[BIOINFO 2025]

Machine learning–based Treg signature predicts clinical outcomes and immune landscape in ovarian cancer

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Ovarian cancer (OC) is the leading cause of death among gynecologic malignancies. Regulatory T cells (Tregs) are critical mediators in driving immune suppression and promoting tumor immune evasion in OC. Therefore, understanding both the abundance and functional state of Tregs within the OC immune microenvironment is essential for improving clinical management and immunotherapy. We analyzed single-cell RNA-seq data from OC (GSE184880 and GSE235329) to define T-cell subpopulations and identify their marker genes using the UMAP algorithm. Through gene set variation analysis (GSVA) and weighted gene co-expression network analysis (WGCNA) of bulk RNA-seq data, we identified 257 Treg-related genes (TRGs) that characterize the immunosuppressive microenvironment of OC. To develop a prognostic tool, we then integrated ten machine learning algorithms into 80 model combinations and selected the best-performing model to construct a Treg-related prognostic signature (TRPS). This signature was validated across TCGA and three independent GEO cohorts (GSE26712, GSE9891, and GSE13876). We further compared clinicopathological features, mutational profiles, immune cell infiltration, and predicted immunotherapy responses between the high-risk (HR) and low-risk (LR) TRPS groups. Moreover, using machine-learning approaches identified four genes (CXCL10, HMGA1, SYNGR2, and SORL1) as diagnostic markers with strong predictive power. Notably, patients in the LR group exhibited superior overall survival, higher tumor mutational burden (TMB), enhanced immune-cell infiltration, and greater sensitivity to immunotherapy than those in the HR group. Overall, our study established an optimal Treg-related prognostic signature for ovarian cancer, which serves as a robust indicator of prognosis, enables precise risk stratification but also offers valuable insights for therapeutic decision.