Informatics and Data Science

298

Improving AI Assessment of Cutaneous Chronic Graft-Versus-Host Disease using Unlabeled Patient Photographs†

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OBJECTIVES/GOALS: Measuring the area of skin involvement in chronic graft-versus-host disease (cGVHD) relies on costly, time-consuming manual assessment, with high disagreement among experts (>20%). Our published AI method, trained on labeled 3D photos, showed promise for delineating affected areas. We aim to improve its performance using unlabeled 2D photos. METHODS/STUDY POPULATION: Our published AI model (baseline) was trained on 360 labeled photos of 36 cGVHD patients,from a 3D camera with calibrated distance and lighting.Our gold standard labels were contours around affected skin, marked by a trained expert. A second unlabeledcohort of 974 standard 2D photos of 8 cGVHD patients was used to improve the baseline model. First the baseline model predicted affected areas on the unlabeled photos. Photos with good predictions were added to the training set with their AI-predicted labels. The model was then re-trained with the expanded labeled set. Models were successively trained with more AI labels until performance stopped improving. AI performance was assessed on a test set of 20 photos from 20 patients unseen during training, labeled by 4 experts to improve accuracy. RESULTS/ANTICIPATED RESULTS: Model performance was calculated by comparing against the gold standard labels on the test set. To quantify the spatial overlap of labeled areas the Dice coefficient was used (0 is no overlap, 1 is complete agreement), where higher values are better. To estimate clinical error we used surface area error (Error), where lower values are better. On the test set, the baseline model had a median Dice of 0.57 [interquartile range: 0.39 – 0.82] and Error of 57.6% [20.2 – 103.3%]. Re-training with additional AI-predicted labels from 8 new patients, the model yielded a median Dice of 0.60 [0.35 – 0.80] and Error of 50% [12.5 – 103.8%]. This approach is being expanded to a further 300 unlabeled patients, where we anticipate significant improvements to AI performance and consistency. DISCUSSION/SIGNIFICANCE: Evaluating AI models in standard photos could provide a consistent method of assessing and tracking cutaneous cGVHD and relieve the burden of costly expert assessment. A reliable automated AI tool would provide a meaningful improvement to the current standard of manual assessment and could be easily applied to large patient cohorts.

299

A CTS team approach to assess the in vitro toxicity of microplastic fibers to human lung epithelial cells cultured at an air-liquid interface†

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OBJECTIVES/GOALS: Our goal is to determine whether microplastic fibers (MPFs) provide signals for dendritic cell-induced Th2 polarization via epithelial-cell-derived thymic stromal lymphopoietin (TSLP). We seek to highlight a potential mechanism for MPF-induced airway toxicity associated with asthma exacerbation. METHODS/STUDY POPULATION: Primary human bronchial epithelial cells (NHBEs) were grown and differentiated at an air-liquid interface. Dyed and undyed polyester MPFs (14x45 μm) generated using a cryomicrotome were delivered to NHBEs through a custom designed mesh-hopper system. After the exposure period (6, 12, 24 hrs), cell viability was assessed using alamarBlue, and RT-qPCR was performed to determine mRNA expression of asthma associated genes (i.e., TSLP, IL-13, IL-33, etc.,) in NHBEs. Bulk mRNA-sequencing followed by bioinformatics will be performed to observe other plausible pathways tweaked by lung cell exposure to MPFs. RESULTS/ANTICIPATED RESULTS: Through gravimetric analysis, it was determined that the mesh-hopper system can achieve delivery efficiencies of at least 85% for as low as 500 fibers. Following exposure, results show polyester MPFs (500 - 1,000 fibers) exposed to NHBEs at multiple time points (6, 12, 24 hrs) did not result in a statistically significant decrease in cell viability. Treatment with 500 undyed MPFs resulted in a slight increase in TSLP expression at 6 hrs that decreased over time, whereas all other treatment groups resulted in TSLP downregulation. Similarly, 500 undyed MPFs resulted in an increase in IL-13 expression at both 6 and 12 hrs with all other treatment groups leading to IL-13 downregulation. We anticipate the RNA-seq results will show pro-inflammatory pathways are highly targeted following NHBE exposure to MPFs. DISCUSSION/SIGNIFICANCE: This study is one of the first to mechanistically assess the impact of MPFs on lung cells while simultaneously addressing the need for a reliable system that delivers MPFs to ALI cultures to better mimic inhalation and avoid inadequate resuspension of particles in liquid medium.

