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(54) Title: PROTEASE-ACTIVATING CD45-GATE CAR

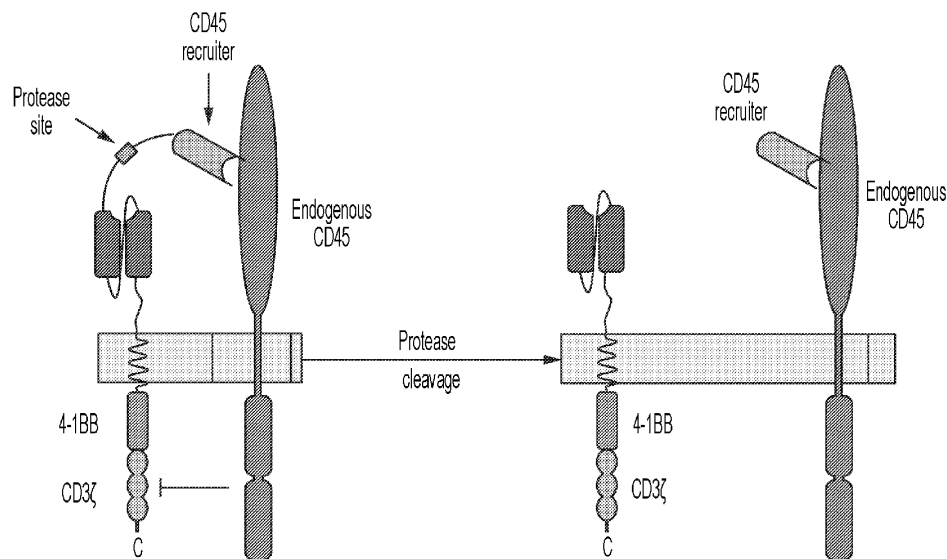


Fig. 1A

(57) **Abstract:** A reversibly gated effector polypeptide e.g. a chimeric antigen receptor (protease-activating CD45-gate CAR) comprising an extracellular CD45 recruiting domain, a protease-cleavable linker, and a polypeptide comprising an extracellular ligand binding domain, a transmembrane domain, and an intracellular domain. Nucleic acids including vectors and expression vectors that encode the protease-activating CD45-gate CAR and cells including immune cells such as T cells that comprise and express the nucleic acids. Methods of treatment of various conditions including various forms of cancer comprising administering the cells including CAR T cell therapy. In some embodiments, the CD45 gate at least partially inhibits activation of the protease-activating CD45-gate CAR when the protease-activating CD45-gate CAR binds antigen. The inhibition is at least partially diminished, relieved and/or eliminated when the protease-activating CD45-gate CAR is exposed to a protease that can cleave the linker.

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