Research Week 2021

Identification and Characterization of Neoplastic Hybrid Cells in Uveal Melanoma

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Keywords

cancer biology, metastasis, single cell RNA sequencing, uveal melanoma

Abstract

Uveal melanoma (UM) is a rare but aggressive disease, with >50% of tumors propagating metastatic disease spread—associated with nearly uniform fatality. Despite significant advances in molecular prognostic tests for identifying patients at risk for developing metastatic disease, the biological process underlying development of metastasis in UM remains poorly understood. A unique subtype of neoplastic cells, characterized by co-expression of neoplastic and immune cell genotypes and phenotypes, can be found within peripheral blood of patients with UM. These cells, termed hybrid cells, have been shown to successfully seed at distant metastatic sites and are detected in circulation at higher numbers than their circulating tumor cell counterparts. To complement our detection of hybrid cells in peripheral blood of UM patients, we identified hybrid cells in primary and metastatic UM tumors from a single cell RNA sequencing (scRNA-seq) dataset. Differential gene expression and subsequent pathway utilization analyses of these hybrid cells revealed genotypes consistent with a pro-metastatic signature, including upregulated migratory and stem/developmental genes and pathways. Further characterization of neoplastic hybrid cells within UM will assist in the identification of targetable pathways that may mediate metastatic disease development. In addition, this work provides a platform for identifying and evaluating neoplastic hybrid cells that can be applied to existing scRNA-seq datasets of other cancer types.