CLAIMS

1. A targeting construct, comprising a modified IL-1 family cytokine characterized by a reduced affinity for its receptor, and a targeting moiety.
2. The targeting construct, according to claim 1, wherein said modified IL-1 family cytokine is a mutant IL-1 family cytokine.
3. The targeting construct according to claim 1 or 2, wherein said targeting moiety is targeting to a marker expressed on a IL-1 family cytokine receptor expressing cell.
4. The targeting construct, according to claim 2, wherein said mutant IL-1 family cytokine is a mutant IL-1β.
5. The targeting construct, according to claim 4, wherein said targeting moiety is targeting to a marker expressed on an IL-1R1 and/or IL-1RacP expressing cell.
6. The targeting construct according to any of the preceding claims, wherein said targeting moiety is directed to a tissue specific marker.
7. The targeting construct according to any of the claims 1-5, wherein said targeting moiety is directed to Her2.
8. The targeting construct according to any of the previous claims, wherein said targeting moiety is an antibody.
9. The targeting construct according to claim 8, wherein said antibody is a nanobody.
10. The targeting construct according to any of the preceding claims, wherein the modified IL-1 family cytokine is an IL-1β mutant, selected from the group consisting of A117G/P118G, R120GR120X, L122A, T125G/L126G, R127G, Q130X, Q131G, K132A, S137G/Q138Y, L145G, H146X, L145A/L147A, Q148X, Q148G/Q150G, Q150G/D151A, M152G, F162A, F162A/Q164E, F166A, Q164E/E167K, N169G/D170G, I172A, V174A, K208E, K209A K209X, K209A/K210A, K219X, and E221KX, E221S/N224A, N224S/K225S, E244K and N245Q
11. A targeting construct according to any of the claims 1-10 for use as a medicament.
12. The targeting construct according to any of the claims 1-10 for use in stimulation of the immune response.
13. The targeting construct according to any of the claims 1-10 for use in treatment of cancer.

CLAIMS

1. A composition comprising a targeting construct, comprising:

(1) a mutated IL-1β characterized by a reduced affinity for its receptor as compared to wild type IL-1β, wherein the mutated IL-1β comprises one or more mutations selected from R120X, Q131G, L145G, H146X, L147A, Q148X, F162A, Q164E, and K208E, where X is a non-conservative change, and

(2) a targeting moiety comprising a variable domain of camelid heavy chain antibodies (VHH) or a variable domain of new antigen receptors (VNAR).

2. The targeting construct, according to claim 1, wherein said mutant IL-1β comprises one or more mutations selected from R120G, Q131G, L145G, H146A, L147A, Q148G, F162A, Q164E, and K208E.

3. The composition, according to claim 1, wherein said targeting moiety is targeting to a marker expressed on an IL-1 R1 and/or IL-1 RacP expressing cell.

4. The composition according to any one of the preceding claims, wherein said targeting moiety is directed to Her2 or leptin receptor.

5. The composition according to any of the preceding claims, wherein the mutated IL-1β comprises one or more of:

(i) Q131G and Q148G,

(ii) Q148G and K208E,

(iii) R120G and Q131G,

(iv) R120G and H146A,

(v) R120G and K208E,

(vi) R120G, F162A, and Q164E,

(vii) F162A and Q164E,

(viii) Q164E and E167K, and

(ix) L145A and L147A.

6. A composition according to any one of the preceding claims for use as a medicament.

7. The composition according to any one of the preceding claims for use in stimulation of the immune response.

8. The composition according to any one of the preceding claims for use in treatment of cancer.

9. Use of a composition according to any one of claims 1-6 in the manufacture of a medicament for stimulation of the immune response.

10. Use of a composition according to any one of claims 1-7 in the manufacture of a medicament for treatment of cancer.

11. A composition for use in a method of stimulating an immune response in a cell, the method comprising contacting the cell with a composition comprising a targeting construct comprising:

(1) a mutated IL-1β characterized by a reduced affinity for its receptor as compared to wild type IL-1β, wherein the mutated IL-1β comprises one or more mutations selected from R120X, Q131G, L145G, H146X, L147A, Q148X, F162A, Q164E, and K208E, where X is a non-conservative change, and

(2) a targeting moiety comprising a variable domain of camelid heavy chain antibodies (VHH) or a variable domain of new antigen receptors (VNAR).

12. The composition for use of claim 11, wherein NFκB is activated.

13. The composition for use of claim 11 or 12, wherein the mutated IL-1β comprises one or more of:

(i) Q131G and Q148G,

(ii) Q148G and K208E,

(iii) R120G and Q131G,

(iv) R120G and H146A,

(v) R120G and K208E and

(vi) R120G, F162A, and Q164E,

(vii) F162A and Q164E,

(viii) Q164E and E167K, and

(ix) L145A and L147A.

14. The composition for use of any one of claims 11-13, wherein the targeting moiety comprises a variable domain of a camelid heavy chain antibody (VHH) against HER2.

15. The composition for use of any one of claims 11-13, wherein the targeting moiety comprises a variable domain of a camelid heavy chain antibody (VHH) against leptin receptor.