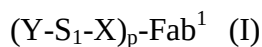


CLAIMS

1. A conjugate represented by the following formula (I):



wherein

Fab¹ is an anti-human CEACAM5 antibody Fab fragment selected from the group consisting of

(a) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment including a heavy chain variable region consisting of the amino acid sequence of amino acids 1 to 121 of SEQ ID NO: 2 and a light chain including a light chain variable region consisting of the amino acid sequence of amino acids 1 to 112 of SEQ ID NO: 4, and

(b) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment including a heavy chain variable region which consists of the amino acid sequence of amino acids 1 to 121 of SEQ ID NO: 2 and in which glutamic acid of amino acid 1 of SEQ ID NO: 2 is modified to pyroglutamic acid, and a light chain including a light chain variable region consisting of the amino acid sequence of amino acids 1 to 112 of SEQ ID NO: 4,

the Fab¹ is bound to X via p amino groups or thiol groups in the Fab¹;

X is a peptide linker or a bond;

S₁ is a spacer or a bond;

Y is a ligand; and

p is a natural number of 1 to 25 and represents the number of (Y-S₁-X) bound to Fab¹;

provided that when X is a bond, S₁ is -CH₂-(1,4-phenylene)-NH-C(=S)- or a bond, and Y is 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid.

2. The conjugate according to claim 1, wherein Fab¹ is selected from the group consisting of

(a) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 2 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4, and

(b) an anti-human CEACAM5 antibody Fab fragment comprising a heavy chain fragment which consists of the amino acid sequence shown in SEQ ID NO: 2 and in which glutamic acid of amino acid 1 of SEQ ID NO: 2 is modified to pyroglutamic acid, and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4.

3. The conjugate according to claim 2, wherein Fab¹ includes a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 2 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4.

4. The conjugate according to any one of claims 1 to 3, wherein X is a peptide linker including a peptide consisting of 2 to 4 amino acids having an amino acid sequence cleaved by a renal brush border membrane enzyme or a lysosomal enzyme.

5. The conjugate according to any one of claims 1 to 4, wherein S₁ is

-C(=O)-CH₂O-(1,3-phenylene)-C(=O)-,

-C(=O)-(CH₂CH₂O)₄-(1,3-phenylene)-C(=O)-,

-C(=O)-(1,3-phenylene)-C(=O)-,

-NH-CH₂-(1,3-phenylene)-C(=O)-,

-NH-(CH₂)₂-C(=O)-,

-CH₂-(1,4-phenylene)-NH-C(=S)-, -NH-(CH₂CH₂O)₃-CH₂-C(=O)-NH-CH₂-(1,3-phenylene)-C(=O)-,

-NH-CH₂-(1,4-phenylene)-NH-C(=O)-,

-NH-(CH₂)₃-C(=O)-,

-NH-(CH₂CH₂O)₃-CH₂-C(=O)-,

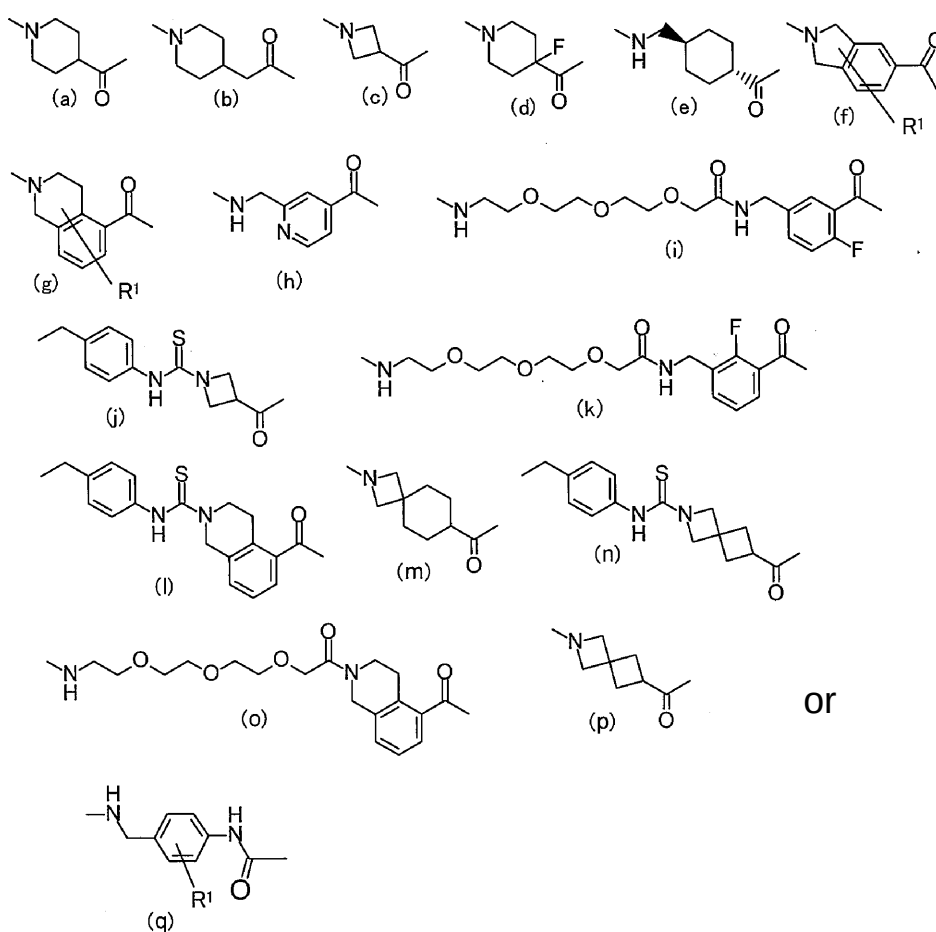
-NH-CH₂-(1,4-phenylene)-C(=O)-,

-CH₂-(1,4-phenylene)-NH-C(=S)-NH-CH₂-(1,3-phenylene)-C(=O)-,

-CH₂-(1,4-phenylene)-NH-C(=S)-NH-(CH₂CH₂O)₃-CH₂-C(=O)-NH-CH₂-(1,3-phenylene)-C(=O)-,

a spacer represented by any of the following formulas (a) to (q), or a bond,

[Chemical Formula 126]



wherein R^1 is a hydrogen atom, a halogen, or C_{1-6} alkyl, or halo C_{1-6} alkyl; and

