

CLAIMS

1. A conjugate of a chelating agent chelated with a radionuclide, and an antibody, wherein the radionuclide is a metal nuclide emitting α particle or positron, and the antibody is a humanized antibody specifically binding to mucin subtype 5AC,
- wherein the antibody is a humanized antibody having a heavy chain variable region consisting of
- (1) the amino acid sequence shown in SEQ ID NO: 1 (H01),
 - (2) the amino acid sequence shown in SEQ ID NO: 2 (H02),
 - (3) the amino acid sequence shown in SEQ ID NO: 3 (H03), or
 - (4) the amino acid sequence shown in SEQ ID NO: 4 (H04), and
- a light chain variable region consisting of
- (5) the amino acid sequence shown in SEQ ID NO: 5 (L01),
 - (6) the amino acid sequence shown in SEQ ID NO: 6 (L02),
 - (7) the amino acid sequence shown in SEQ ID NO: 7 (L03), or
 - (8) the amino acid sequence shown in SEQ ID NO: 8 (L04).
2. The conjugate according to claim 1, wherein the antibody is a humanized antibody having
- (1) a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 1 (H01), and
 - (7) a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 7 (L03).
3. The conjugate according to claim 1 or 2, wherein the metal nuclide emitting α particle is actinium-225, and the metal nuclide emitting positron is Zr-89.
4. The conjugate according to any one of claims 1 to 3, comprising not less than 1 molecule and not more than 8 molecules of the chelating agent per 1 molecule of the antibody.
5. The conjugate according to any one of claims 1 to 4, wherein

the chelating agent site-specifically modifies an Fc region of the antibody via a linker.

6. The conjugate according to claim 5, wherein the linker
5 comprises a peptide consisting of not less than 13 and not more than 17 amino acid residues, is formed by a crosslinking reaction between the peptide modified with a crosslinking agent and the antibody, and is represented by the following formula (i);

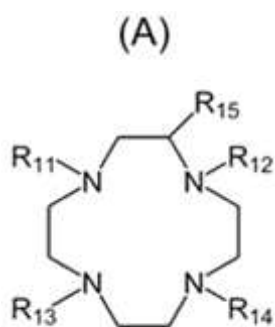
10 (Xa)-Xaa1-(Xb)-Xaa2-(Xc)-Xaa3-(Xd) ... (i)

wherein Xa, Xb, Xc and Xd are each continuous X in the number of a, continuous X in the number of b, continuous X in the number of c, and continuous X in the number of d, respectively, X is an amino acid residue having neither a thiol group nor a
15 haloacetyl group in the side chain,

a, b, c and d are each independently an integer of not less than one and not more than 5, and satisfy $a+b+c+d \leq 14$, Xaa1 and Xaa3 are each independently an amino acid residue derived from an amino acid having a thiol group in the side
20 chain, or

one is an amino acid residue derived from an amino acid having a thiol group in the side chain and the other is an amino acid residue derived from an amino acid having a haloacetyl group in the side chain, and Xaa1 and Xaa3 are linked, and
25 Xaa2 is a lysine residue, arginine residue, cysteine residue, aspartic acid residue, glutamic acid residue, 2-aminosuberic acid, or diamino propionic acid, and modified with the crosslinking agent.

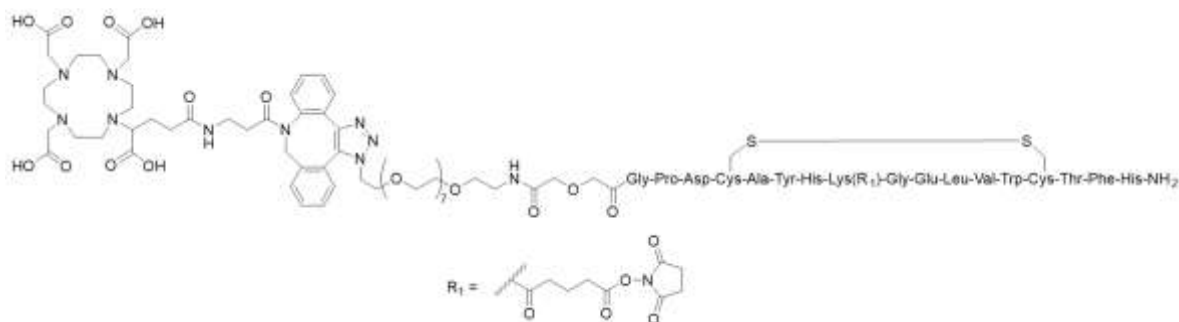
30 7. The conjugate according to any one of claims 1 to 6, wherein the chelating agent has a structure derived from a compound represented by the following formula (A) or a salt thereof:



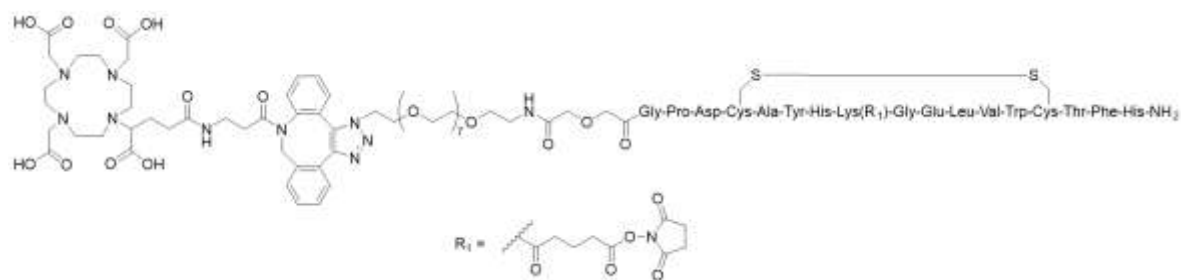
wherein in the formula (A), R_{11} , R_{13} and R_{14} are each independently a group consisting of $-(CH_2)_pCOOH$, $-(CH_2)_pC_5H_5N$, $-(CH_2)_pPO_3H_2$, $-(CH_2)_pCONH_2$ or $-(CHCOOH)(CH_2)_pCOOH$, one of R_{12} and R_{15} is a hydrogen atom, a carboxyl group, or a carboxyalkyl group having 2 or 3 carbon atoms, the other is a substituent for conjugating with the antibody, p is an integer of not less than 0 and not more than 3, R_{15} is a hydrogen atom when R_{12} is a substituent for conjugating with the antibody, and R_{15} is a substituent for conjugating with the antibody when R_{12} is not a substituent for conjugating with the antibody.

8. The conjugate according to claim 2, wherein the antibody comprises a heavy chain constant region consisting of the amino acid sequence shown in SEQ ID NO: 25 and a light chain constant region consisting of the amino acid sequence shown in SEQ ID NO: 26.

9. The conjugate according to claim 8, wherein the Fc region of the antibody is site-specifically modified by a chelating agent and linker of the formula:



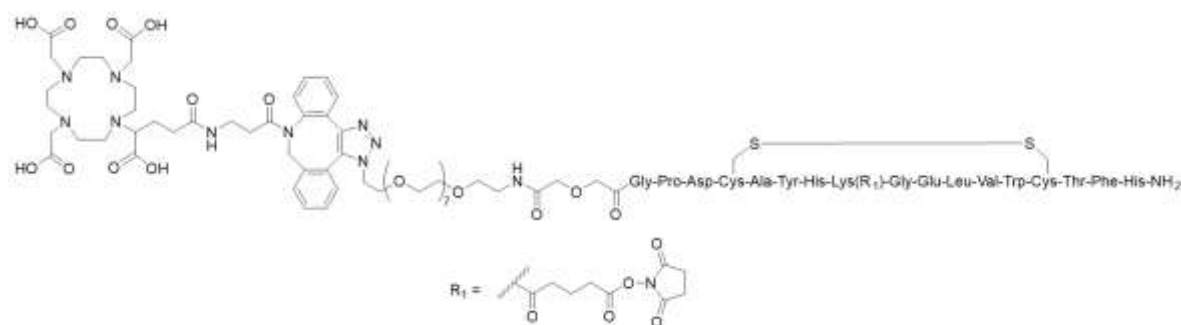
or



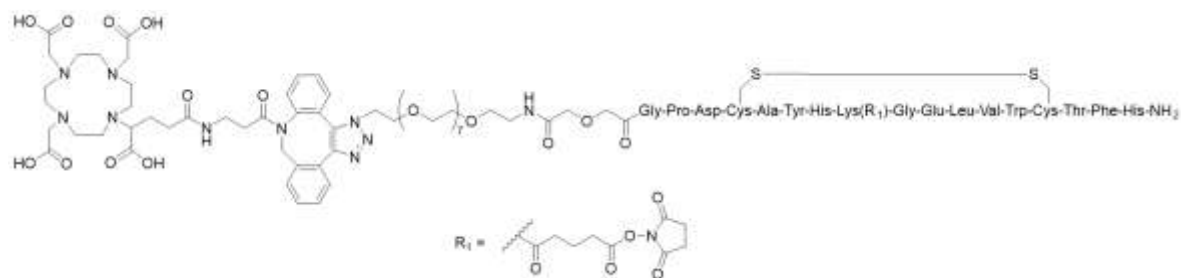
and

the radionuclide is actinium-225.

- 5 10. The conjugate according to claim 10, wherein the Fc region of the antibody is site-specifically modified by a chelating agent and the linker of the formula:



or



10

and

the radionuclide is zirconium-89.

11. The conjugate according to claim 9 or 10, wherein the Fc
15 region of the antibody is site-specifically modified by reaction between R_1 and a Lys252 residue according to the EU nunebring in the Fc region of the antibody.

12. A radiopharmaceutical comprising the conjugate according to

any one of claims 1 to 11 as the active ingredient.

13. The radiopharmaceutical according to claim 12 for use in RI
internal therapy for cancer, wherein the radionuclide is a
5 metal nuclide emitting α particle.

14. The radiopharmaceutical for use according to claim 13,
wherein the radiopharmaceutical is to be administered to a
subject at a dose of not more than 250 kBq/kg one time in the
10 RI internal therapy.

15. The radiopharmaceutical for use according to claim 14,
wherein the dose is not more than 80 kBq/kg one time.

15 16. The radiopharmaceutical according to claim 12 for use in
the diagnosis of cancer, wherein the radionuclide is a metal
nuclide emitting positron.

17. A radiopharmaceutical for use in the diagnosis of cancer in
20 RI internal therapy, wherein the RI internal therapy utilizes
the radiopharmaceutical according to any one of claims 13 to 15,
and wherein the radiopharmaceutical comprises a conjugate of a
chelating agent chelated with a radionuclide, and an antibody,
wherein the antibody is a humanized antibody specifically
25 binding to mucin subtype 5AC.