

CLAIMS

1. A fusion polypeptide comprising:

(i) a DNAX-activating protein 10 (DAP10) polypeptide comprising the sequence of
5 SEQ ID NO: 1, or a functional variant thereof, wherein the functional variant

(a) comprises an amino acid sequence having at least 80% sequence identity to
SEQ ID NO: 1, or

(b) is a truncated version of SEQ ID NO: 1 comprising or consisting of amino acids
19-93, 19-69, 1-71, 19-71, 19-48, 49-69, 49-93, or 70-93 of SEQ ID NO: 1; and

(ii) a DNAX-activating protein 12 (DAP12) polypeptide comprising the sequence of
10 SEQ ID NO: 9, or a functional variant thereof, wherein the functional variant

(a) comprises an amino acid sequence having at least 80% sequence identity to
SEQ ID NO: 9, or

(b) is a truncated version of SEQ ID NO: 9 comprising or consisting of amino acids
15 22-113, 62-113, 22-61 or 41-61 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

20 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.

25 3. The fusion polypeptide according to any previous claim, comprising the functional variant of DAP10 polypeptide, wherein the functional variant of DAP10 polypeptide comprises an amino acid sequence having at least 85%, at least 90%, at least 95%, at least 97%, at least 98% or at least 99% sequence identity to the DAP10 polypeptide of SEQ ID NO: 1.

4. 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: 1-8.
5. The fusion polypeptide according to any previous claim, comprising the functional variant of DAP12 polypeptide, wherein the functional variant of DAP12 polypeptide
5 comprises an amino acid sequence having at least 85%, at least 90%, at least 95%, at least 97%, at least 98% or at least 99% sequence identity to the DAP12 polypeptide of SEQ ID NO: 9.
6. The fusion polypeptide of any one of claims 1-4, wherein the DAP12 polypeptide or functional variant thereof comprises or consists of any one of SEQ ID Nos: 9-13.
- 10 7. The fusion polypeptide according to any previous claim, wherein the fusion polypeptide comprises or consists of the sequence of any one of SEQ ID NOs: 60 to 63.
8. 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; and/or
 - 15 (c) does not comprise SEQ ID NO: 85; and/or
 - (d) does not comprise SEQ ID NO: 86; and/or
 - (e) does not comprise both SEQ ID NO: 85 and SEQ ID NO: 86.
9. 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
20 wherein the fusion polypeptide is in electrostatic association with a NKG2D polypeptide, optionally wherein the NKG2D polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98% or at least 99% sequence identity to the human NKG2D polypeptide of SEQ ID NO: 14.
10. The fusion polypeptide according to claim 9, wherein the NKG2D polypeptide is a
25 functional variant of a NKG2D polypeptide which is a truncated version of SEQ ID NO: 14, optionally wherein the truncated version of NKG2D comprises or consists of amino acids 52-216, 73-216 or 82-216 of SEQ ID NO: 14.
11. The fusion polypeptide according to claim 9 or claim 10, wherein the fusion polypeptide is part of a contiguous chimeric polypeptide further comprising a NKG2D polypeptide and
30 the contiguous chimeric polypeptide comprises or consists of the sequence of any one of SEQ ID NOs: 64-69.

12. 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 least 99% sequence identity with a nucleic acid encoding any of SEQ ID NOs: 60-69 or
5 wherein the isolated nucleic acid comprises or consists of the nucleotide sequence of any one of SEQ ID NOs: 70-79.
13. A vector comprising the nucleic acid according to claim 12, optionally wherein the vector is a lentiviral vector or a retroviral vector.
14. A host cell comprising the fusion polypeptide according to any of claims 1-11, the
10 nucleic acid according to claim 12 or the vector according to claim 13.
15. An immunoresponsive cell selected from a T-cell or a NK cell comprising the fusion polypeptide according to any of claims 1-11, the nucleic acid according to claim 12 or the vector according to claim 13.
16. A method for making an immunoresponsive cell, comprising the steps of:
- 15 (i) transducing the nucleic acid sequence of claim 12 or vector of claim 13 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.
17. A pharmaceutical composition comprising the fusion polypeptide of any of claims 1-11,
20 nucleic acid of claim 12, vector of claim 13, host cell of claim 14, or immunoresponsive cell of claim 15 and a pharmaceutically or physiologically acceptable diluent and/or carrier.
18. The fusion polypeptide of any of claims 1-11, nucleic acid of claim 12, vector of claim 13, host cell of claim 14, immunoresponsive cell of claim 15 or pharmaceutical composition according to claim 17 for use in the treatment of a pathological disorder, optionally wherein
25 the pathological disorder is cancer.