

The present disclosure provides a set of antibodies comprising:

i) a first antibody that binds to an antigen expressed on the surface of a target cell, and which further comprises a V_H domain of an antigen binding site for a radiolabelled compound, but which does not comprise a V_L domain of an antigen binding site for the radiolabelled compound; and

ii) a second antibody that binds to the antigen expressed on the surface of the target cell, and which further comprises a V_L domain of an antigen binding site for the radiolabelled compound, but which does not comprise a V_H domain of the antigen binding site for the radiolabelled compound,

10 wherein said V_H domain of the first antibody and said V_L domain of the second antibody are together capable of forming a functional antigen binding site for the radiolabelled compound.

In one aspect, the present disclosure provides a set of antibodies comprising:

i) a first antibody that binds to an antigen expressed on the surface of a target cell, and which further comprises a V_H domain from a functional antigen binding site for a radiolabelled compound, but which does not comprise a V_L domain from the functional antigen binding site for the radiolabelled compound; and

ii) a second antibody that binds to said antigen expressed on the surface of the target cell, and which further comprises a V_L domain from a functional antigen binding site for the
20 radiolabelled compound, but which does not comprise a V_H domain from the functional antigen binding site for the radiolabelled compound,

wherein said V_H domain of the first antibody and said V_L domain of the second antibody are together capable of forming the functional antigen binding site for the radiolabelled compound when the first and second antibodies are bound to said antigen,

wherein the radiolabelled compound comprises Pb-DOTAM, and

wherein the V_H domain from the functional antigen binding site for the radiolabelled compound comprises:

- a) a heavy chain CDR1;
- b) heavy chain CDR2 comprising the amino acid sequence FIGSRGDTYYASWAKG (SEQ ID NO:2), or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 2, wherein these substitutions do not include Phe50, Asp56 and/or Tyr58, and optionally also do not include Gly52 and/or Arg54;
- c) heavy chain CDR3 comprising the amino acid sequence ERDPYGGGAYPPHL (SEQ ID NO:3), or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 3, wherein these substitutions do not include Glu95, Arg96, Asp97, Pro98, Ala100C, Tyr100D, and Tyr99 and optionally also do not include Pro100E;

10 and wherein the VL domain from the functional antigen binding site for the radiolabelled compound comprises:

- d) light chain CDR1 comprising the amino acid sequence QSSHSVYSDNDLA (SEQ ID NO:4) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 4, wherein these substitutions do not include Tyr28 and Asp32;
- e) a light chain CDR2; and
- f) light chain CDR3 comprising the amino acid sequence LGGYDDESDTYG (SEQ ID NO:6) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 6, wherein these substitutions do not include Gly91, Tyr92, Asp93, Thr95c and Tyr96; wherein numbering is according to Kabat.

20 Neither the first nor the second antibody comprise, on their own, a functional antigen binding site for a radiolabelled compound. The first antibody has only a V_H domain from the functional binding site for the radiolabelled compound, and not the V_L domain. The second antibody has only the V_L domain, and not the V_H domain.

A functional antigen binding site for the radiolabelled compound is formed when the V_H and V_L domains of the first and second antibodies are associated. This may occur, for example, when the first and second antibodies are bound to the same individual target cell or to adjacent cells.

The first and second antibodies described herein may be referred to herein as “single domain split antibodies”, “split antibodies” or “demibodies”. The V_H and V_L domain which together form an antigen binding site capable of binding to the radiolabelled compound are split between two antibodies, and not present as part of the same antibody.

The split domain format means that the radiolabelled compound cannot bind to either the first antibody on its own or to the second antibody on its own. In the blood, there is little or no stable association between the first and the second antibody, and so little or no stable binding of the radiolabelled compound.

10 An antigen expressed on the surface of a target cell may be referred to herein as a “target antigen” or “TA”. According to the present disclosure, the first and the second antibody described above have a binding site for the same target antigen. (For the avoidance of doubt, where it stated that the antibodies bind the same target antigen, this means that they have a binding site capable of binding to the same target antigen and includes the possibility

cell or a set of host cells comprising a vector or set of vectors of the present disclosure. In addition there is provided a method of producing an antibody comprising culturing the host cell(s) so that the antibody is produced.

In some examples, antibodies as described herein find use in a method of pre-targeted radioimmunotherapy (PRIT) or in a method of pre-targeted radioimaging.

