26 TUMOR INFILTRATING CD8/CD103/TIM-3 EXPRESSING LYMPHOCYTES IN EPITHELIAL OVARIAN CANCER CO-EXPRESS CXCL13 AND ASSOCIATE WITH IMPROVED SURVIVAL

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Background Reactivation of tumor infiltrating T lymphocytes (TILs) with immune checkpoint inhibitors or co-stimulators has proven to be an effective anti-cancer strategy for a broad range of malignancies. However, epithelial ovarian cancer (EOC) remains largely refractory to current T cell-targeting immunotherapeutics. Therefore, identification of novel immune checkpoint targets and biomarkers with prognostic value for EOC is warranted. TIL populations in many cancers often express checkpoint receptor TIM-3. However, TIM-3 expression in TILs and the biological consequences thereof are subject of debate, as associations with both poor and favorable prognosis have been reported across multiple malignancies. Here, we identified a small population of CD8/CD103/TIM3 triple-positive T cells in EOC tissue using immunofluorescence microscopy. Upon analysis of an EOC Tissue Micro Array, tumor infiltration of this immune cell subset associated with improved patient survival.

Methods Methods used in my research are the following:

- Analysis of Single Cell mRNA Sequencing Data
- Multicolor immunofluorescent staining
- Perform Flow Cytometry analysis after isolating Tumor Infiltrated Lymphocytes (TILs) from Fresh Tumor Tissues.

Results Combining multicolor immunofluorescent staining's with single cell RNA-sequencing analysis, we here identified a TIM-3/CXCL13-positive tissue-resident memory (CD8/CD103-positive) T cell (Trm) population in EOC. Analysis of a cohort of ~175 patients with high-grade serous EOC revealed TIM-3-positive Trm were significantly associated with improved patient survival. As CXCL13-positive CD8-positive T cells have been strongly linked to patient response to anti-PD1 immune checkpoint blockade, combinatorial TIM-3 and PD-1 blockade therapy may be of interest for the (re)activation of anti-cancer immunity in EOC.

Conclusions We identified a small set of CD8/CD103/TIM-3-expressing tumor infiltrated T cells in EOC patients associated with improved EOC patient survival. Therefore, CD8/CD103/TIM-3 triple-positive TILs may be a prognostic marker for EOC and represents a target population of interest for reactivation by immunotherapeutics. Further, differential gene expression (DEG) analysis revealed upregulated expression of co-stimulatory, cytotoxic, and exhaustive genes, and notably that of CXCL13 within the terminally exhausted CD8-positive T cell fraction. Due to the co-expression pattern of TIM-3 and CXCL13, TIM-3 might also serve as a surrogate marker for prognostically favorable CXCL13-positive CD8-positive TILs.

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