

Claims

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

H6L;

M10L; and

P78L.

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, further comprising amino acid substitution G84E.

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.

5. The engineered human IL-21 polypeptide of claim 4, 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.

6. The engineered human IL-21 polypeptide of claim 4, wherein the engineered human CD360 protein ectodomain is modified at M70.

7. The engineered human IL-21 polypeptide of claim 4, wherein the engineered human CD360 protein ectodomain comprises amino acid substitution M70G.

8. The engineered human IL-21 polypeptide of claim 4, wherein the engineered human CD360 protein ectodomain comprises amino acid substitutions M70G and Y129F.

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.
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 M70I and D73E; and (b) the engineered human IL-21 polypeptide of any one of claims 1-3.
11. A pharmaceutical composition comprising the engineered human IL-21 polypeptide of any one of claims 1-8; and a pharmaceutically acceptable excipient.
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.
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.