Development of a molecular targeted cytokine that specifically expands Vγ9Vδ2 T cells and potentiates anti-tumor activity


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Introduction

• The ability of Vγ9Vδ2 T cells to selectively eliminate transformed cells due to recognition of stress-related ligands makes them an ideal candidate for cancer immunotherapy.
• One limitation restraining Vγ9Vδ2 T cell anti-tumor responses is their low abundance in peripheral blood.
• Previous efforts to expand Vγ9Vδ2 T cells have relied on treatment with bisphosphonates and IL-2 which are limited by rapid clearance, competition, and dose-limiting toxicities.
• We have developed our Cisleukin™ platform which targets IL-2 to the human Vγ9Vδ2 T cell, an engineered Vδ2-X with reduced receptor affinity.
• Pairing IL-2 with a high affinity single-domain antibody targeting the human Vγ9Vδ2 T cell allows us to overcome many of the limitations of previous IL-2 approaches by preferentially targeting the human Vγ9Vδ2 T cells due to recognition of stress-related ligands making them an ideal candidate for cancer immunotherapy.

Results

Anti-Vγ9xIL2-X specifically binds Vγ9Vδ2 T cells and activates IL-2 signaling

Treatment with anti-Vγ9xIL2-X upregulates expression of molecules that promote cytotoxicity

Improved tumor cell killing activity by PBMCs treated with anti-Vγ9xIL2-X

Conclusions

• Anti-Vγ9xIL2-X specifically binds Vγ9Vδ2 T cells activating IL-2 signaling and promoting proliferation.
• Expanded Vγ9Vδ2 T cells demonstrate broad anti-tumor killing activity while selectively sparing healthy cells.
• Combination with a tumor targeting bioptic or conventional antibody further potentiates Vγ9Vδ2 T cell killing activity.
• The selective targeting by our Vδ2-Cisleukin™ molecule allows a safer, more effective approach to expand Vγ9Vδ2 T cells for cancer immunotherapy.

References