TARGETING GLYCANS TO ENHANCE ADOPTIVE CELL THERAPY

Peng Wu, James C Paulson, Eleanor Bashian*. The Scripps Research Institute, San Diego, CA, USA; The Scripps Research Institute, Laguna Niguel, CA, USA

Background Adoptive cell therapy (ACT) is a promising immunotherapy modality in which autologous lymphocytes are expanded *ex vivo* to enhance anti-tumor activity. Prior to the expansion process, T cells can be engineered to recognize specific antigens, such as in the case of chimeric antigen receptor (CAR)-T or T cell receptor-engineered (TCR)-T cells. However, efficacy of ACT is still limited, especially in solid tumors, by low anti-tumor activity, poor trafficking ability, and reduced tumor infiltration.

Low anti-tumor activity results from immune suppression due, in part, to the presence of immune checkpoint receptors. Common examples include interactions between PD-1 expressed on T cells and PD-L1 expressed on antigen-presenting cells (APCs), or CTLA-4 expressed on T cells and CD80/86 expressed on APCs. However, immunosuppressive interactions between proteins and glycans have also been reported. Densely present on the surface of T cells, glycans are transcriptionally regulated through differential expression of glycosyltransferases.

Methods We aim to improve the therapeutic efficacy of adoptive cell therapy by remodeling the glycome of T cells through genetic ablation of enzymes involved in glycan biosynthesis.

Results We show that knockout of a single glycosyltransferase in adoptively transferred T cells improves tumor control and survival in a murine melanoma model.

Conclusions This demonstrates that the glycome of T cells can be genetically edited to enhance anti-tumor activity.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0397