PROGNOSTIC GENE SIGNATURE REFLECTING CD8+ T CELL ENRICHMENT IN EARLY-STAGE TRIPLE-NEGATIVE BREAST CANCER

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Background Triple-negative breast cancer (TNBC) is the most challenging subtype of breast cancer, and its prognosis is poor compared to the other subtypes.1 Immune cells have critical role in tumor rejection and prognosis of patient with TNBC.2 In early TNBC, CD8+ T cells infiltration is positively associated with response to neo-adjuvant chemotherapy and prognosis of patients.3 Recently, combination of immune checkpoint inhibitor, pembrolizumab, with standard chemotherapy has been approved for the neo-adjuvant setting.4 However, there are no valid prognostic biomarkers that reflect the CD8+ T cell enriched tumor in patients with early TNBC. To establish an elaborate therapeutic strategy for TNBC, identification of biomarkers that reflecting feature of CD8+ T cell enriched TNBC is needed.

Methods 76 patients with TNBC were enrolled for gene expression profiles and GSE 169246 data were collected for single cell RNA (scRNA) profiles. Median Follow-up period of enrolled patients was 51.5 months (range: 4.6–230.8). Of the enrolled patients, 13 patients had recurrence or metastasis. Using the HiSeq 4000 sequencer, RNA sequencing was conducted to analyze the gene expression profiles of tumor samples from TNBC patients. Single cell RNA analysis was performed using Seurat package (v.4.0.5). Differentially expressed genes (DEGs) were defined as satisfying both conditions that satisfying in Cox regression analysis and Wilcoxon analysis in gene expression profiles, and that satisfying in logistic regression analysis in CD8+ t cell profiles of scRNA analysis. Gene signature was analyzed by combination of above DEGs. Gene signature was marked on t-SNE of scRNA profiles. Statistical analyses were conducted using R language (v.3.4.3).

Results We identified gene signature reflecting CD8+ T cell enriched feature that stratified patients with TNBC by risk score. Gene-set signatures related to CD8+ T cells were identified as following; GADD45B_ H2AFX_PTRA_RILPL2 - RORA_ZC3H13_ZHX2 (sensitivity = 92.31%; specificity = 93.65%; accuracy = 93.42%). In Kaplan Meier (KM) analysis, patients with tumors with high-risk gene signatures (n=16, median iDFS = 42.7) showed significantly shorter iDFS than those with low-risk gene signatures (n=60, median iDFS not reached). CD8+ t cells related gene signature was marked on CD8+ T cell near the CD4+ T cell in t-SNE.

Conclusions the gene-set signatures reflecting CD8+ T cells enrichment showed high performance to predict prognosis of TNBC. Further analysis of gene signatures related to macrophages will be additionally presented at the conference.

REFERENCES