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(54) Title: MASKED IL-2 CYTOKINES AND METHODS OF USE THEREOF

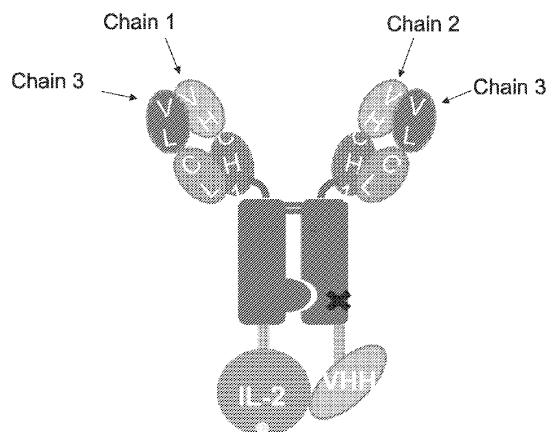


FIG. 1

(57) Abstract: The present invention provides, among other things, a masked cytokine comprising an interleukin 2 (IL-2) polypeptide, a VHH masking moiety, an anti-PD1 targeting moiety, and an engineered Fc domain comprising a tumor-associated protease cleavage site. In such masked cytokine, the IL-2 polypeptide is engineered to be activatable by a protease at a target site, such as in a tumor microenvironment. The VHH masking moiety blocks, occludes, inhibits (e.g., decreases) or otherwise prevents (e.g. masks) the activity or binding of the cytokine to its cognate receptor or protein. Upon proteolytic cleavage of the cleavage site in the Fc domain, the IL-2 polypeptide becomes activated, which renders it capable of binding to its cognate receptor or protein with increased affinity.

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