

PROPOSED CLAIM AMENDMENTS

1. An engineered human IL-21 polypeptide that comprises amino acid substitutions, numbered relative to SEQ ID NO: 2:

H6L;

~~R9K;~~

M10L; and

P78L;

~~and optionally comprises G84E or P104A or a combination thereof;~~

~~and optionally comprises one of K73V or K73I.~~

2. The engineered human IL-21 polypeptide of claim 1, further comprising amino acid substitution K73V or K73I.

~~3. The engineered human IL-21 polypeptide of claim 1, comprising amino acid substitution K73I.~~

~~4.3.~~ The engineered human IL-21 polypeptide of claim 1, further comprising amino acid substitution G84E.

~~5. The engineered human IL-21 polypeptide of claim 1, comprising amino acid substitution P104A.~~

~~6.4.~~ The engineered human IL-21 polypeptide of any one of claims 1-3, wherein the polypeptide binds to an engineered human CD360 protein ectodomain.

~~7.5.~~ The engineered human IL-21 polypeptide of claim ~~64~~, wherein the engineered human CD360 protein ectodomain is modified at one or more residues selected from Y10, Q33, Q35, Y36, E38, L39, F67, H68, F69, M70, A71, D72, D73, I74, L94, A96, E97, P126, A127, Y129, M130, K134, S190, and Y191.

~~8-6.~~ The engineered human IL-21 polypeptide of claim ~~64~~, wherein the engineered human CD360 protein ectodomain is modified at M70.

~~9. The engineered human IL-21 polypeptide of claim 6, wherein the engineered human CD360 protein ectodomain is modified at M70 and Y129.~~

~~10-7.~~ The engineered human IL-21 polypeptide of claim ~~84~~, wherein the engineered human CD360 protein ectodomain comprises amino acid substitution M70G.

~~11-8.~~ The engineered human IL-21 polypeptide of claim ~~94~~, wherein the engineered human CD360 protein ectodomain comprises amino acid substitutions M70G and Y129F.

~~12. The engineered human IL-21 polypeptide of claim 1, comprising amino acid substitutions K73V and G84E.~~

~~13. The engineered human IL-21 polypeptide of claim 1, comprising amino acid substitutions K73I and P104A.~~

~~14. An engineered human IL-21 polypeptide that comprises a set of amino acid substitutions, numbered relative to SEQ ID NO: 2: H6L, R9K, M10L, K73V, P78L, and G84E.~~

~~15. An engineered human IL-21 polypeptide that comprises a set of amino acid substitutions, numbered relative to SEQ ID NO: 2: H6L, R9K, M10L, K73I, P78L, and P104A.~~

~~16-9.~~ A system for selective activation of a receptor in a cell, the system comprising: (a) an engineered receptor comprising the human CD360 protein ectodomain including an amino acid substitution at M70G; and (b) the engineered human IL-21 polypeptide of any one of claims 1-3.

~~17-10.~~ A system for selective activation of a receptor in a cell, the system comprising: (a) an engineered receptor comprising the human CD360 protein ectodomain including amino acid substitutions at ~~M70G-M70I~~ and ~~Y129FD73E~~; and (b) the engineered human IL-21 polypeptide of any one of claims 1-3.

~~18. The system of claim 16, wherein the engineered human CD360 receptor is expressed by a mammalian cell.~~

~~19. The system of claim 17, wherein the engineered human CD360 receptor is expressed by a mammalian cell.~~

~~20. The system of claim 18, wherein the mammalian cell is an immune cell or a stem cell.~~

~~21. The system of claim 19, wherein the mammalian cell is an immune cell or a stem cell.~~

~~22. The system of claim 20, wherein the mammalian cell is an immune cell, and the immune cell is a T cell.~~

~~23. The system of claim 21, wherein the mammalian cell is an immune cell, and the immune cell is a T cell.~~

~~24.11.~~ A pharmaceutical composition comprising the engineered human IL-21 polypeptide of any one of ~~claims~~ 1-8; and a pharmaceutically acceptable excipient.

~~25. A kit comprising the system of claim 16.~~

~~26. A kit comprising the system of claim 17.~~

12. The engineered human IL-21 polypeptide of claim 1, wherein the engineered human IL-21 polypeptide is fused to an Fc domain of IgG or to albumin.

~~27.13. The engineered human IL-21 polypeptide of claim 1, further comprising amino acid substitution R9K.~~

~~14. The engineered human IL-21 polypeptide of claim 4, wherein the engineered human CD360 protein ectodomain comprises amino acid substitutions M70I and D73E.~~

~~15. A pharmaceutical composition comprising the system of any one of claims 9 and 10; and a pharmaceutically acceptable excipient.~~