10 In another aspect, the present disclosure refers to use of the set of antibodies as disclosed herein in the manufacture of a medicament for use in a method of pretargeting radioimmunotherapy of a tumour or cancer, comprising i) that the set of antibodies as disclosed herein is to be administered, wherein the first and second antibodies are to be administered simultaneously or sequentially, in either order, wherein the antibodies bind to the target antigen and localise to the surface of a cell expressing the target antigen; and wherein association of the first and second antibody forms a functional binding site for the radiolabelled compound; and ii) subsequently that a radiolabelled compound is to be administered, wherein the radiolabelled compound binds to functional binding site for the radiolabelled compound; wherein the target antigen is a cancer- or tumour-associated antigen expressed by the tumour or cancer.

In one example, the present disclosure provides a method of pre-targeted radioimmunotherapy which comprises:

- 20 i) administering to a subject a first antibody and a second antibody as described above; and
ii) subsequently administering to said subject a radiolabelled compound.

In another aspect, the present disclosure refers to use of a set of antibodies as disclosed herein in the manufacture of an imaging agent for use in a method of targeting a radioisotope to a tissue or organ for radioimaging comprising: i) that the first and second antibodies are to be administered simultaneously or sequentially, in either order, wherein the antibodies bind to a target antigen and localise to the surface of a cell expressing the target antigen, wherein association of the first and second antibody forms a functional binding site for the radiolabelled compound; and ii) subsequently that a radiolabelled compound is to be administered, wherein the radiolabelled compound binds to the functional binding site for the radiolabelled compound; wherein the tissue or organ for radioimaging expresses the target antigen.

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In another example, the present disclosure provides a first and a second antibody described above for use in a method of treatment comprising administering the first antibody and the second antibody to a subject, and subsequently administering to said subject a radiolabelled compound. In another example, the disclosure provides a first antibody as described above for use in a method of treatment comprising administering the first antibody and the second antibody to a subject, and subsequently administering to said subject a radiolabelled compound. In another example the disclosure provides the second antibody as described above for use in a method of treatment comprising administering the first antibody and the second antibody to a subject, and subsequently administering to said subject a radiolabelled compound.

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In another example, the present disclosure provides a method of radioimaging which comprises:

- i) administering to a subject a first and a second antibody as described herein, wherein the antibodies bind to the target antigen and localise to the surface of a cell expressing the target antigen;
- ii) subsequently administering a radiolabelled compound; and optionally
- iii) imaging the tissue or organ where the radionuclide has localised.

In another example, the present disclosure provides a first and a second antibody as described herein for use in a method of diagnosis carried out on the human or animal body, wherein the method comprises

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- i) administering to subject a first and a second antibody as described herein, wherein the antibodies bind to the target antigen and localise to the surface of a cell expressing the target antigen;

WHAT IS CLAIMED IS:

1. A set of antibodies comprising:

i) a first antibody that binds to an antigen expressed on the surface of a target cell, and which further comprises a VH domain from a functional antigen binding site for a radiolabelled compound, but which does not comprise a VL domain from the functional antigen binding site for the radiolabelled compound; and

ii) a second antibody that binds to said antigen expressed on the surface of the target cell, and which further comprises a VL domain from a functional antigen binding site for the radiolabelled compound, but which does not comprise a VH domain from the functional antigen binding site for the radiolabelled compound,

wherein said VH domain of the first antibody and said VL domain of the second antibody are together capable of forming the functional antigen binding site for the radiolabelled compound when the first and second antibodies are bound to said antigen,

wherein the radiolabelled compound comprises Pb-DOTAM, and

wherein the VH domain from the functional antigen binding site for the radiolabelled compound comprises:

a) a heavy chain CDR1;

b) heavy chain CDR2 comprising the amino acid sequence FIGSRGDTYYASWAKG (SEQ ID NO:2), or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 2, wherein these substitutions do not include Phe50, Asp56 and/or Tyr58, and optionally also do not include Gly52 and/or Arg54;

c) heavy chain CDR3 comprising the amino acid sequence ERDPYGGGAYPPHL (SEQ ID NO:3), or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 3, wherein these substitutions do not include Glu95, Arg96, Asp97, Pro98, Ala100C, Tyr100D, and Tyr99 and optionally also do not include Pro100E;

and wherein the VL domain from the functional antigen binding site for the radiolabelled compound comprises:

d) light chain CDR1 comprising the amino acid sequence QSSHSVYSDNDLA (SEQ ID NO:4) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 4, wherein these substitutions do not include Tyr28 and Asp32;

e) a light chain CDR2; and

f) light chain CDR3 comprising the amino acid sequence LGGYDDESDTYG (SEQ ID NO:6) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 6, wherein these substitutions do not include Gly91, Tyr92, Asp93, Thr95c and Tyr96; wherein numbering is according to Kabat.

