

CLAIMS

The invention claimed is:

1. An interleukin-12 (IL-12) composition wherein said composition has been modified to have a reduced half-life compared to a corresponding non-modified IL-12 composition.
2. The composition of claim 1, wherein said IL-12 composition comprises one or more amino acid substitutions which increase the rate of proteolysis of said composition compared to the rate of proteolysis of a corresponding IL-12 composition not having said one or more amino acid substitutions.
3. The composition of claim 2, wherein said IL-12 composition is a heterodimer of p40 and p35 polypeptides.
4. The composition of claim 2, wherein the corresponding non-modified IL-12 composition is a heterodimer of human IL-12 p40 and human IL-12 p35 polypeptides.
5. The composition of claim 2, wherein said IL-12 composition is a single chain IL-12 polypeptide.
6. The composition of claim 2, wherein said IL-12 composition is a topologically manipulated single chain IL-12 polypeptide.
7. The composition of claim 2, wherein said IL-12 composition comprises a p40 polypeptide which comprises any one or more amino acid substitutions selected from the group consisting of:

K126L
K124G / K126L
K124A / K126L
K124S / K126L
K124G / N125G / K126L
K124A / N125A / K126L
M45L
N248L
K247A / N248L
L246A / K247A / N248L
L246S / K247A / N248L
A172P
A172P / T174A
D40A / P42L

G161P / D164L
K126L
K124G / K126L
K124A / K126L
K124S / K126L
K124G / N125G / K126L
K124A / N125A / K126L
M45L
D287S
K302S / N303S
V180S
K280L / S281V / K282P / E284G / K285S
S176L / A177V / E178P / V180T / R181S
K280L / S281V / K282P / E284G / K285V
S176L / A177V / E178P / V180S / R181S
N248S / S249G
K282G / K285V
S249G
K282G / K307V

wherein these substitution positions correspond to amino acid positions as shown in SEQ ID NO: 2.

8. The composition of claim 2, wherein said IL-12 composition comprises a p35 polypeptide which comprises any one or more amino acid substitutions selected from the group consisting of:

Q186L
S215L
Y223L
K214P
K214P / S216A
C144P / S147L
C144P / L145S / S147L
G142R / R148G
K149S
K149A
E135S
Q186S
S216R
D111A / K112R
Q213R / K214L / S215R / S216A
A146V / S147P / K149G / T150S / S151K

N132V / S133P / E135G / T136S / S137K
S147P / K149I / T150I / S151K
N132F / S133P / E135G / S137K
N77I / L78P / S83R
T210L / Q213R / K214G
R148G / K149R
N207S / S208G / E209R
E209G / T210R

wherein these substitution positions correspond to amino acid positions as shown in SEQ ID NO: 4.

9. An interleukin-12 (IL-12) composition wherein said composition has been modified to comprise a membrane linking (tethering/anchoring/binding) moiety.

10. The composition of claim 9, wherein said IL-12 composition comprises one or more amino acid substitutions which increase the rate of proteolysis of said composition compared to the rate of proteolysis of a corresponding IL-12 composition not having said one or more amino acid substitutions.

11. The composition of claim 9, wherein said IL-12 composition comprises a heterodimer of p40 and p35 polypeptides.

12. The composition of claim 10, wherein the corresponding non-modified IL-12 composition is a heterodimer of human IL-12 p40 and human IL-12 p35 polypeptides.

13. The composition of claim 9, wherein said IL-12 composition comprises a single chain IL-12 polypeptide.

14. The composition of claim 9, wherein said IL-12 composition comprises a topologically

manipulated single chain IL-12 polypeptide.

15. The composition of any one of claims 9 to 14, wherein said membrane anchoring, linking, or tethering) moiety is selected from the group consisting of: a covalent membrane surface linking moiety, a hydrophobic membrane surface linking moiety, a hydrophillic membrane surface linking moiety, an ionic membrane surface linking moiety, an integral membrane polypeptide, and a transmembrane polypeptide.

16. The composition in any one of claims 9 to 14, wherein IL-12 expression is inducibly regulated by a gene switch.

17. The composition of claim 15, wherein IL-12 expression is inducibly regulated by a gene switch.

18. The composition of claim 16, wherein said gene switch is an ecdysone receptor-based (EcR-based) switch.

19. The composition of claim 17, wherein said gene switch is an ecdysone receptor-based (EcR-based) switch.

20. The composition of claim 18, wherein said gene switch is an ecdysone receptor-based (EcR-based) switch.

21. The composition of claim 19, wherein said IL-12 is expressed by a modified T cell.

22. The composition of claim 20, wherein said IL-12 is expressed by a modified T cell.