received glucocorticoids, vasopressors, and respiratory support, suffering progressive symptoms of cytokine release syndrome, and death (table 2).

Conclusions The IL-1 inhibitor, anakinra, has shown efficacy in ameliorating signs and symptoms of cytokine release syndrome caused by immunotherapy administration. Mechanistic similarities between cytokine release syndrome and COVID-19 related pulmonary damage suggest that this pharmacotherapeutic intervention could decrease mortality and need for mechanical ventilation in patients infected with COVID-19.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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Machine learning, artificial intelligence, and computational modeling

DEVELOPING GENERALIZABLE DEEP LEARNING MODELS FOR TUMOR SEGMENTATION IN PATHOLOGY IMAGES TO ENABLE THE IDENTIFICATION OF PREDICTIVE BIOMARKERS FOR IMMUNOTHERAPIES

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Background Despite recent advances in cancer immunotherapies, their efficacies vary significantly among patients. To better understand the mechanisms of drug resistance, it is essential to characterize immune responses to immunotherapies in the tumor immune microenvironment (TME) from intact patient tissues. To this end, quantitative spatial immune profiling of pathology images has been the focus for many recent studies. Such analysis often depends critically on the automated image segmentation of tumor and stromal compartments. However, current segmentation approaches, even these based on deep learning, often fail to perform well when given datasets to segment, which differ from the data on which they were trained. Specifically, tissue segmentation models trained for one type of organ (source) face challenges in performance when applied directly to images of another organ type (target), even when the targeted regions to segment are highly similar in morphology between the source and target. Here, we present a segmentation approach to adapt knowledge learned from source data of one cancer type to unlabelled target data of another organ cancer type via unsupervised domain adaptation (UDA) frameworks. This research will help build deep learning models that significantly reduce the need for expert manual annotations.

Methods Annotated colorectal cancer (CRC) (target domain) and prostate cancer (source domain) were used for tumor tissue segmentation model development, containing image tiles from 38 and 20 whole slide images, respectively. We compared the performance and robustness of four approaches. First, we implemented two output-space domain-adversarial based UDA’s. We then implemented a self-training-based approach. Additionally, we designed a two-stage UDA approach by first conducting self-training and then further aligning target domain features with category-anchors generated from source data after a first stage of self-training.

Results Directly applying a tumor tissue segmentation model trained on prostate cancer images (source) to CRC images (target) resulted in an intersection-over-union (IOU) score of 62.5%, which was 19% IOU lower (domain gap) than using a model trained on target data. Methods based on output-space domain adversarial training reduced the domain gap by up to 8% IOU, a performance result which was better than with self-training-based methods, which only reduced the domain gap by 4%. Both sets of approaches improved precision by 10%.

Conclusions We demonstrate the feasibility of designing tumor segmentation models that are robust and generalizable to multiple indications. The UDA approaches have the potential to speed our understanding of factors influencing immunotherapy efficacy through automated annotation of tissue regions required.

REFERENCES

FIVE IMMUNOTYPIC SIGNATURES IDENTIFIED IN HUMAN GLOBLASTOMA CORRELATE WITH TUMOR CONTACT WITH THE LATERAL VENTRICLE, IMMUNE SUPPRESSION, AND PATIENT OUTCOME

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Background Glioblastomas make up more than 60% of adult primary brain tumors and carry a median survival of less than 15 months despite aggressive therapy. Immunotherapy, now standard of care for many peripheral solid tumors, offers an appealing alternative platform that may improve survival outcomes for patients with glioblastoma; however, predictive features that could inform responsiveness to different immunotherapeutic modalities remains to be elucidated. Recent studies have demonstrated that patients whose tumors show radiographic contact with the lateral ventricle have diminished...
survival outcomes compared to patients whose tumors do not contact the lateral ventricle. While greater immune infiltrate correlates with more favorable outcomes and more effectual responses to immunotherapy, the anti-tumor immune response in the ventricle is unknown. We hypothesized that ventricle contact may provide a uniquely immunosuppressive microenvironment within the brain that promotes tumor growth by suppressing anti-tumor immunity, that may be overcome with appropriate targeting strategies.