X is a peptide linker selected from the group consisting of

- (1) -Met-Ile-NH-(CH₂)₂-Z₁-,
- (2) -Gly-Lys*-Z₂-,
- (3) -Gly-Phe-Lys*-Z₂-,
- (4) -Met-Val-Lys*-Z₂-,
- (5) -Gly-Tyr*-CH₂-C(=O)-NH-(CH₂)₂-Z₁-,
- (6) -Gly-Lys-Lys*-Z₂-,
- (7) -Gly-Arg-Lys*-Z₂-,
- (8) -Gly-Lys*-C(=S)-NH-(1,4-phenylene)-NH-C(=S)-,
- (9) -Met-Ile-NH-(CH₂)₂-NH-C(=S)-NH-(1,4-phenylene)-NH-C(=S)-,
- (10) -Asp-Gly-Lys*-Z₂-,
- (11) -Met-Gly-Lys*-Z₂-,
- (12) -Met-Ile-Lys*-Z₂-,
- (13) -Gly-Tyr*-CH₂-C(=O)-Lys*-Z₂-,

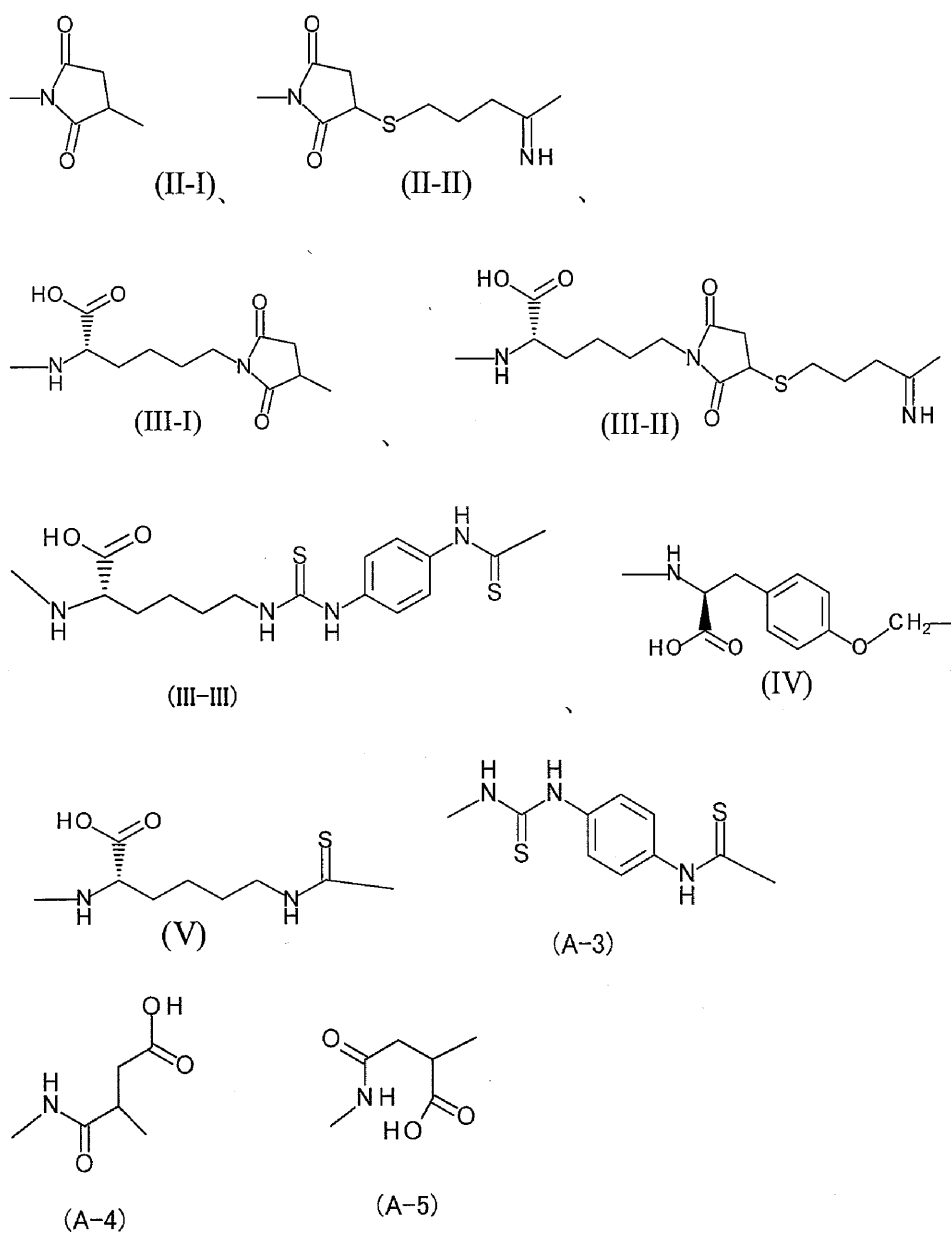
- (14) -Val-NH-(CH₂)₂-Z₁-,
- (15) -Ile-NH-(CH₂)₂-Z₁-,
- (16) -Gly-Val-NH-(CH₂)₂-Z₁-,
- (17) -Gly-Ile-NH-(CH₂)₂-Z₁-,
- (18) -Met-Phe-Lys*-Z₂-,
- (19) -Gly-Tyr-Lys*-Z₂-,
- (20) -Gly-Tyr*-CH₂-C(=O)-NH-(CH₂O)₃-CH₂-C(=O)-NH-(CH₂)₂-Z₁-,
- (21) -Gly-(3-(2-naphthyl)alanine)-Lys*-Z₂-,
- (22) -Gly-diphenylalanine-Lys*-Z₂-,
- (23) -Gly-Tyr-NH-(CH₂)₅-Z₁-,
- (24) -Met-Ile-NH-(CH₂)₂-(A-4)-,
- (25) -Met-Ile-NH-(CH₂)₂-(A-5)-,
- (26) -Met-Ile-NH-(CH₂)₂-(II-II)-,
- (27) -Met-Ile-NH-(CH₂)₂-(A-3)-,
- (28) -Met-Gly-Lys*-Z₃-, and

or

- (29) a bond,

wherein Met represents methionine, Ile represents isoleucine, Gly represents glycine, Lys represents lysine, Phe represents phenylalanine, Val represents valine, Tyr represents tyrosine, Arg represents arginine, Asp represents aspartic acid, Z₁ represents a group represented by the following formula (II-I) or (II-II), -Lys*-Z₂- represents a group represented by the following formula (III-I) or (III-II), -Tyr*-CH₂- represents a group represented by the following formula (IV), -Lys*-C(=S)- represents a group represented by the following formula (V), -Lys*-Z₃- represents a group represented by the following formula (III-III), and group (A-3), (A-4), or (A-5) is as represented by the following formulas.

