CHARACTERIZATION OF ANTIBODIES AGAINST BTN2A1 FOR Vδ2+ γδ T CELL-BASED TUMOR IMMUNOTHERAPY

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Abstracts

Background Human γδ T cells are ideal candidates for tumor immunotherapy because of their natural tropism for tumor microenvironment, elicit rapid innate-like immune responses upon tumor recognition and the ability to orchestrate other tumor-infiltrating immune cells for tumor cell killing. Our group has recently defined aspects of the mechanism of T-cell receptor (TCR) dependent activation of Vy9Vδ2+ T cells by tumors following the presentation of phosphoantigens via the B7 immunoglobulin family-like butyrophilin 2A1 (BTN2A1) and BTN3A1. Dysregulation of the mevalonate pathway in tumors can cause activation of Vy9Vδ2+ T cells via phosphoantigen accumulation and induces γδ T cell chemotaxis toward tumor cells. Most clinical studies so far have used aminobisphosphonates (to promote accumulation of phosphoantigens in cells) or synthetic phosphoantigen analogues such as bromohydrin pyrophosphate (BrHPP) and 2-methyl-3-butenyl-1-pyrophosphate (2M3B1PP) to activate Vy9Vδ2+ T cells in cancer patients. More recently, agonist antibodies against BTN3A (e.g., clone 20.1, ICT-01 and CTX-2026) have been identified and used as a phosphoantigen-independent approach to activate Vy9Vδ2+ T cells for targeted cell killing.

Methods We are currently characterizing a number of anti-BTN2A1 antibodies that can potentially be used to modulate the activity of Vy9Vδ2+ T cells in vitro assays.

Results We have also established a pre-clinical humanized tumor model using NOD scid gamma (NSG) mice and showed delayed tumor growth in mice that received 4 rounds of human Vδ2+ γδ T cell adoptive cell transfer in combination with clone 20.1 agonist antibody, which will allow further characterization of our anti-BTN2A1 antibodies.

Conclusions Taken together, our study has demonstrated the potential to target BTN2A1 and BTN3A1 for Vy9Vδ2+ T cell-based cancer immunotherapy development.

REFERENCES

Ethics Approval ‘This study was approved by Australian Red Cross for the isolation of human Vδ2+ γδ 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 Vδ2+ γδ T cells into NSG mice, AEC Reference number: A2020/05661.’