CHARACTERIZING HUMAN V\(\delta 1^+\) AND V\(\delta 2^+\) T CELLS FOR TUMOR IMMUNOTHERAPY DEVELOPMENT

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Background Immunotherapy has revolutionized the treatment of cancer, and has been instated as a ‘pillar’ of modern cancer treatments alongside chemotherapy, radiotherapy and surgery. Most tumor immunotherapy developments to date have focused on cytotoxic CD8\(^+\) T cells. Increasingly, \(\gamma\delta\) T cells are being considered as the next-generation tumor immunotherapy against difficult to treat solid tumors due to their potent cytotoxic and cytolytic functions, and natural tropism for the tumor microenvironment. Moreover, \(\gamma\delta\) T cells can recognize a broad range of tumors and infected cells without the requirement of antigen presentation via major histocompatibility complex (MHC) molecules. Previous studies have shown that a high number of \(\gamma\delta\) T cells within tumors is strongly correlated with overall patient survival across 25 cancer types.

Methods We have isolated and expanded human V\(\delta 1^+\) and V\(\delta 2^+\) T cells and performed in vitro T cell killing assay. In vitro isolated human V\(\delta 2^+\) T cells were used for adoptive cell transfer in tumor-bearing NSG mice.

Results In our hands, we show that human V\(\delta 1^+\) and V\(\delta 2^+\) T cell constitute only 0.05 to 0.62\% and 0.34 to 3.02\%, respectively of total circulating T cells. We are now routinely isolating and expanding human V\(\delta 1^+\) and V\(\delta 2^+\) T cells and have immunophenotyped and validated their capability to kill different types of tumor cells in vitro. Additionally, we show that in vitro isolated human V\(\delta 2^+\) T cells can slow tumor growth in vivo and prolong the survival of tumor-bearing NSG mice when adoptively transferred.

Conclusions Collectively, our data showed that human \(\gamma\delta\) T cells are promising targets for tumor immunotherapy development.

Ethics Approval ‘This study was approved by Australian Red Cross for the isolation of human V\(\delta 2^+\) \(\gamma\delta\) T cells from healthy donors’ peripheral blood mononuclear cells, agreement number: 21-07VIC-09.’

‘This study was approved by Austin Health Animal Ethics Committee for adoptive cell transfer of human V\(\delta 2^+\) \(\gamma\delta\) T cells into NSG mice, AEC Reference number: A2020/05661.’

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