

CLAIMS

1. A fusion polypeptide comprising:

(i) a DNAX-activating protein 10 (DAP10) polypeptide comprising the sequence of SEQ ID NO: 1, or a functional variant thereof, wherein the functional variant is a truncated version of SEQ ID NO: 1 comprising or consisting of amino acids 19-93 or 49-93 of SEQ ID NO: 1; and

(ii) a DNAX-activating protein 12 (DAP12) polypeptide comprising the sequence of SEQ ID NO: 9, or a functional variant thereof, wherein the functional variant is a truncated version of SEQ ID NO: 9 comprising or consisting of amino acids 22-113 or 62-113 of SEQ ID NO: 9.

2. The fusion polypeptide according to claim 1, having the formula, from N-terminus to C-terminus:

A-B-C-D-E,

wherein

A = an optional N-terminal sequence

B = the DAP10 polypeptide or functional variant thereof

C = an optional linker sequence

D = the DAP12 polypeptide or functional variant thereof

E = an optional C-terminal sequence.

3. The fusion polypeptide of claim 1 or claim 2, wherein the DAP10 polypeptide or functional variant thereof comprises or consists of any one of SEQ ID Nos: 1, 2 or 7.

4. The fusion polypeptide of any one of claims 1-3, wherein the DAP12 polypeptide or functional variant thereof comprises or consists of any one of SEQ ID Nos: 9-11.

5. The fusion polypeptide according to any previous claim, wherein the fusion polypeptide comprises or consists of the sequence of SEQ ID NO: 60.

6. The fusion polypeptide according to claim 1 or claim 2, wherein the fusion polypeptide:

(a) does not comprise SEQ ID NO: 84; and/or

(b) does not comprise an anti-EpCAM peptide.

5 7. The fusion polypeptide according to any previous claim, wherein the fusion polypeptide is part of a contiguous chimeric polypeptide further comprising a NKG2D polypeptide or wherein the fusion polypeptide is in electrostatic association with a NKG2D polypeptide, wherein

10 (i) the NKG2D polypeptide comprises or consists of the human NKG2D polypeptide of SEQ ID NO: 14, or

(ii) is a functional variant of a NKG2D polypeptide which is a truncated version of SEQ ID NO: 14 comprising or consisting of amino acids 52-216 of SEQ ID NO: 14.

15 8. The fusion polypeptide according to claim 7, wherein the fusion polypeptide is part of a contiguous chimeric polypeptide further comprising a NKG2D polypeptide and the contiguous chimeric polypeptide comprises or consists of the sequence of SEQ ID NO: 64.

9. An isolated nucleic acid sequence encoding the fusion polypeptide according to any previous claim, optionally wherein the isolated nucleic acid sequence comprises a nucleotide sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97% or at
20 least 99% sequence identity with a nucleic acid encoding SEQ ID NOs: 60 or 64 or wherein the isolated nucleic acid comprises or consists of the nucleotide sequence of SEQ ID NOs: 70 or 74.

10. A vector comprising the nucleic acid according to claim 9, optionally wherein the vector is a lentiviral vector or a retroviral vector.

25 11. A host cell comprising the fusion polypeptide according to any of claims 1-8, the nucleic acid according to claim 9 or the vector according to claim 10.

12. An immunoresponsive cell selected from a T-cell or a NK cell comprising the fusion polypeptide according to any of claims 1-8, the nucleic acid according to claim 9 or the vector according to claim 10.

30

13. A method for making an immunoresponsive cell, comprising the steps of:

- (i) transducing the nucleic acid sequence of claim 9 or vector of claim 10 into the immunoresponsive cell; and
- (ii) culturing the immunoresponsive cell such that a fusion polypeptide is expressed and associates with a NKG2D polypeptide to form a CAR.

5

14. A pharmaceutical composition comprising the fusion polypeptide of any of claims 1-8, nucleic acid of claim 9, vector of claim 10, host cell of claim 11, or immunoresponsive cell of claim 12 and a pharmaceutically or physiologically acceptable diluent and/or carrier.

15. The immunoresponsive cell of claim 12 or pharmaceutical composition comprising such an immunoresponsive cell according to claim 14 for use in the treatment of a pathological disorder, optionally wherein the pathological disorder is cancer.

10