and .06 in Cohort 2). Via the IDI, there was added predictive utility of child assets (i.e., social competence) in both cohorts (IDI=0.008 in Cohort 1 and 0.02 in Cohort 2), as well as added predictive utility of parenting assets (i.e., parenting involvement/self-efficacy) in Cohort 1 (IDI=0.004). Preliminary evidence for barriers/facilitators regarding early childhood mental health screening in pediatric primary care and preschool settings will also be discussed, as part of a roadmap for future implementation of the calculator in routine care. DISCUSSION/SIGNIFICANCE OF IMPACT: Improving early mental health risk algorithms through a strengths-based lens is essential for evidence-based and equitable decision-making. We have laid the groundwork for future implementation of a mental health decision tool in routine care of young children, from pediatric primary care to preschool.

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Suiting up T cells: Strengthening membrane "armor" to improve anti-cancer immunity†

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OBJECTIVES/GOALS: The plasma membrane (PM) is the nexus for cell signaling, where lipid composition governs receptor organization and T cell function. We aim to define PM dynamics in T cell states and develop PM-based strategies to preserve anti-tumor activity. METHODS/STUDY POPULATION: As such, we induced a dysfunctional T cell state, known as T cell exhaustion, through chronic stimulation or TGF-β1, hypoxia, and tumor cell co-culture and measured membrane biophysical properties through ratiometric confocal imaging of molecular probe Di-4-ANEPPDHQ. Complementary biochemical data from shotgun lipidomic analysis, immunofluorescence staining, and biochemical fluorescent assays paint a more complex picture of membrane fluidity changes during T cell exhaustion. RESULTS/ANTICIPATED RESULTS: In both cases, we observed

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