Unified Transcriptomic Melanoma Reference Map Reveals Predictive Molecular Signatures for Patient Prognosis

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Melanoma is the most fatal type of skin cancer, taking over 50,000 lives annually. While advances in checkpoint immunotherapy have decreased mortality rates, it is difficult to determine which patients will benefit from treatment, and how tumor biology predicts prognosis. Studies have published bulk RNA-seq datasets for melanoma; however, these datasets have never been unified to decode underlying molecular processes in a generalizable manner. In this study, I combined seven datasets representing 1,040 patient samples and created a transcriptomic reference map using dimension reduction via Uniform Manifold Approximation and Projection (UMAP). Analysis of tumor samples from the same patient before vs. during immunotherapy revealed transcriptomic changes which I used to create a predictive gene signature for immunotherapy response. I compared regions of the UMAP based on sample proximity using hierarchical clustering and identified areas with distinct biological features. The keratinocyte-enriched region correlated with poor prognosis, whereas the immune activated region correlated with good prognosis. Finally, I analyzed chromosome arm-level changes and found that increased aneuploidy correlated with poor survival. Based on these novel biological findings, I ultimately created an XGboost-based machine learning model to predict a given patient's response to immunotherapy and survival, with an AUROC of 0.88. Finally, I integrated my findings into a free web-based tool available for clinicians and researchers without computational training to make new discoveries and potentially guide patient treatment decisions. This work redefines melanoma precision medicine, increasing predictability and understanding of patients' underlying tumor biology and treatment response.

Awards Won:
Second Award of $2,400