[Chemical Formula 127]



6. The conjugate according to any one of claims 1 to 5, wherein S_1 is $-C(=O)-CH_2O-$ (1,3-phenylene)- $C(=O)-$, $-C(=O)-(CH_2CH_2O)_4-(1,3-phenylene)-C(=O)-$, or $-C(=O)-(1,3-phenylene)-C(=O)-$, and

X is a peptide linker selected from the group consisting of

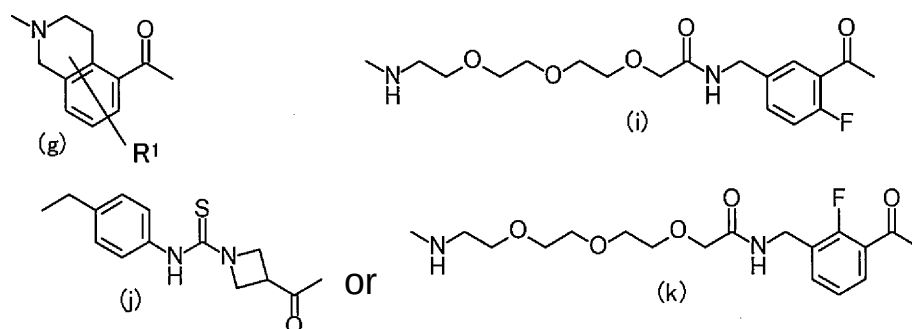
- (1) $-Met-Ile-NH-(CH_2)_2-Z_1-$,
- (2) $-Gly-Lys^*-Z_2-$,
- (3) $-Gly-Phe-Lys^*-Z_2-$,
- (5) $-Gly-Tyr^*-CH_2-C(=O)-NH-(CH_2)_2-Z_1-$,

(6) -Gly-Lys-Lys*-Z₂-, and

(8) -Gly-Lys*-C(=S)-NH-(1,4-phenylene)-NH-C(=S)-.

7. The conjugate according to any one of claims 1 to 5, wherein S₁ is -C(=O)-CH₂O-(1,3-phenylene)-C(=O)-, -C(=O)-(CH₂CH₂O)₄-(1,3-phenylene)-C(=O)-, -NH-CH₂-(1,3-phenylene)-C(=O)-, -NH-CH₂-(1,4-phenylene)-NH-C(=O)-, -NH-CH₂-(1,4-phenylene)-C(=O)-, -C(=O)-(1,3-phenylene)-C(=O)-, or the following formula

[Chemical Formula 128]



and X is a peptide linker selected from the group consisting of

(1) -Met-Ile-NH-(CH₂)₂-Z₁-,

(2) -Gly-Lys*-Z₂-,

(3) -Gly-Phe-Lys*-Z₂-,

(5) -Gly-Tyr*-CH₂-C(=O)-NH-(CH₂)₂-Z₁-,

(6) -Gly-Lys-Lys*-Z₂-,

(8) -Gly-Lys*-C(=S)-NH-(1,4-phenylene)-NH-C(=S)-,

(24) -Met-Ile-NH-(CH₂)₂-(A-4)-,

(25) -Met-Ile-NH-(CH₂)₂-(A-5)-,

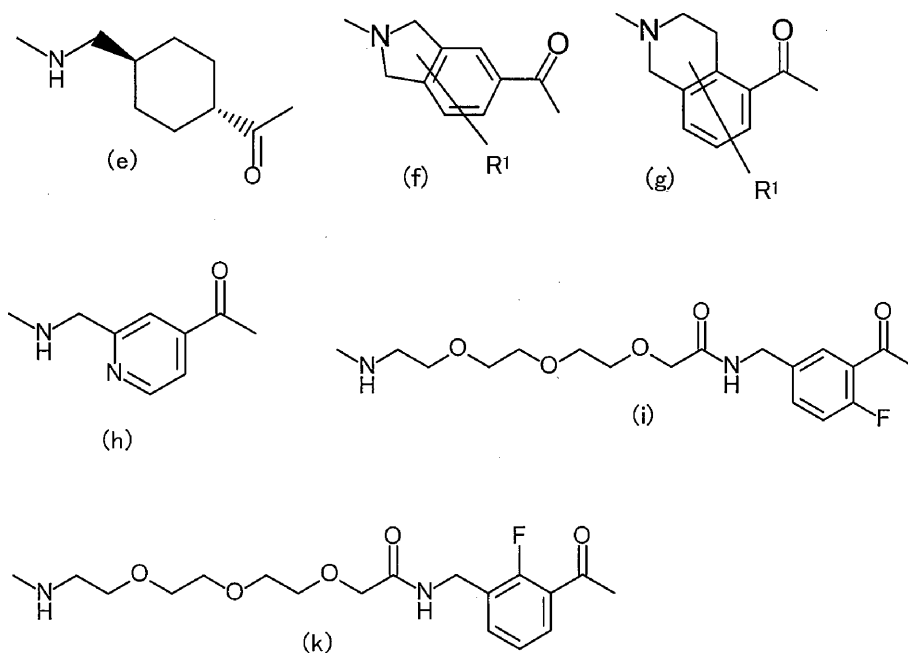
(26) -Met-Ile-NH-(CH₂)₂-(II-II)-,

(27) -Met-Ile-NH-(CH₂)₂-(A-3)-, and

(28) -Met-Gly-Lys*-Z₃-.

