

Claims

1. An at least bispecific antigen binding protein comprising
 - (i) a heavy chain variable domain (V_H) and a light chain variable domain (V_L),
5 wherein said V_H comprises a complementary determining region 1 (CDR1), a CDR2 and a CDR3; and the CDR3 is the CDR3 as comprised in SEQ ID NO: 43; and
said V_L comprises a CDR1, a CDR2 and a CDR3 as comprised in SEQ ID NO: 42, and optionally wherein each of the CDR1, the CDR2 and the CDR3 comprises up to three amino acid substitutions compared to the CDR1, CDR2 and the CDR3 as comprised in SEQ ID NO: 42; and
10
 - (ii) a variable alpha domain ($V\alpha$) and a variable beta domain ($V\beta$),
wherein
said $V\alpha$ comprises CDR1a according to SEQ ID NO: 23, CDR2a according to SEQ
15 ID NO: 26 and CDR3a according to SEQ ID NO: 25; and
said $V\beta$ comprises CDR1b according to SEQ ID NO: 31, CDR2b according to SEQ ID NO: 34 and CDR3b according to SEQ ID NO: 35.
2. The at least bispecific antigen binding protein according to claim 1, wherein said V_H
20 comprises the CDR1 and the CDR2 as comprised in SEQ ID NO: 43, and optionally wherein each of the CDR1 and the CDR2 comprises up to three amino acid substitutions compared to the CDR1 and the CDR2 as comprised in SEQ ID NO: 43.
3. The at least bispecific antigen binding protein according to claim 1 or 2, wherein said
25 antigen binding protein recruits T cells.
4. The at least bispecific antigen binding protein according to any one of claims 1 to 3, wherein said antigen binding protein targets the $TCR\alpha\beta$.
- 30 5. The at least bispecific antigen binding protein according to any one of claims 1 to 4, wherein said V_H comprises or consists of SEQ ID NO: 43.
6. The at least bispecific antigen binding protein according to any one of claims 1 to 5, wherein said V_L comprises or consists of SEQ ID NO: 42.

7. The at least bispecific antigen binding protein according to any of claims 1 to 6, wherein said V_H and V_L form an antigen binding site D, and wherein said antigen binding site D recruits T cells.
- 5 8. The at least bispecific antigen binding protein according to any one of claims 1 to 7, wherein said $V\alpha$ and said $V\beta$ form an antigen binding site B, and preferably wherein the antigen binding site B binds to a target antigenic (TA) peptide/MHC complex.
9. The at least bispecific antigen binding protein according to claim 8, wherein the antigen
10 binding site B comprises or consists of a T cell receptor (TCR) or (a) fragment(s) thereof or an antibody or (a) fragment(s) thereof
10. The at least bispecific antigen binding protein according to claim 8 or 9, wherein the TA
15 antigenic peptide is a tumour associated antigen (TAA) peptide, and wherein said TAA is selected from the group of TAA antigenic peptides comprising or consisting of the MAGE-A antigenic peptide consisting of the amino acid sequence 'KVLEHVVRV' of SEQ ID NO: 10, wherein the MHC is a HLA-A*02.
11. The at least bispecific antigen binding protein according to any of claims 8 to 10, wherein
20 the antigen binding site B comprises a TCR alpha chain variable domain ($v\alpha$) and a TCR beta chain variable domain ($v\beta$), wherein
 - i) the $v\alpha$ comprises or consists of the amino acid sequence selected from the group consisting of

25 'EDVEQSLFLSVREGDSVVINCTYTDSSSTYLYWYKQEPGKGLQLLTYIYS
SQDSKQDQRLTVLLNKKDKHLSLRIADTQTGDSAIYFCAEMTSESKIIFGS
GTRLSIRP' SEQ ID NO: 20,

'EDVEQSLFLSVREGDSVVINCTYTDSSSTYLYWYKQEPGKGLQLLTYIYS
SQDQKQDQRLTVLLNKKDKHLSLRIADTQTGDSAIYFCAEMTSESKIIFGS
GTRLSIRP' 'SEQ ID NO: 21,

30 'EDVEQSLFLSVREGDSVVINCTYTESSTYLYWYKQEPGKGLQLLTYIYSS
QDQKQDQRLTVLLNKKDKHLSLRIADTQTGDSAIYFCAEMTSESKIIFGSG
TRLSIRP' SEQ ID NO: 22; or

an amino acid sequence at least 85% identical to the amino acid sequence selected from the group consisting of SEQ ID NO: 20, 21 and 22 and

wherein the amino acid sequence is at least 85% identical to the amino acid sequence of SEQ ID NO: 20 and comprises CDRa1, CDRa2, CDRa3, wherein CDRa1 comprises SEQ ID NO: 23, CDRa2 comprises SEQ ID NO: 24 and CDRa3 comprises SEQ ID NO: 25, and

5 wherein the amino acid sequence is at least 85% identical to the amino acid sequence of SEQ ID NO: 21 and comprises CDRa1, CDRa2, CDRa3, wherein CDRa1 comprises SEQ ID NO: 23, CDRa2 comprises SEQ ID NO: 26 and CDRa3 comprises SEQ ID NO: 25, and

