Abstract

The present application discloses modified enhanced immune cells targeting HPV and their pharmaceutical uses. The present invention provides T cell receptors targeting HPV E7 antigen or fragments thereof, as well as their pharmaceutical applications. In addition, modified immune cells that simultaneously express HPV-targeted TCRs and chimeric switch receptors and their pharmaceutical uses are provided. The modified immune cells of the present application replace the intracellular inhibitory signaling domain of immunosuppressive receptors with the intracellular activating signaling domain of co-stimulatory molecules, thereby converting inhibitory signals triggered by the binding of immunosuppressive factors or ligands into activating signals. Such design can effectively block immunosuppressive molecule-induced T cell exhaustion, increase cytokine secretion, and improve cell proliferative capacity and tumor cell cytotoxicity. The invention is expected to address a series of challenges confronting adoptive T cell immunotherapy, including tumor heterogeneity, poor penetration through tumor barriers, short duration of therapeutic efficacy, and localized immunosuppressive tumor microenvironment.

FIG. 39