8. The conjugate according to any one of claims 1 to 5, wherein S₁ is -NH-CH₂-(1,3-phenylene)-C(=O)-, -CH₂-(1,4-phenylene)-NH-C(=S)-, -NH-(CH₂CH₂O)₃-CH₂-C(=O)-NH-CH₂-(1,3-phenylene)-C(=O)-, -CH₂-(1,4-phenylene)-NH-C(=S)-NH-CH₂-(1,3-phenylene)-C(=O)-, -NH-CH₂-(1,4-phenylene)-NH-C(=O)-, a spacer represented by any of the following formulas (e) to (i) or (k), or a bond,

[Chemical Formula 129]



and X is a peptide linker selected from the group consisting of

- (1) -Met-Ile-NH-(CH₂)₂-Z₁-,
- (2) -Gly-Lys*-Z₂-,
- (3) -Gly-Phe-Lys*-Z₂-,
- (9) -Met-Ile-NH-(CH₂)₂-NH-C(=S)-NH-(1,4-phenylene)-NH-C(=S)-,
- (10) -Asp-Gly-Lys*-Z₂-,
- (11) -Met-Gly-Lys*-Z₂-,
- (12) -Met-Ile-Lys*-Z₂-,
- (21) -Gly-(3-(2-naphthyl)alanine)-Lys*-Z₂-,
- (24) -Met-Ile-NH-(CH₂)₂-(A-4)-,
- (25) -Met-Ile-NH-(CH₂)₂-(A-5)-,
- (26) -Met-Ile-NH-(CH₂)₂-(II-II)-,
- (27) -Met-Ile-NH-(CH₂)₂-(A-3)-, and
- (28) -Met-Gly-Lys*-Z₃-.

9. The conjugate according to any one of claims 1 to 5, wherein X is a peptide linker selected from the group consisting of

- (1) -Met-Ile-NH-(CH₂)₂-Z₁-,
- (9) -Met-Ile-NH-(CH₂)₂-NH-C(=S)-NH-(1,4-phenylene)-NH-C(=S)-,
- (12) -Met-Ile-Lys*-Z₂-,

(24) -Met-Ile-NH-(CH₂)₂-(A-4)-,

(25) -Met-Ile-NH-(CH₂)₂-(A-5)-,

(26) -Met-Ile-NH-(CH₂)₂-(II-II)-,

(27) -Met-Ile-NH-(CH₂)₂-(A-3)-.

10. The conjugate according to any one of claims 1 to 5, wherein X is a peptide linker selected from the group consisting of

(11) -Met-Gly-Lys*-Z₂-, and

(28) -Met-Gly-Lys*-Z₃-.

11. The conjugate according to any one of claims 1 to 10, wherein Y is deferoxamine or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid.

12. The conjugate according to claims 11, wherein Y is deferoxamine.

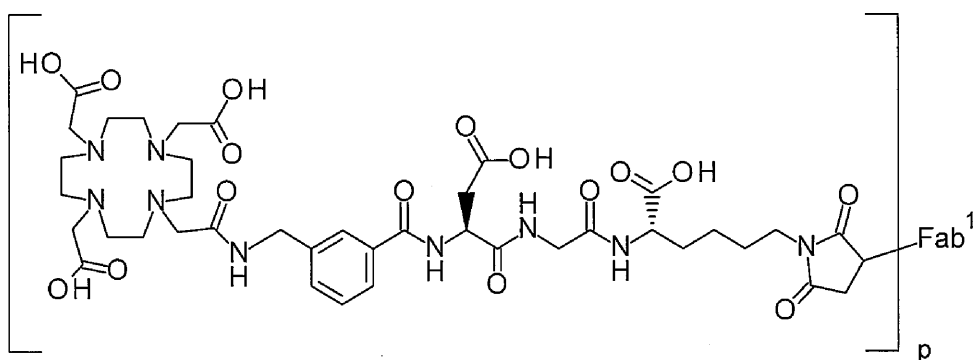
13. The conjugate according to claim 11, wherein Y is 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid.

14. The conjugate according to claim 13, wherein Y is 3arm DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid) or 4arm DOTA.

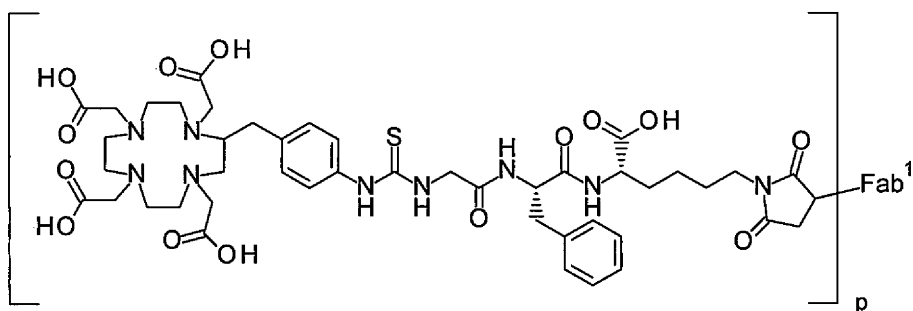
15. The conjugate according to claim 14, wherein Y is 3arm DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid).

16. The conjugate according to any one of claims 11 or 13 to 15, wherein the conjugate is a conjugate selected from the group consisting of the compounds represented by the following formulas, and Fab¹ is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab¹.

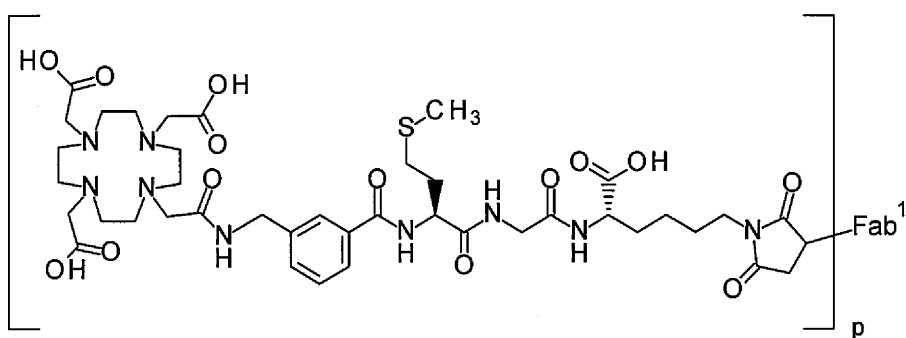
[Chemical Formula 130]