10 wherein the amino acid sequence is at least 85% identical to the amino acid sequence of SEQ ID NO: 22 and comprises CDRa1, CDRa2, CDRa3 wherein CDRa1 comprises SEQ ID NO: 27, CDRa2 comprises SEQ ID NO: 26 and CDRa3 comprises SEQ ID NO: 25, and preferably wherein the amino acid of said first variable domain comprises the amino acids 19V and/or 48K, and the $v\beta$ comprises or consists of the amino acid sequence

15 ‘DAGVIQSPRHEVTEMGQEVTLRCKPIPGHDYLFWYRQTM MRGLELLFYF CYGTPCDDSGMPEDRFS AKMPNASFSTLKIQPSEPRDSAVYFCASRADTGE LFFGEGSRLTVL’ SEQ ID NO: 30 or an amino acid sequence at least 85% identical to the amino acid sequence consisting of SEQ ID NO 30, and wherein the amino acid sequence is at least 85% identical to the amino acid sequence of SEQ

20 ID NO: 30 and comprises CDRb1, CDRb2, and CDRb3, wherein CDRb1 comprises SEQ ID NO: 31, CDRb2 comprises SEQ ID NO: 34 and CDRb3 comprises SEQ ID NO: 35, respectively, and optionally comprises the amino acid 54F and/or 66C, or

(ii) the $v\alpha$ or $v\gamma$ comprises or consists of the amino acid sequence SEQ ID NO: 48 or

25 an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 48, wherein an amino acid sequence is at least 85% identical to the amino acid sequence of SEQ ID NO: 48 and comprises and CDRa1, CDRa2, CDRa3, wherein CDRa1 comprises SEQ ID NO: 49, CDRa2 comprises SEQ ID NO: 50 and CDRa3 comprises SEQ ID NO: 51 and

30 the $v\beta$ or $v\delta$ comprises or consists of the amino acid sequence of SEQ ID NO: 44 or an amino acid sequence at least 85% identical to SEQ ID NO: 44 wherein said amino acid sequence is at least 85% identical to the amino acid sequence of SEQ ID NO: 44 and comprises CDRa1, CDRa2, CDRa3, wherein CDRb1 comprises

SEQ ID NO: 45, CDRb2 comprises SEQ ID NO: 46 and CDRb3 comprises SEQ ID NO: 47.

12. The at least bispecific antigen binding protein according to any of claims 1 to 11, further
5 comprising one or more of the following:
- (i) a diagnostic agent;
 - (ii) a therapeutic agent; or
 - (iii) a pharmacokinetics (PK) modifying moiety.
- 10 13. A nucleic acid or two separate nucleic acids comprising a sequence encoding an at least bispecific antigen binding protein according to any one of claims 1 to 12, or a nucleic acid vector comprising said nucleic acid or two separate nucleic acids.
14. A recombinant host cell comprising the at least bispecific antigen binding protein
15 according to any one of claims 1 to 12, or the nucleic acid or two separate nucleic acids or the nucleic acid vector according to claim 13,
preferably wherein said host cell is
- a) a stem cell, more preferably a mesenchymal stem cell; or
 - b) a cell for recombinant expression, such as a Chinese Hamster Ovary (CHO) cell.
- 20 15. A method of producing an at least bispecific antigen binding protein, comprising
- a) providing a suitable host cell,
 - b) providing a genetic construct comprising a coding sequence encoding the at least bispecific antigen binding protein according to any of claims 1 to 12,
 - 25 c) introducing said genetic construct into said suitable host cell, and
 - d) expressing said genetic construct by said suitable host cell,
preferably wherein the method comprises the isolation and/or purification of the at least bispecific antigen binding protein from the suitable host cell.
- 30 16. An at least bispecific antigen binding protein obtainable by the method of claim 15.
17. A pharmaceutical composition comprising the at least bispecific antigen binding protein according to any one of claims 1 to 12 or 16, the nucleic acid or two separate nucleic

acids, or the nucleic acid vector according to claim 13, or the host cell according to claim 14, and a pharmaceutically acceptable carrier, diluent, stabilizer and/or excipient.

- 5 18. The pharmaceutical composition according to claim 17, wherein the at least bispecific antigen binding protein is dissolved or dispersed in a pharmaceutically acceptable carrier or aqueous medium.
19. An at least bispecific antigen binding protein obtainable by the method of claim 18.
- 10 20. Use of the at least bispecific antigen binding protein according to any one of claims 1 to 12, 16 or 19, the nucleic acid or two separate nucleic acids or the nucleic acid vector according to claim 13, the host cell according to claim 14 or the pharmaceutical composition according to claim 17 or 18 for the manufacture of a medicament for treating a disease.
- 15 21. Use of the at least bispecific antigen binding protein according to any one of claims 1 to 12, 16 or 19, the nucleic acid or two separate nucleic acids or the nucleic acid vector according to claim 13, the host cell according to claim 14 or the pharmaceutical composition according to claim 17 or 18 for the manufacture of a medicament for the
- 20 diagnosis of a proliferative disease.
22. Use of the at least bispecific antigen binding protein according to any one of claims 1 to 12, 16 or 19, the nucleic acid or two separate nucleic acids or the nucleic acid vector according to claim 13, the host cell according to claim 14 or the pharmaceutical
- 25 composition according to claim 17 or 18 for the manufacture of a medicament for the treatment of a proliferative disease.
23. The use according to claims 21 or 22, wherein the proliferative disease is cancer.