ImmunoNet: A Novel in-silico Platform to Personalize Immunotherapy for Breast Cancer Treatment

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The tumor immune microenvironment (TIME) of breast cancer is a known source of tumor heterogeneity and it has been increasingly recognized as having a role in the course of disease. In the present study, I used a computational approach to dissect the landscape of TIME states among TCGA breast cancer patients. Our central hypothesis is that the pre-existing TIME states represent a dimension which is informative about the prognosis and the response to immunotherapy. In order to test this hypothesis, I first classified breast cancer patients according to their primary TIME status. Next, I describe a TIME-based classification with prognostic value for overall survival among the TCGA patients. I further demonstrated that absolute quantification of mast cells, M0 macrophages, CD8 T cells and neutrophils were predictive of overall survival. In order to identify the TIME states which, predict response to immune checkpoint blockade, I performed a similar analysis of 11 different mouse models of primary invasive breast carcinoma that were subsequently treated with immune checkpoint inhibitor (ICI) therapy. These analyses revealed that the TIME content of M1 macrophages, monocytes and resting dendritic cells were predictive of sensitivity to ICI therapy. Taken together, these results indicate that (1) the landscape of human primary TIME states is diverse and can identify patients with more or less aggressive disease and (2) that pre-existing TIME states may be able to identify patients, of all molecular subtypes of breast cancer, who are good candidates for ICI therapy.