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(54) Title: METHODS AND COMPOSITIONS FOR THE REDUCTION OF CHIMERIC ANTIGEN RECEPTOR TONIC SIGNALING

(57) Abstract: The present disclosure relates to methods and compositions related to Chimeric Antigen Receptors ("CARs") and modifications to the framework sequences to eliminate tonic signaling. The compositions include modified binding members having a binding specificity to chondroitin sulfate proteoglycan 4 (CSPG4) and are stable when prepared as single chain antibody (scFv) and incorporated into CARs. The methods further include nucleic acid constructs for the expression of CSPG4 CARs, and the application of the CSPG4 CAR to therapeutic methods for the treatment of cancer. The present disclosure also relates to the modification of humanized framework sequences.

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