

POSTER PRESENTATION

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Wnt pathway activation functionally reprograms human antigen-specific T cells

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Polyfunctionality is a hallmark of protective immunity, yet the molecular mechanisms governing polyfunctional T cells are poorly understood. After TCR activation, naïve CD8⁺ T cells undergo proliferation and differentiation, which lead to effector functions and memory subset development. However only a portion of activated T cells develop into memory CD8⁺ T cells and with chronic stimulation become terminally differentiated and exhausted CD8⁺ T cells, as defined by CCR7⁻/CD45RA⁺, and functionally impair effective immune responses [1]. We therefore probed the ability to reverse terminally differentiated antigen-specific cells using pharmacological agents. Stimulating human memory CD8⁺ T cells with cognate TCR stimulation in the presence of Wnt agonist enhances polyfunctionality and stemness. Both M1-influenza⁺ and CMV⁺ CD8⁺ T cell responses were reprogrammed and revealed sustained effects from initial Wnt pathway activation *in vitro*. Future work with cancer antigens and reprogramming of differentiated CD8⁺ responses could lead to improved *in vitro* culture conditions for adoptive immunotherapy.

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