2. The set of antibodies of claim 1, wherein the first and second antibody each comprise i) an antibody fragment comprising an antigen binding site specific for said antigen expressed on the surface of a target cell and ii) either a VL domain or a VH domain from a functional antigen binding site for the radiolabelled compound, optionally wherein the antibody fragment is selected from at least one Fv, scFv, or Fab or cross-Fab fragment.

3. The set of antibodies according to claim 1 or claim 2, wherein the first and second antibody each further comprise an Fc domain.

4. The set of antibodies of claim 3, wherein the Fc domain is modified to reduce or eliminate effector function.

5. The set of antibodies according to claims 3 or claim 4, wherein the first antibody comprises or consists of:

- i) a complete light chain;
- ii) a complete heavy chain;
- iii) an additional Fc chain; and
- iv) a polypeptide comprising or consisting of the VH domain from a functional antigen binding site for the radiolabeled compound;

wherein the light chain of (i) and the heavy chain of (ii) together provide an antigen binding site for said antigen; and wherein the polypeptide comprising or consisting of the VH domain from the functional antigen binding site for the radiolabeled compound is fused, optionally via a linker, by its N-terminus to the C-terminus of either (ii) or (iii); and

wherein the second antibody comprises or consists of

- v) a complete light chain;
- vi) a complete heavy chain;
- vii) an additional Fc chain; and
- viii) a polypeptide comprising or consisting of the VL domain from a functional antigen binding site for the radiolabeled compound;

wherein the light chain of (v) and the heavy chain of (vi) together provide an antigen binding site for said antigen; and wherein the polypeptide comprising or consisting of the VL domain from the functional antigen binding site for the radiolabeled compound is fused by its N-terminus, optionally via a linker, to the C-terminus of either (vi) or (vii); wherein the antibody heavy chain variable domain (VH) of the polypeptide of (iv) and the antibody light chain variable domain (VL) of the polypeptide of (viii) are together capable of forming the functional antigen binding site for the radiolabelled compound.

6. The set of antibodies according to claim 3 or claim 4, wherein each of the first and second antibody comprise a) an Fc domain b) at least one antibody fragment, such as an scFv, Fv, Fab or cross-Fab fragment, comprising an antigen binding site for the target antigen and c) a polypeptide comprising either a VL domain or a VH domain from a functional antigen binding site for the radiolabelled compound, wherein the C-terminus of the antibody fragment of (b) is fused to the N-terminus of one chain of the Fc domain, and the C-terminus of the polypeptide of (c) is fused to the N-terminus of the other chain of the Fc domain.

7. The set of antibodies of claim 6, wherein the first antibody comprises:

- i) a complete light chain;
- ii) a complete heavy chain;
- iii) an additional Fc chain; and
- iv) a polypeptide comprising or consisting of the VH domain from a functional antigen binding site for the radiolabeled compound;

wherein the light chain of (i) and the heavy chain of (ii) together provide an antigen binding site for the target antigen; and wherein the polypeptide comprising or consisting of the VH domain from the functional antigen binding site for the radiolabeled compound is fused by its C-terminus via a linker to the N-terminus of (iii); and

the second antibody comprises:

- v) a complete light chain;
- vi) a complete heavy chain;
- vii) an additional Fc chain; and
- viii) a polypeptide comprising or consisting of the VL domain from a functional antigen binding site for the radiolabeled compound;

wherein the light chain of (v) and the heavy chain of (vi) together provide an antigen binding site for the target antigen; and wherein the polypeptide comprising or consisting of the VL

domain from the functional antigen binding site for the radiolabeled compound is fused by its C-terminus via a linker to the N-terminus of (vii).