300

Psilocybin-induced changes in neural reactivity to alcohol and emotional cues in patients with alcohol use disorder: An fMRI pilot study†

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OBJECTIVES/GOALS: This pilot study investigated psilocybin-induced changes in neural reactivity to alcohol and emotional cues in patients with alcohol use disorder (AUD). METHODS/STUDY POPULATION: Participants were recruited from a phase II, randomized, double-blind, placebo-controlled clinical trial investigating psilocybin-assisted therapy (PAT) for the treatment of AUD (NCT02061293). Eleven adult patients completed task-based blood oxygen dependent functional magnetic resonance imaging (fMRI)

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approximately 3 days before and 2 days after receiving 25 mg of psilocybin (n = 5) or 50 mg of diphenhydramine (n = 6). Visual alcohol and emotionally valanced (positive, negative, or neutral) stimuli were presented in block design. RESULTS/ANTICIPATED RESULTS: Across both alcohol and emotional cues, psilocybin increased activity in the medial and lateral prefrontal cortex (PFC) and left caudate, and decreased activity in the insular, motor, temporal, parietal, and occipital cortices, and cerebellum. Unique to negative cues, psilocybin increased supramarginal gyrus activity; unique to positive cues, psilocybin increased right hippocampus activity and decreased left hippocampus activity. DISCUSSION/SIGNIFICANCE: Greater PFC and caudate engagement and concomitant insula, motor, and cerebellar disengagement suggests enhanced goal-directed action, improved emotional regulation, and diminished craving. The robust changes in brain activity observed in this pilot study warrant larger neuroimaging studies to elucidate neural mechanisms of PAT.

302

Diagnostic Evidence Gauge of Spatial Transcriptomics (DEGAS-ST): Using transfer learning to map clinical data to spatial transcriptomics in prostate cancer†

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OBJECTIVES/GOALS: The 'field effect' is a concept in pathology that pre-malignant tissue changes forecast health. Spatial transcriptomics could detect these changes earlier than histopathology, suggesting new early cancer screening methods. Knowing how normal tissue damage relates to cancer's origin and progression may improve long-term outcomes. METHODS/STUDY POPULATION: We trained DEGAS, our machine learning framework, with prostate cancer data, combining both general cancer patterns and in-depth genetic information from individual tumors. The Tumor Cancer Genome Atlas (TCGA) shows how gene patterns in tumors relate to patient outcomes, emphasizing the differences between tumors from different patients (intertumor). On the other hand, spatial transcriptomics (ST) shows the genetic variety within a single tumor (intratumor) but has limited samples, making it hard to know which genetic differences are important for treatment. DEGAS bridges these areas by finding tissue sections that resemble those in TCGA profiles and are key indicators of patient survival. DEGAS serves as a valuable tool for generating clinically-important hypotheses. RESULTS/ANTICIPATED RESULTS: DEGAS identified benign-appearing glands in a normal prostate as being highly associated with poor progression-free survival. These glands have transcriptional signatures similar to high-grade prostate cancer. We confirmed this finding in a separate prostate cancer ST dataset. By integrating single cell (SC) data we demonstrated that cells annotated as cancerous in the SC data map to regions of benign glands in the ST dataset. We pinpoint several genes, chiefly Microseminoprotein-β (MSMB, PSP94), where reduced expression is highly correlated with poor progression-free survival. Cell type specific differential expression analysis further revealed that loss of MSMB expression associated with poor outcomes occurs specifically in luminal epithelia, the putative progenitor of prostate cancer. DISCUSSION/SIGNIFICANCE: DEGAS reveals that normal-appearing tissue can be highly-associated with tumor progression and underscores the importance of the 'field effect' in cancer research. Traditional analysis may miss such nuance, hiding key transitional cell states. Validating gene markers could boost early cancer detection and understanding of metastasis.

303

Social Network Analysis of Patient Sharing Among Providers: Implications for Analyzing Disparities in Cancer Screening

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OBJECTIVES/GOALS: Many providers share patients resulting in networks where clinical information is exchanged, and which can impact the quality and efficiency of care. Here we analyzed the network properties of a primary care service area (PCSA) in Harris County TX, motivating our ongoing analysis of how they are associated with disparities in cancer screening. METHODS/STUDY POPULATION: Data.All providers (n=731, Medicare 2018) from the PCSA with the most providers in Harris County TX, with gender, specialty, and the number of shared patients. Method. Modeled the data as a network consisting of provider nodes, connected in pairs by edges if they shared >11 patients (an empirically-determined threshold). Analyzed the network structure using (1) modularity maximization and its significance to identify densely-connected communities; (2) degree centralization to measure whether a few providers shared many patients, and betweenness centralization to measure whether a few providers connected densely-connected communities; and (3) chi-squared to measure if pairs of connected providers tended to be of the same gender compared to disconnected provider pairs. RESULTS/ANTICIPATED RESULTS: The results (Fig. 1, http://www.skbhavnani.com/DIVA/Images/Fig-1-SNA-Network.jpg [http://www.skbhavnani.com/DIVA/Images/Fig-1-SNA-Network.jpg]) revealed a fragmented network with 120 small components (connected subnetworks, not part of any larger connected subnetwork), and 1 large component. The large component (n=244) had strong and significant modularity (Q=0.73, z=53.13, P<.001) with communities of providers that shared more patients than expected by chance; low degree centralization (dc=0.11) suggesting that no provider dominated patient sharing, in addition to high and significant betweenness centralization (bc=0.5, P<.01) suggesting that a few providers were responsible for connecting the densely-connected communities; and a significant gender bias (X2=10.05, df=1, P< .01) among those that shared patients, versus those that did not. DISCUSSION/SIGNIFICANCE: The analysis revealed a specific type of vulnerability (betweenness) for network fragmentation, and a gender bias in how patients were shared. These results motivated our ongoing analysis on how the network properties are associated with disparity in cancer screening within PCSAs across Texas.

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