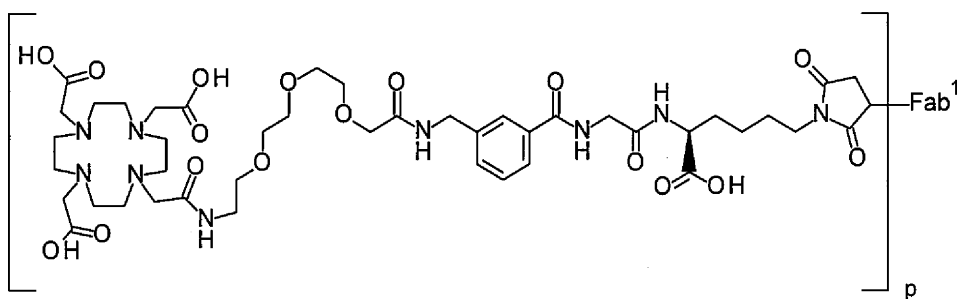
[Chemical Formula 131]



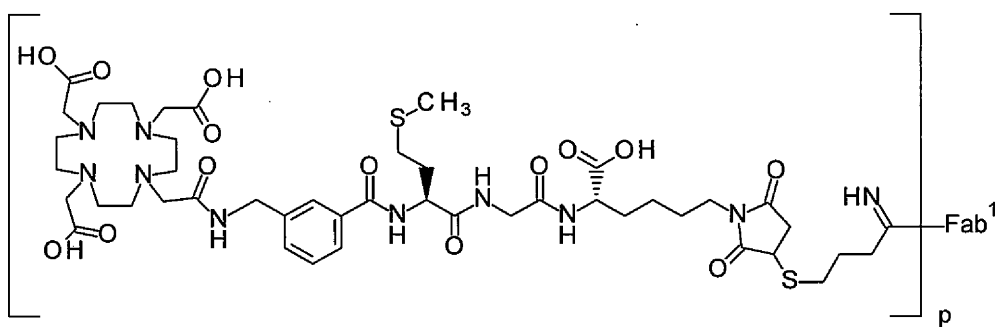
[Chemical Formula 132]



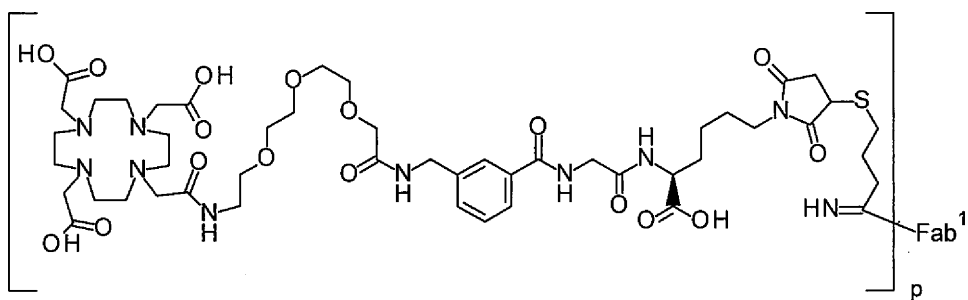
[Chemical Formula 133]



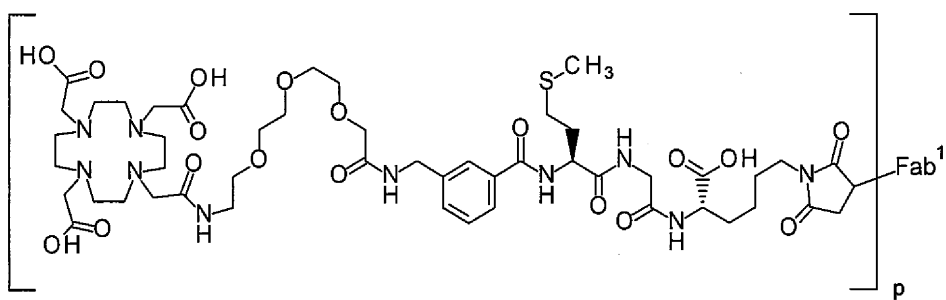
[Chemical Formula 134]



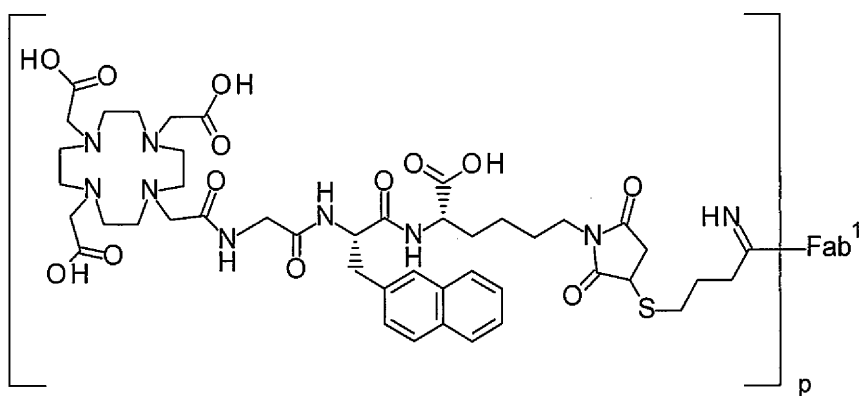
[Chemical Formula 135]



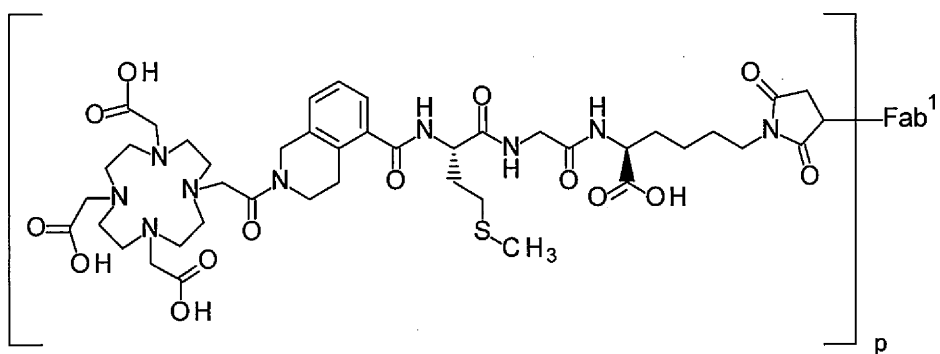
[Chemical Formula 136]