8. The set of antibodies of claim 3 or claim 4, wherein the first antibody comprises
- a) a first full length antibody and consisting of two antibody heavy chains and two antibody light chains, wherein at least one arm of the full length antibody binds said antigen; and
 - b) a polypeptide consisting of
 - i) an antibody heavy chain variable domain (VH); or
 - ii) an antibody heavy chain variable domain (VH) and an antibody constant domain (CH1),

wherein said polypeptide is fused by the N-terminus of the VH domain to the C-terminus of one of the two heavy chains of said first full-length antibody, optionally via a linker, and

wherein the second antibody comprises:

- c) a second full length antibody and consisting of two antibody heavy chains and two antibody light chains, wherein at least one arm of the antibody binds to said antigen; and
- d) a polypeptide consisting of
 - i) an antibody light chain variable domain (VL); or
 - ii) an antibody light chain variable domain (VL) and an antibody light chain constant domain (CL),

wherein said polypeptide is fused by the N-terminus of the VL domain to the C-terminus of one of the two heavy chains of said second full-length antibody, optionally via a linker,

wherein the polypeptide of (b) and the polypeptide of (d) are together capable of forming the functional antigen-binding site for the radiolabelled compound.

9. The set of antibodies of claim 8, wherein each of the first and second antibodies is bivalent for said antigen, optionally wherein both arms of the full-length antibody bind to the same epitope of said antigen, or wherein each of the first and second antibodies is biparatopic for said antigen.

10. The set of antibodies according to any one of the preceding claims, wherein the functional binding site for Pb-DOTAM binds with a dissociation constant (K_d) value of the binding affinity of 100pM, 50pM, 20pM, 10pM, 5pM, 1pM or less, e.g. 0.9pM or less, 0.8pM or less, 0.7pM or less, 0.6pM or less or 0.5pM or less.

11. The set of antibodies according to any one of the preceding claims, wherein the functional binding site for Pb-DOTAM binds to Pb-DOTAM and to Bi-DOTAM.

12. The set of antibodies of any one of the preceding claims, wherein the VH domain of the antigen binding site for the radiolabelled compound comprises:

a) a heavy chain CDR1 comprising the amino acid sequence GFSLSTYSMS (SEQ ID NO:1) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 1;

b) heavy chain CDR2 comprising the amino acid sequence FIGSRGDTYYASWAKG (SEQ ID NO:2), or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 2, wherein these substitutions do not include Phe50, Asp56 and/or Tyr58, and optionally also do not include Gly52 and/or Arg54;

c) heavy chain CDR3 comprising the amino acid sequence ERDPYGGGAYPPHL (SEQ ID NO:3), or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 3, wherein these substitutions do not include Glu95, Arg96, Asp97, Pro98, Ala100C, Tyr100D, and Tyr99 and optionally also do not include Pro100E;

and/or wherein the VL domain of the antigen binding site for the radiolabelled compound comprises:

d) light chain CDR1 comprising the amino acid sequence QSSHSVYSDNDLA (SEQ ID NO:4) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 4, wherein these substitutions do not include Tyr28 and Asp32;

e) light chain CDR2 comprising the amino acid sequence QASKLAS (SEQ ID NO: 5) or a variant thereof having at least 1, 2 or 3 substitutions in SEQ ID NO: 5, optionally not including Gln50; and

f) light chain CDR3 comprising the amino acid sequence LGGYDDSDTYG (SEQ ID NO:6) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 6, wherein these substitutions do not include Gly91, Tyr92, Asp93, Thr95c and Tyr96.

13. The set of antibodies of any one of the preceding claims, wherein

the VH domain from the functional antigen binding site for the radiolabelled compound comprises (a) CDR-H1 comprising the amino acid sequence of GFSLSTYSMS (SEQ ID NO:1); (b) CDR-H2 comprising the amino acid sequence of FIGSRGDTYYASWAKG (SEQ ID NO:2) and (c) CDR-H3 comprising the amino acid sequence of ERDPYGGGAYPPHL (SEQ ID NO:3); and

the VL domain from the functional antigen binding site for the radiolabelled compound comprises (d) CDR-L1 comprising the amino acid sequence of QSSHSVYSDNDLA (SEQ ID NO:4); (e) CDR-L2 comprising the amino acid sequence of QASKLAS (SEQ ID NO:5); and (f) CDR-L3 comprising the amino acid sequence of LGGYDDESPTYG (SEQ ID NO:6).

14. The set of antibodies of any one of the preceding claims, wherein

the VH domain from the functional antigen binding site for the radiolabelled compound comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 7 and SEQ ID NO 9, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 7 or SEQ ID NO: 9; and

the VL domain from the functional antigen binding site for the radiolabelled compound comprises an amino acid sequence of SEQ ID NO: 8, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 8.

