MASKED CYTOKINE POLYPEPTIDES

ABSTRACT

Provided herein are cytokines or functional fragments thereof that, in some embodiments, are engineered to be masked by a masking moiety at one or more receptor binding site(s) of the cytokine or functional fragment thereof. In some embodiments, the cytokines are engineered to be activatable by a protease at a target site, such as in a tumor microenvironment, by including a proteolytically cleavable linker. In some embodiments, the proteolytically cleavable linker links the cytokine to the masking moiety, links the cytokine to a half-life extension domain, and/or links the masking moiety to a half-life extension domain. The 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 cleavable linker at the target site, the cytokine becomes activated, which renders it capable of binding to its cognate receptor or protein with increased affinity.

Fig. 1A