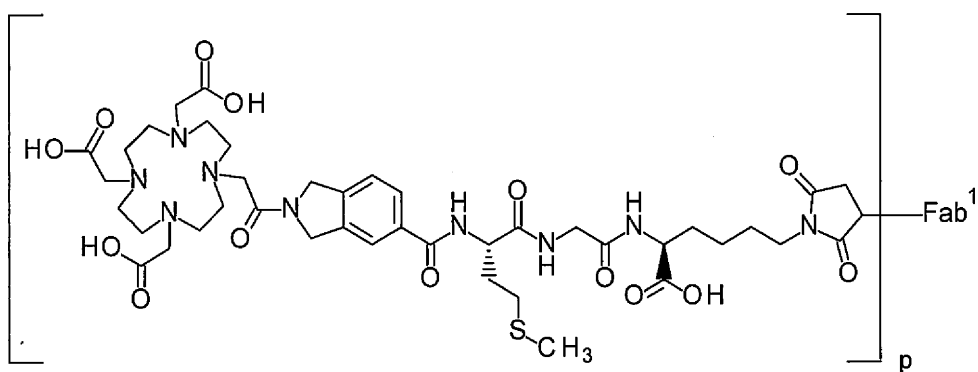
[Chemical Formula 137]



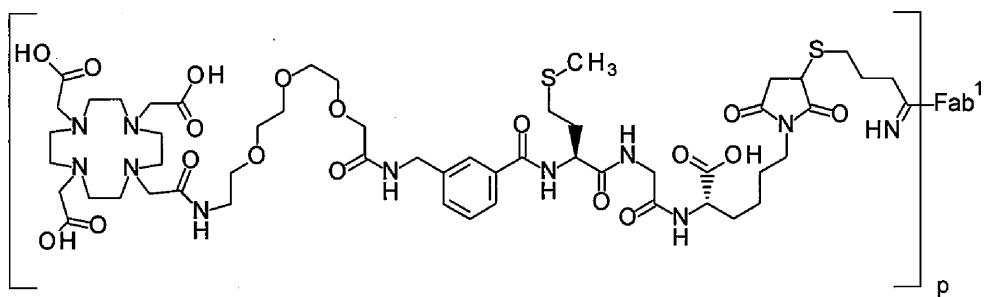
[Chemical Formula 138]



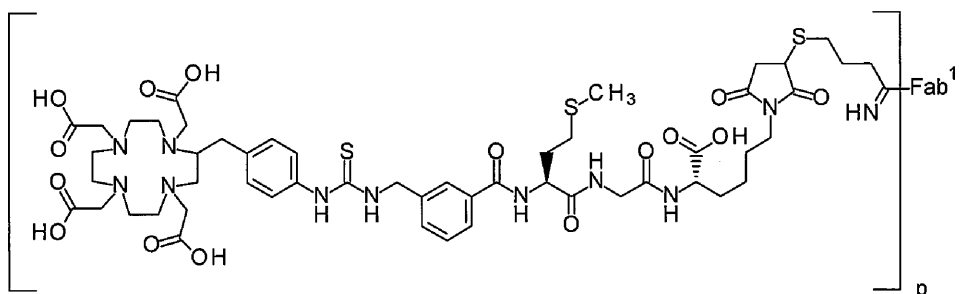
[Chemical Formula 139]



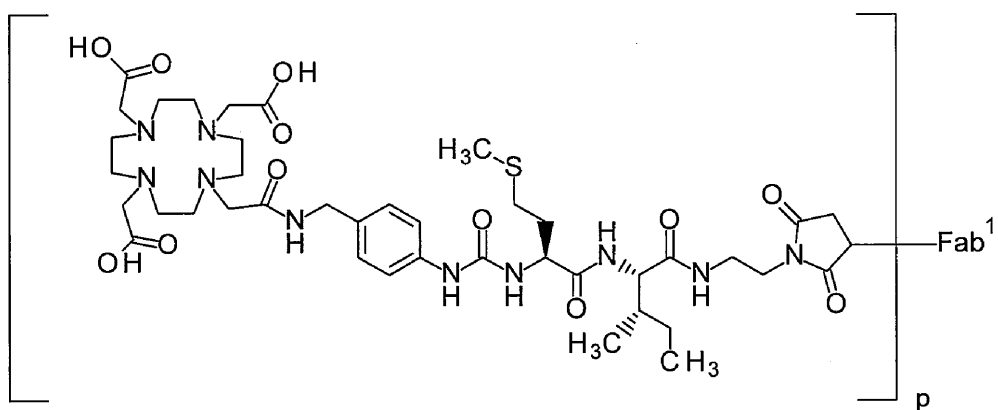
[Chemical Formula 140]



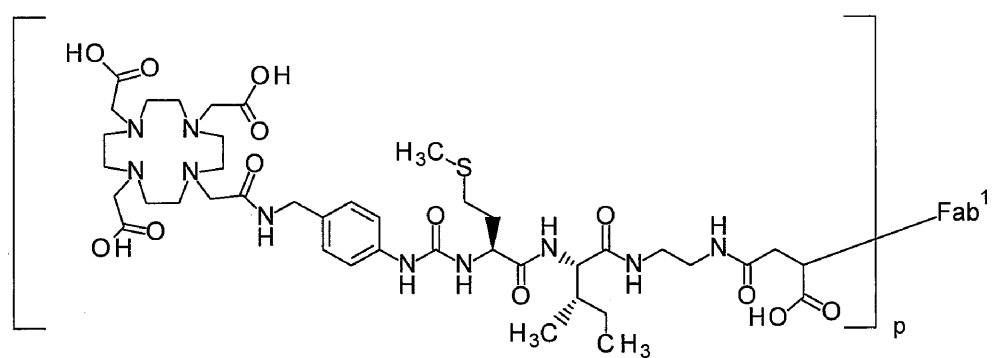
[Chemical Formula 141]



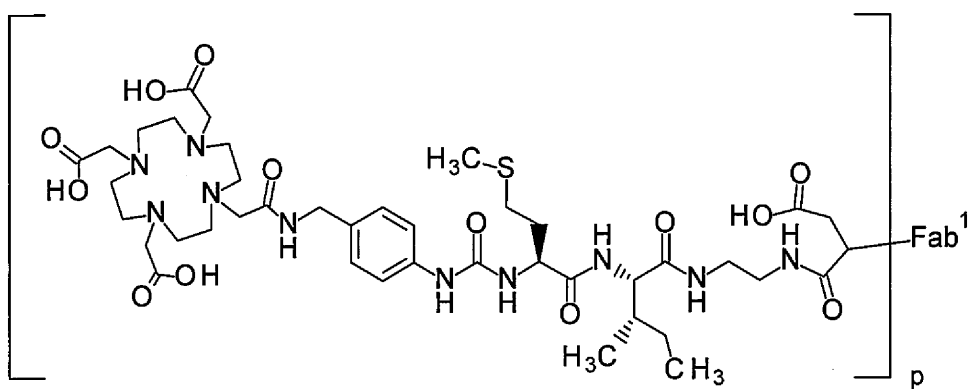
[Chemical Formula 142]



