CLAIMS

1. A construct, comprising (i) three copies of a cytokine chain of a member of the TNF superfamily, wherein the resulting cytokine is modified so that the affinity towards its receptor is lowered (ii) a linker sequence and (iii) a targeting moiety, wherein said linker sequence is linking the cytokine copies to the targeting moiety.
2. The construct of claim 1, wherein said construct is a fusion protein.
3. The construct according to claim 1 or 2, wherein at least one copy of the said cytokine chain of a member of the TNF superfamily is mutated.
4. The construct according to any of the preceding claims, wherein said cytokine is selected from the group, consisting of FasL, TRAIL, TNF, CD30L, CD40L, OX40L, RANKL, TWEAKL, LTalpha, LTbeta, LIGHT, CD27L, 41BBL, GITRL, APRIL, EDA, VEGI, and BAFF.
5. The construct according to any of the preceding claims wherein said targeting moiety is an antibody or a nanobody.
6. The construct according to any of the preceding claims, wherein said mutated cytokine copy is selected from the group consisting of TNF Y87Q, TNF Y87F, TNF I97A, TNF I97S, TNF Y115A, TNF Y115G.
7. The construct according to any of the preceding claims, wherein said targeting moiety is directed towards a target selected from the group consisting of CD20, Her2, c-Met, EGFR, tenascin C, $\alpha_v\beta_3$ integrin and CD13.
8. The construct according to any one of claims 1 to 7 for use as a medicament.
9. The construct according to any one of claims 1 to 7 for use in treatment of cancer.

CLAIMS

1. A composition comprising a fusion protein, wherein the fusion protein is a single chain comprising:

(i) a modified human TNF, comprising three copies of a TNF chain, wherein the modified TNF has reduced affinity towards its receptor as compared to wild-type TNF;

(ii) a linker sequence; and

(iii) a single targeting moiety, wherein said linker sequence links the TNF copies to the targeting moiety, and

wherein the composition only shows significant biological activity towards cells that are targeted by the targeting moiety.

2. The composition according to claim 1, wherein the modified TNF is human TNF having a mutation at position Y87, optionally selected from Y87Q, Y87L, Y87A, and Y87F.

3. The composition according to claim 1, wherein the modified TNF is human TNF having a mutation at position I97, optionally selected from I97A, I97Q and I97S.

4. The composition according to claim 1, wherein the modified TNF is human TNF having a mutation at position Y115, optionally selected from Y115A and Y115G.

5. The composition according to claim 1, wherein the targeting moiety comprises an antibody or a nanobody.

6. The composition according to claim 5, wherein the targeting moiety is directed towards a target selected from CD20, Her2, c-Met, EGFR, tenascin C, αvβ3 integrin, and CD13.

7. The composition according to claim 6, wherein the targeting moiety is directed towards CD20.

8. The composition according to claim 6, wherein the targeting moiety is directed towards Her2.

9. A composition comprising a single chain fusion protein, wherein the fusion protein comprises

(i) a modified human TNF comprising three copies of a TNF chain, wherein the human TNF has reduced affinity towards its receptor as compared to wild-type TNF and comprises a mutation at position Y87;

(ii) a linker sequence; and

(iii) a targeting moiety comprising a nanobody directed to CD20, wherein:

said linker sequence links the TNF copies to the targeting moiety and

the composition only shows significant biological activity towards cells expressing CD20.

10. The composition of claim 9, wherein the mutation is selected from Y87Q, Y87L, Y87A, and Y87F.

11. A composition for use in treating cancer, the use comprising administering an effective amount of the composition comprising a single chain fusion protein to a patient in need thereof, wherein the fusion protein comprises:

(i) a modified human TNF comprising three copies of a TNF chain, wherein the human TNF has reduced affinity towards its receptor as compared to wild type TNF and comprises a mutation at position Y87 or Y115;

(ii) a linker sequence; and

(iii) a targeting moiety directed to a cellular target, wherein:

said linker sequence links the TNF copies to the targeting moiety and

the composition only shows significant biological activity towards cells that are targeted by the targeting moiety.

12. The composition for use of claim 11, wherein the mutation is selected from Y87Q, Y87L, Y87A, and Y87F.

13. The composition for use of claim 11, wherein the mutation is selected from Y115A and Y115G.