Washington University in St. Louis
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OPTIMIZED MHC-INDEPENDENT T CELL RECEPTORS AS A CAR-T ALTERNATIVE

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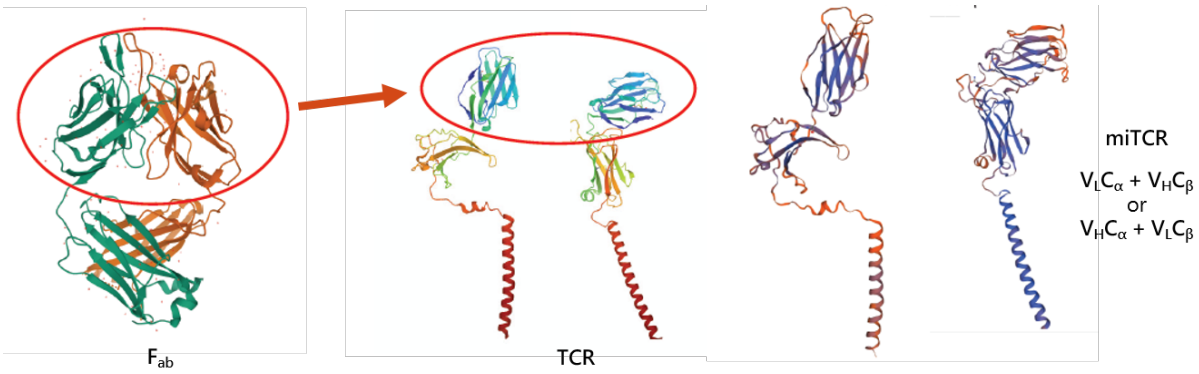
Technology Description

Researchers in Nathan Singh's lab at Washington University have developed a construct for cell therapy that combines facets of existing CAR-T therapy and the endogenous T cell receptor (TCR) to better regulate adoptive cell activation. Unlike the traditional TCR, this receptor does not require MHC engagement for activation and instead uses antibody variable domains. Unlike CARs, this receptor is fully able to complex with other co-receptors that regulate cell activation, preventing rapid cell exhaustion.

This MHC-independent TCR (miTCR) contains the constant regions of TCRα and β, each attached to an antibody variable region heavy or light chain targeting CD19. The researchers have optimized the design of this construct to produce the most effective miTCR.



Stage of Research

The researchers have designed and validated the miTCR molecules *in vitro*, including performing structural analysis and optimization of the molecule. Jurkat cells expressing the miTCR (and without endogenous TCRα and β expression) were effective at destroying $CD19^+$ leukemia cells with sustained cell activation. *In vivo* experiments are ongoing.

Applications

- Cell therapy in oncology

Key Advantages

- Recruits other members of TCR complex to regulate activation

- Lessens risk of cytokine release syndrome, neurotoxicity

Patents: Pending

Related Web Links: Singh Profile & Lab