1039 THE PROGNOSTIC VALUE OF TUMOUR-SPECIFIC T CELLS IN ASIAN TNBC: USING CD39$^+$CD8$^+$ T CELLS AS A SURROGATE MARKER

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Background Triple-negative breast cancer (TNBC) is the most aggressive histologic and the only subtype of breast cancer responding to immunotherapy. The immunologic portrait of TNBC is featured with unique microenvironment of high levels of tumour lymphocyte infiltration (TILs) and PD-L1 expression.[1-3] In our previous work, we demonstrated that CD39$^+$CD8$^+$T cells represent tumour antigen-specific CD8$^+$T cells as well as a potential biomarker that predicts response to PD-1/PD-L1 blockade in treatment-naive non-small cell lung cancer.[4] From these perspectives, we hypothesized that accurate quantitation of CD39$^+$CD8$^+$T cell subset would predict prognosis in TNBC.[5-7]

Methods Tumour specific T cells and CD39$^+$CD8$^+$T cells were detected with flow cytometry in peripheral blood mononuclear cells (PBMCs) and TILs from 4T1.2 tumour-bearing mice as well as TNBC patients respectively. 315 Asian TNBC cases recruited from Singapore General Hospital were comprised in our cohort and multiplex immunohistochemistry/immunofluorescence (mIHC/IF) was used to detect the expression of CD39, CD8 and other immune lineage biomarkers. Associations between overall survival (OS), disease free survival (DFS) and biomarkers expression were investigated.

Results In 4T1.2 mice model, tumour-specific CD8$^+$T cells (gp70 tetramer$^+$) expressed significantly higher CD39 in PBMCs and TILs, especially after anti-PD1 and anti-CD137 immunization. CD39$^+$CD8$^+$T cells were also detected in TNBC patients' PBMCs and TILs. Furthermore, CD39$^+$CD8$^+$T cell and other CD39$^+$ sub-population immune infiltrates including CD39$^+$CD68$^+$ macrophages and CD39$^+$FOXP3$^+$ regulatory T cells were detected in TNBC tumour samples subjected to mIHC/IF. Multivariate analysis showed that tumours with high CD39$^+$ immune infiltrates harboured significantly increased OS (HR 0.41, P=0.0029) and DFS (HR 0.59, P=0.0243), and the increase of OS was significant even after adjusting for clinicopathological parameters (HR 0.25, P=0.0154). In addition, the proportion of CD39$^+$CD8$^+$ T cells (HR 0.50, P=0.0317), but not CD39$^-$CD8$^+$T cells (HR 0.62, P=0.1420), was associated with improved OS and the prognostic significance was independent of clinicopathological parameters. Notably, multivariate analysis demonstrated that CD39$^+$CD8$^+$T cell proportion was similarly associated with improved OS (HR=0.49; 95% CI 0.27-0.90; P=0.0181) and DFS (HR=0.62; 95% CI 0.41-0.96; P=0.0287). For other sub-populations of CD39$^+$ immune infiltrates, CD39$^+$CD68$^+$ and CD39$^+$FOXP3$^+$ immune infiltrates were not associated with improved OS or DFS.

Conclusions Our present study provided further support for previous findings that CD39$^+$CD8$^+$T cells may serve as a surrogate marker of tumour-specific T cells in TNBC. High CD39$^+$CD8$^+$T cells proportion is associated with improved clinical outcomes in TNBC. Further studies will quantitate and monitor the trajectory changes of these tumour-specific T cells in an immunotherapy treated TNBC cohort.

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