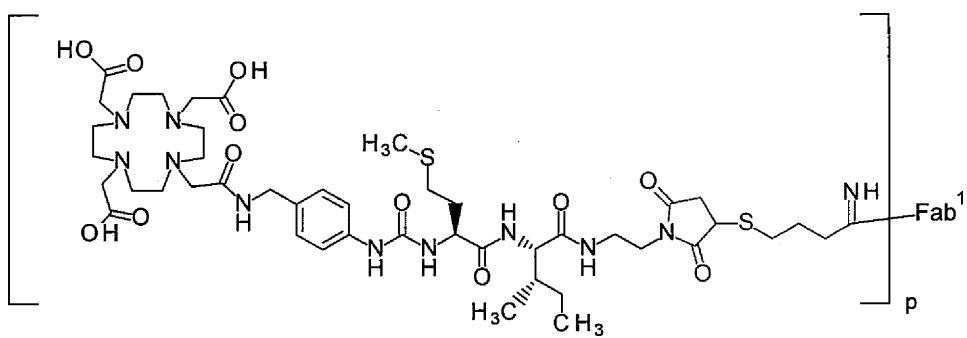
[Chemical Formula 143]



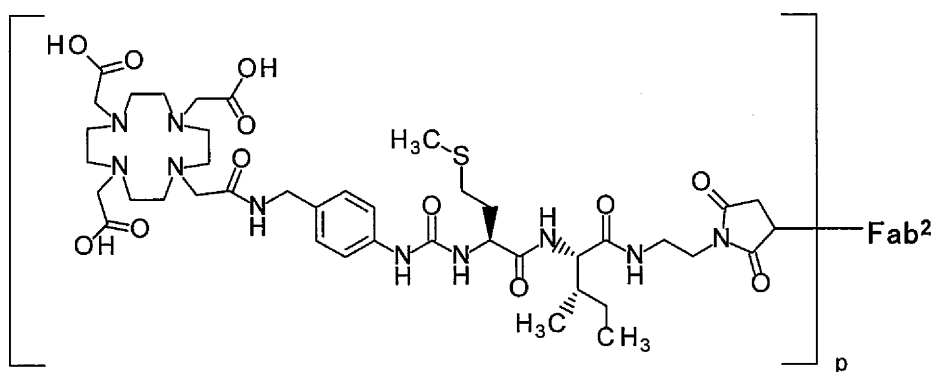
[Chemical Formula 144]



[Chemical Formula 145]



[Chemical Formula 149]



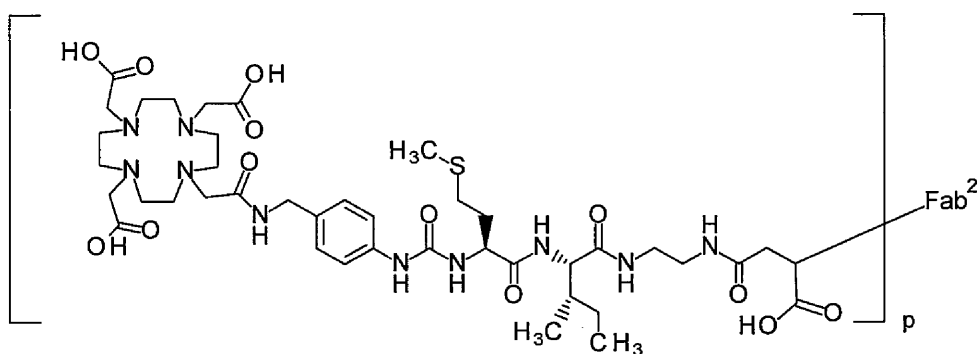
wherein Fab² is a Fab fragment including a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 2 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4;

p is a natural number of 1 to 25; and

Fab² is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab².

19. A conjugate represented by the following formula:

[Chemical Formula 150]



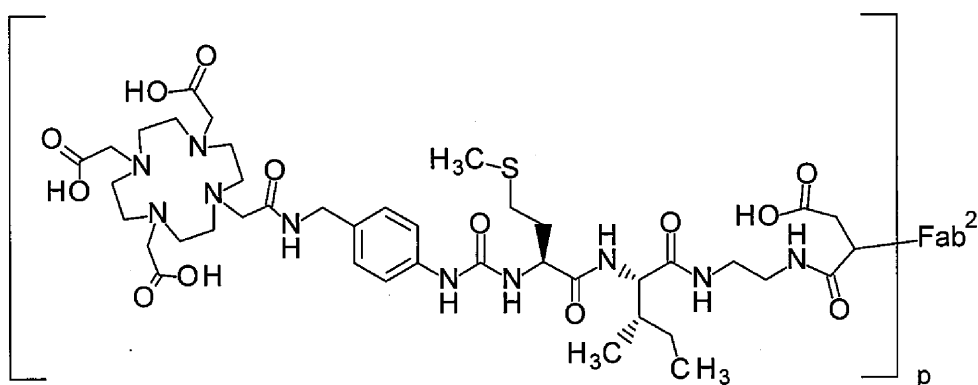
wherein Fab² is a Fab fragment including a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 2 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4;

p is a natural number of 1 to 25; and

Fab² is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab².

20. A conjugate represented by the following formula:

[Chemical Formula 151]



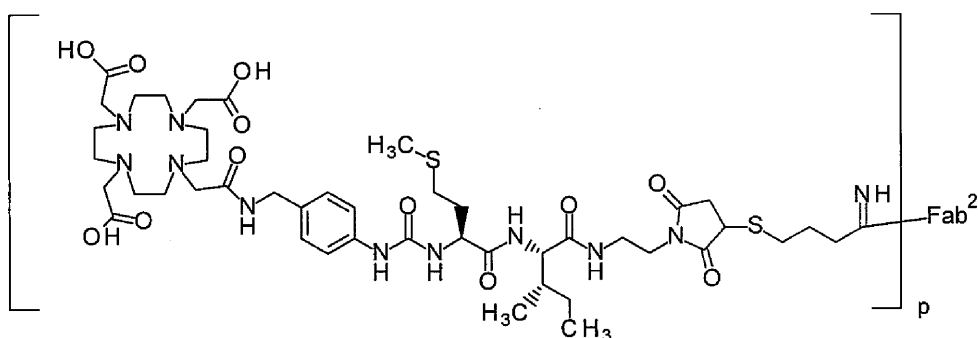
wherein Fab² is a Fab fragment including a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 2 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4;

p is a natural number of 1 to 25; and

Fab² is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab².

