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response prediction to immunotherapy**

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ABSTRACT

Immune checkpoint inhibitors (ICIs) have transformed the treatment of metastatic urothelial carcinoma (mUC) and metastatic renal cell carcinoma (mRCC), yet objective response rates (ORR) remain low (~15-25%), highlighting the need for predictive tools to stratify cancer patients for ICI treatments. We previously developed LogitDA, a logistic regression-based predictor that incorporates feature selections, including domain adaptation. LogitDA with the identified gene signatures in mUC and mRCC outperformed established immune-related signatures in predicting response to Atezolizumab. Here, we present ImmunoResponse Predictor, a web-based graphical user interface (GUI) built on LogitDA, and introduce a novel ORR-informed cosine distance metric (iCosineDist) that leverages domain knowledge of ORRs, and the percentage of support which quantifies the applicability of LogitDA predictions to future mUC/mRCC datasets. This GUI preprocesses user-uploaded RNA-seq data, predicts ICI response, and reports the percentage of support. Specifically, using independent datasets from

the PCD4989g trial, LogitDA achieved prediction AUCs of 0.75 (mUC) and 0.72 (mRCC), with prediction accuracies of 0.71 and 0.83 and corresponding percentages of support of 81% and 72% for mUC and mRCC, respectively. ImmunoResponse Predictor enables accurate and accessible prediction of immunotherapy response, thereby enhancing the clinical applicability of LogitDA.

Availability. ImmunoResponse-Predictor is open source and publicly available at <https://github.com/rajatbutola/ImmunoResponsePredictor>, and it can be accessed online at <https://logitda.shinyapps.io/immunoresponsepredictor/>.