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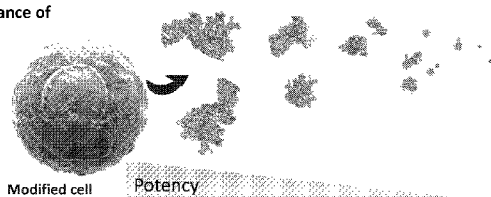
(54) Title: IMPROVED THERAPEUTIC CONTROL OF HETERODIMERIC AND SINGLE CHAIN FORMS OF INTERLEUK-
IN-12

FIGURE 1

Schematic depiction of approaches to improved therapeutic control of IL-12

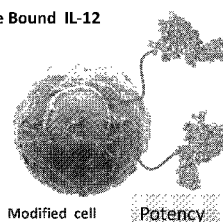
Rapid breakdown/clearance of
Protease sensitive IL-12

- Protease site
- Protease
site/destabilization



Locally Acting Membrane Bound IL-12

- Protease
site/destabilization



(57) Abstract: The present invention relates to modified forms of IL-12. These modified forms of IL-12 may be engineered to have a shortened in vivo half-life compared and/or enhanced localization of biological effects compared to that of corresponding non-modified form of IL-12. Short half-life and membrane bound forms of IL-12 may provide greater therapeutic control for in vivo therapeutic delivery, in particular when used in combination with ligand inducible delivery of IL-12. Modified forms of IL-12 engineered to have shortened in vivo half-life and/or enhanced localization of biological effects include heterodimeric p35/p40, single chain and membrane bound forms of IL-12 wherein a naturally occurring IL-12 amino acid sequence is genetically modified to enhance susceptibility of the IL-12 molecule to in vivo proteolytic degradation.