21. A conjugate represented by the following formula:

[Chemical Formula 152]



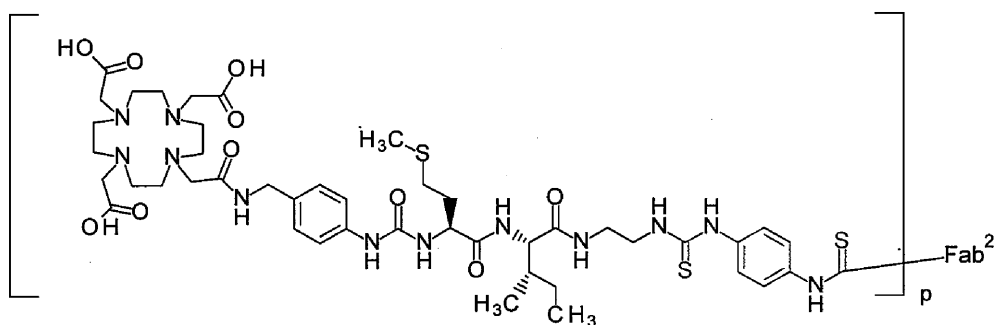
wherein Fab² is a Fab fragment including a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 2 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4;

p is a natural number of 1 to 25; and

Fab² is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab².

22. A conjugate represented by the following formula:

[Chemical Formula 153]



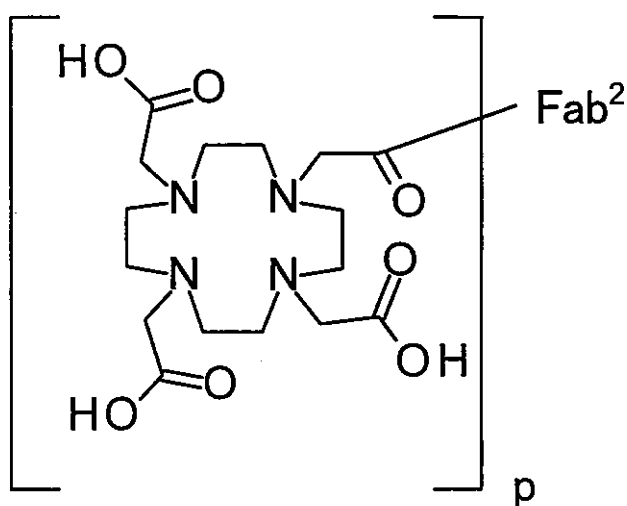
wherein Fab² is a Fab fragment including a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 2 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4;

p is a natural number of 1 to 25; and

Fab² is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab².

23. A conjugate represented by the following formula:

[Chemical Formula 154]



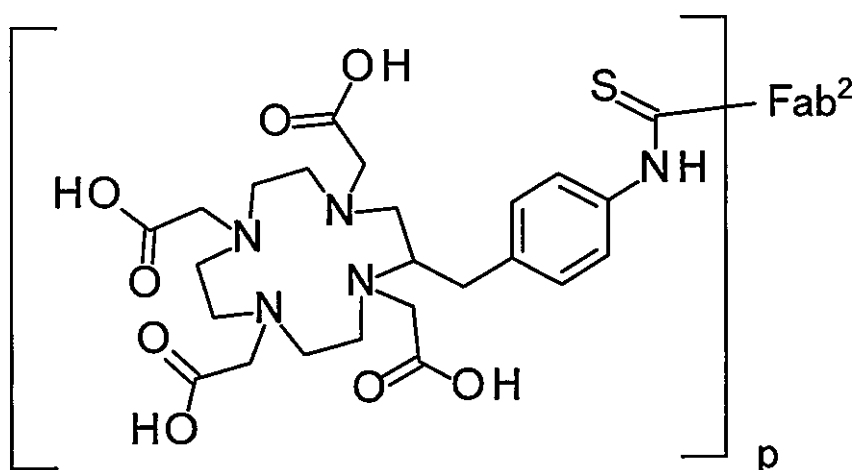
wherein Fab² is a Fab fragment including a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 2 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4;

p is a natural number of 1 to 25; and

Fab² is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab².

24. A conjugate represented by the following formula:

[Chemical Formula 155]



wherein Fab² is a Fab fragment including a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 2 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 4;

p is a natural number of 1 to 25; and

Fab² is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab².

25. The conjugate according to any one of claims 1 to 24, wherein p is a natural number of 1 to 5.
26. The conjugate according to any one of claims 1 to 15, wherein a metal is coordinated to Y.
27. The conjugate according to any one of claims 16 to 24, wherein a metal is coordinated.
28. The conjugate according to claim 26 or 27, wherein the metal is a metal radioisotope.
29. The conjugate according to claim 28, wherein the metal is ⁸⁹Zr.
30. The conjugate according to claim 26 or 27, wherein the metal is a paramagnetic metal ion.
31. The conjugate according to claim 30, wherein the metal is Gd³⁺.

32. The conjugate according to any one of claims 26 to 31, wherein the conjugate is a PET tracer.
33. A diagnostic composition comprising one or more conjugates according to any one of claims 26 to 32 and a pharmaceutically acceptable carrier.
34. A pharmaceutical composition comprising one or more conjugates according to any one of claims 26 to 31 and a pharmaceutically acceptable carrier.
35. The pharmaceutical composition according to claim 34, wherein the pharmaceutical composition is a pharmaceutical composition for treating a cancer expressing human CEACAM5.
36. The pharmaceutical composition according to claim 35, wherein the cancer is colorectal cancer, breast cancer, lung cancer, thyroid cancer, or a cancer resulting from metastasis thereof.
37. Use of the conjugate according to any one of claims 26 to 31 for production of a diagnostic composition for a cancer and/or in the manufacture of a medicament in the form of a pharmaceutical composition for the treatment of cancer.