00528 Specific Targeting of Human Acute Myeloid Leukemia Using in Vitro Expanded Gamma Delta T Cells Derived From Cord Blood

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Aims: To explore the potentials of in vitro expanded gamma delta (γδ) T cells derived from human cord blood (CB) to target human AML cells.

Methodology: γδ T cells were purified from CB units and expanded in vitro for up to 3 weeks. Phenotypes of the expanded cells were FACS analysed and their cytotoxicity against human AML cells were determined by chromium51 release assay. The efficacies of these cells in targeting human AML cells in vivo were also examined using primary AML patient derived xenograft (PDX) mouse models.

Result: Our data showed that in keeping with the neonatal origin of CB, γδ T cells in CB display a predominately central memory (Tcm) and naïve (Tn) phenotype, making these cells favourable for extensive in vitro expansion. Using our in-house optimized in vitro expansion protocol, we were able to achieve up to 105-fold expansion of the starting γδ T cells over a period of 21 days. The expanded γδ T cells exhibit potent in vitro cytotoxicity against a range of human AML cell lines in a dose dependent manner, yet display minimal cytotoxicity against $CD34^+$ cells isolated from allogeneic CB samples. Intravenous infusion of the expanded γδ T cells into NOD/SCID/IL2Rγ-/-(NSG) mice that had been xenografted with primary AML patient samples resulted in significant reduction of BM leukemic burden compared to untreated control. On the other hand, infusion of these cells into human CB engrafted mice did not lead to significant reduction in normal human cell chimerism in the mouse marrow.

Conclusion: In summary, our data demonstrates that in vitro expanded CB derived γδ T cells show potent AML-specific cytotoxicity both in vitro and in vivo, making it a promising alternative cell source for immunotherapy. Further investigations to enhance the mechanistic understanding would be needed to seed for future clinical translation.