15. The set of antibodies of claim 14, wherein one or more alanine residues are added to the C-terminus of the VH domain from the functional antigen binding site for the radiolabelled compound, or wherein one or more residues from the N-terminus of the CH1 domain are added to the C-terminus of the VH domain from the functional antigen binding site for the radiolabelled compound, optionally wherein residues AST are added to the C-terminus of the VH domain from the functional antigen binding site for the radiolabelled compound.

16. The set of antibodies of any one of the preceding claims, wherein the first and second antibody bind to the same epitope of the antigen expressed on the surface of a target cell.

17. The set of antibodies of any one of claims 1 to 15, wherein the first antibody binds to a different epitope of the antigen from the second antibody.

18. The set of antibodies of any one of the preceding claims, wherein the antigen expressed on the surface of a target cell is a tumour-associated antigen.

19. The set of antibodies of any one of the preceding claims, wherein the antigen expressed on the surface of a target cell is selected from the group consisting of carcinoembryonic antigen (CEA), CD20, HER2, EGP-1 (epithelial glycoprotein-1, also known as trophoblast-2), colon-specific antigen-p (CSAp), a pancreatic mucin MUC1, GPRC5D and FAP.

20. The set of antibodies of any one of the preceding claims, wherein the antigen expressed on the surface of a target cell is CEA.

21. The set of antibodies according to claim 20, wherein the first and/or second antibody comprises an antigen-binding site which binds to CEA, comprising:

a) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:19; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:20; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and

a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:22; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:23; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:24; or

b) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:43; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:44; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and

a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:46; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:47; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:48; or

c) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:11; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:12; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:13; and

a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:14; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:15; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:16; or

d) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:59; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:60; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:61; and

a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:62; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:63; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:64; or

e) comprising a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:156; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:157 or 158; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:159; and

a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:160, 161 or 162; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:163, 164 or 165; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:166.

22. The set of antibodies according to claim 21, wherein the first and/or second antibody comprises an antigen-binding site for CEA comprising

a) a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 25, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:25; and

a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 26, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:26; or

b) a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 49, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:49; and

a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 50, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:50; or

c) a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 17, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:17; and

a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 18, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:18; or

d) a heavy chain variable region (VH) comprising an amino acid sequence selected from SEQ ID NO: 169, 170, 171, 172, 173 or 174, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto; and

a light chain variable region (VL) comprising an amino acid sequence selected from SEQ ID NO: 175, 176, 177, 178, 179 or 180, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto; or

e) a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 65, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:65; and

a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 66, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:66.

23. The set of antibodies according to claim 20 wherein the first and/or second antibody comprises an antigen-binding site which binds to CEA, comprising:

(a) a VH domain comprising an amino acid sequence of SEQ ID NO:169 and a VL domain comprising an amino acid sequence of SEQ ID NO:179, or

(b) a VH domain comprising an amino acid sequence of SEQ ID NO:173 and a VL domain comprising an amino acid sequence of SEQ ID NO:179, or

- (c) a VH domain comprising an amino acid sequence of SEQ ID NO:170 and a VL domain comprising an amino acid sequence of SEQ ID NO:179, or
- (d) a VH domain comprising an amino acid sequence of SEQ ID NO:174 and a VL domain comprising an amino acid sequence of SEQ ID NO:178, or
- (e) a VH domain comprising an amino acid sequence of SEQ ID NO:173 and a VL domain comprising an amino acid sequence of SEQ ID NO:178, or
- (f) a VH domain comprising an amino acid sequence of SEQ ID NO:171 and a VL domain comprising an amino acid sequence of SEQ ID NO:178, or
- (g) a VH domain comprising an amino acid sequence of SEQ ID NO:169 and a VL domain comprising an amino acid sequence of SEQ ID NO:178.

24. The set of antibodies according to claim 20, wherein:

the first antibody comprises an antigen-binding site which binds to CEA, comprising

a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:11; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:12; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:13; and

a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:14; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:15; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:16;

and the second antibody comprises an antigen-binding site which binds to CEA, comprising

a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:19; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:20; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and

a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:22; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:23; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:24.

