1035 CD26+ CD4+ T CELLS IMPART ENHANCED ANTI-TUMOR IMMUNITY AND IMPROVED PROGNOSIS IN EARLY-STAGE BREAST CANCER PATIENTS

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Background Tumor-infiltrating lymphocytes (TILs) play a crucial role in anti-tumor responses, primarily through the activity of cytotoxic CD8+ T cells. However, the role of conventional CD4+ T cells in driving anti-tumor immunity and survival outcomes in breast cancer patients is not well understood.

Methods Peripheral blood, breast cancer tissue, and disease-free breast tissue from early-stage breast cancer patients were collected by surgical resection. Flow cytometry was performed to dissect CD4+ T cell subpopulations based on ectoenzyme CD26 expression. Single cell RNA sequencing of human breast cancer samples revealed a distinct transcriptional profile of CD26+ CD4+ T cells. Pseudotime analysis uncovered the lineage relationships among these different CD4+ T cell populations. Cell-cell interaction analysis revealed the potential crosstalk between CD26+ CD4+ T cells and other immune cells. The prognostic value of the CD26+ CD4+ T cell signature was evaluated using public genomic data.

Results Circulating CD26 expressing T cells were found to have increased polyfunctionality and memory potential. Single cell sequencing of tumor infiltrating CD4+ T cells reveals a distinct transcriptional profile of CD26+ CD4+ T cells, with increased expression of pro-survival and pro-migratory T cell features. Pseudotime analysis suggested that CD26+ CD4+ T cells could differentiate into CD26- CD4+ T cells. Through cell-cell interaction analysis, active crosstalk was observed between this subset and dendritic cells, and their potential to enhance the activation of CD8+ T cells and NK cells. Finally, the signature of CD26+ CD4+ T cells was shown to correlate with improved patient survival in both estrogen receptor positive (ER+) and triple negative (TNBC) breast cancer patients.

Conclusions These findings unveil a distinct population of CD4+ T cells with both functional and memory features, imparting their anti-tumor effects and the potential to enhance the activities of other immune cells, which underscores their potential for immunotherapy. Additionally, the identification of their prognostic value could enhance the existing prediction tools for patient selection in various therapeutic regimens.

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Ethics Approval Fresh tumor and peripheral blood were obtained from patients who gave institutional review board (IRB)-approved written informed consent prior to inclusion in the study (City of Hope IRB 05091, IRB 07047, and IRB 14346).

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