Background A population of MR1-restricted T cells (MR1T) which responds to tumor-associated antigens has been studied. The MR1T can kill tumor cells from various tissue origins across the MHC barriers, but inert to non-cancerous cells. These T cells appears to have a potential to be a safe anti-cancer therapeutics overcoming the HLA-restriction of conventional CD8+ T cells. We have developed Panck T cells, pan-cancer-killing CD8+ T cells, to examine their potential as a therapeutic in human trials.

Methods We induced anti-cancer MR1T by stimulating peripheral T cells with cancer cells that were prepared to over express MR1 but not express HLA. MR1T cells with anti-cancer activities were purified and subjected to a rapid expansion in a large scale. These cells were phenotyped, assayed for cancer killing activities in both in vitro, and in vivo. Finally, the TCR sequences of the Panck T cells were analyzed to characterize TCR clones associated with the anti-cancer activities of Panck T cells.

Results We established a method of isolating and expanding MR1-restricted Panck T cells at high purity, and confirmed that these cells showed cytotoxicity, IFN-γ and TNF responses to various target cancer cells. They showed strong anti-cancer activities in animal models of various hematologic and solid cancers. We isolated high purity of CD8+ 4-1BB+ T cells except CD8+ TCRβ7.2+ T cells, which are MAIT cells after primary induction of Panck T. Final products have characteristics of phenotype, usually CD69hi, CD161-, TCRβ7.2-, CD62Lmed, CD45RO+, CD57-, and PD-1-, and have shown anti-cancer activities against multiple cancers in both in vitro, and in vivo animal models. Expression of a representative TCR on T cells mediated anti-cancer effects against multiple cancers comparable to the Panck T itself.

Conclusions In conclusion, we have developed and standardized the isolation and expansion method of Panck T, which showed a strong anti-cancer activity to various types of cancers regardless of their HLA types.

REFERENCES

Ethics Approval Approval has been granted by the Institutional Review Board (IRB) for human-derived material research (NCC2020-0295)

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