Methods Primary glioblastoma tumors obtained in accordance with the Declaration of Helsinki and with institutional IRB approval (#131870) were disaggregated into single-cell suspensions. Radiographic contact with the LV was identified by MRI imaging and confirmed by a trained neurosurgeon. Multi-dimensional single-cell mass cytometry (CyTOF) then measured >30 immune parameters in thirteen immune subpopulations infiltrating human glioblastomas, including T cells, natural killer cells, B cells, microglia, peripheral macrophages, and myeloid-derived suppressors cells (MDSC). Computational machine-learning pipelines including Citrus, t-SNE, FlowSOM, and MEM identified key differences in the abundance and phenotypes of immune infiltrates.

Results On the basis of glioblastoma contact with the ventricle, we computationally identified consequential distinctions in the abundance of T cell, macrophage, and microglia subsets constituting five immunotype signatures among glioblastoma patients. Immunotypes associated with CD69+CD32+CD44+ peripheral macrophages and PD-1+TIGIT+ CD8 T cells correlated with ventricle contact, whereas immunotypes associated with enriched γδ T cells, B, NK cell, and tissue-resident microglial cells correlated with tumors distal to the ventricle. Further, immune infiltration in the tumor microenvironment correlated with patient outcome, with higher lymphocyte infiltrates correlating with more favorable outcomes, and immune exhaustion correlating with less favorable outcomes.

Conclusions Single-cell mass cytometry in conjunction with the machine learning tools identified key differences in immune cell abundance between lateral ventricle contacting and noncontacting glioblastomas. These results provide key insights into the immune microenvironment of glioblastomas and elucidate several clinically actionable immunotherapeutic targets that may be used to optimize treatment strategies for glioblastomas based on ventricle contact status.

Ethics Approval This study was approved by Vanderbilt University’s Institutional Ethics Board, approval number 131870.

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### Abstract 662

**STATISTICAL LEARNING FROM CLINICAL AND IMMUNOGENOMIC VARIABLES TO PREDICT RESPONSE AND SURVIVAL WITH PD-L1 INHIBITION IN ADVANCED UROTHELIAL CANCER**

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**Background** Urothelial cancer patients treated with immune checkpoint inhibitor (ICI) therapy have varied response and survival. Clinical and immunogenomic biomarkers could help predict ICI response and survival to inform decisions about patient selection for ICI treatment.

**Methods** The association of clinical metadata and immunogenomic signatures with response and survival was analyzed in a set of 347 urothelial cancer patients treated with the PD-L1 inhibitor atezolizumab as part of the IMVigor210 study. Data were divided into a discovery set (2/3 of patients) and validation set (1/3 of patients). We analyzed as potential predictors 70 total variables, of which 16 were clinical metadata and 54 were immunogenomic signatures. Categorical variables were converted to dummy variables (89 total variables: 35 clinical, 54 immunogenic). Using the discovery set, elastic net regression with Monte Carlo cross-validation was used to build optimal models for response (logistic regression) and survival (Cox proportional-hazard).

**Results** In the optimal model of response, 17 variables (10 clinical, 7 immunogenic) were selected as informative predictors, including Baseline Eastern Cooperative Oncology Group (ECOG) Score = 0, Neoantigen Burden, Lymph Node Metastases, and Tumor Mutation Burden (figure 1). The final model predicted patient response with good performance (Area Under Curve = 0.828, pAUC = 2.38e-3; True Negative Rate = 91.7%, True Positive Rate = 87.59%, Confusion matrix = 0.0252). In the optimal model of survival, 32 variables (17 clinical, 15 immunogenic) were selected as informative predictors, including baseline ECOG Score = 0, IC Level 2+, Race = Asian, and Consensus Tumor Subtype = Neuroendocrine (figure 2). The final model predicted patient survival

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**Abstract 662 Figure 1** Elastic Net Logistic Regression with Monte Carlo Cross-Validation to Predict Response to Atezolizumab in Urothelial Cancer. (A) Predictive variables with beta coefficient 95% confidence intervals that exclude 0, derived from Monte Carlo cross-validation. (B) Confusion matrix of actual vs. predicted response data in the validation set. (C) Total response proportions of actual and predicted response data in the validation set.

**Abstract 662 Figure 2** Elastic Net Cox Proportional-Hazards Regression with Monte Carlo Cross-Validation to Predict Survival. (A) Predictor variables with beta coefficient 95% confidence intervals that exclude 0, derived from Monte Carlo cross-validation. (B) Predictions vs. survival outcomes in the validation set. (C) Loess models of density curves for survival outcomes in the validation set. (D) Loess fit of predictions vs. survival outcomes in the validation set. 95% confidence interval indicates strength of fit.