25. The set of antibodies according claim 1, wherein the first antibody is selected from the group consisting of:

- a) a first antibody comprising a first heavy chain of SEQ ID NO: 28, a second heavy chain of SEQ ID NO: 32 and a light chain of SEQ ID NO: 34, optionally wherein one or more alanine residues is added to the C-terminus of SEQ ID NO: 32, or wherein the sequence AST is added to the C-terminus of SEQ ID NO: 32;

b) a first antibody comprising a first heavy chain of SEQ ID NO: 51, and second heavy chain of SEQ ID NO: 52 and a light chain of SEQ ID NO: 54, optionally wherein one or more alanine residues is added to the C-terminus of SEQ ID NO:52 or wherein the sequence AST is added to the C-terminus of SEQ ID NO: 32;

c) a first antibody comprising a first heavy chain of SEQ ID NO: 86, a second heavy chain of SEQ ID NO: 87 wherein the C-terminal AST residues are optional and may be absent or replaced by a different C-terminal extension, and a light chain of SEQ ID NO: 89; and

d) a first antibody comprising a first heavy chain of SEQ ID NO: 93, a second heavy chain of SEQ ID NO: 94 wherein the C-terminal AST residues are optional and may be absent or replaced by a different C-terminal extension, and a light chain of SEQ ID NO: 96;

and/or the second antibody is selected from the group consisting of:

e) a second antibody comprising a first heavy chain of SEQ ID NO: 30, a second heavy chain of SEQ ID NO: 33 and a light chain of SEQ ID NO: 34;

f) a second antibody comprising a first heavy chain of SEQ ID NO: 55, and second heavy chain of SEQ ID NO: 56 and a light chain of SEQ ID NO: 58;

g) a second antibody comprising a first heavy chain of SEQ ID NO: 83, and second heavy chain of SEQ ID NO: 84 and a light chain of SEQ ID NO: 89; and

h) a second antibody comprising a first heavy chain of SEQ ID NO:90, and second heavy chain of SEQ ID NO: 91 and a light chain of SEQ ID NO: 96.

26. The set of antibodies according to claim 7, wherein:

i) the first antibody comprises a first heavy chain of SEQ ID NO:112, a second heavy chain of SEQ ID NO: 114 and a light chain of SEQ ID NO: 115; and

ii) the second antibody comprises a first heavy chain of SEQ ID NO:112, a second heavy chain of SEQ ID NO: 113 and a light chain of SEQ ID NO: 115.

27. A set of nucleic acids expressing the set of antibodies of any one of the preceding claims.
28. An expression vector or set of expression vectors comprising the set of nucleic acids according to claim 27.
29. A host cell or set of host cells comprising the expression vector or set of expression vectors of claim 28.
30. Use of the set of antibodies according to any one of claims 1 to 26 in the manufacture of a medicament for use in a method of pretargeting radioimmunotherapy of a tumour or cancer, comprising
- i) that the set of antibodies according to any one of claims 1 to 27 is to be administered, wherein the first and second antibodies are to be administered simultaneously or sequentially, in either order, wherein the antibodies bind to the target antigen and localise to the surface of a cell expressing the target antigen; and wherein association of the first and second antibody forms a functional binding site for the radiolabelled compound; and
 - ii) subsequently that a radiolabelled compound is to be administered, wherein the radiolabelled compound binds to functional binding site for the radiolabelled compound;
- wherein the target antigen is a cancer- or tumour-associated antigen expressed by the tumour or cancer.
31. The use of claim 30, wherein the subject is human.
32. Use of a set of antibodies according to any one of claims 1 to 26 in the manufacture of an imaging agent for use in a method of targeting a radioisotope to a tissue or organ for radioimaging comprising:
- i) that the first and second antibodies are to be administered simultaneously or sequentially, in either order, wherein the antibodies bind to a target antigen and localise to the surface of a cell expressing the target antigen, wherein association of the first and second antibody forms a functional binding site for the radiolabelled compound; and
 - ii) subsequently that a radiolabelled compound is to be administered, wherein the radiolabelled compound binds to the functional binding site for the radiolabelled compound;
- wherein the tissue or organ for radioimaging expresses the target antigen.

33. The use of claim 32, wherein the use further comprises a step of imaging.
34. The use of claim 32 or claim 33, wherein the target antigen is a cancer or tumour-associated antigen and the method is a method of imaging tumours or cancer.
35. The use of any one of claims 30 to 34, wherein the use does not comprise that a clearing or blocking agent is to be administered.