CLAIMS

1. An immunoconjugate comprising a modified antibody or antibody fragment thereof, wherein said modified antibody or antibody fragment comprises a substitution of one or more amino acids with cysteine on its constant region selected from positions 124, 152, 164, 174, and 189 of the heavy chain of said antibody or antibody fragment, and wherein said positions are numbered according to the EU system.

2. The immunoconjugate of claim 1. wherein said antibody or antibody fragment comprises a sequence selected from the group consisting of SEQ ID NOs: 5, 10, 14, 18, and 21.

3. The immunoconjugate of claim 1 or claim 2, wherein said modified antibody or antibody fragment comprises a combination of substitutions of two or more amino acids with cysteine:
   a. on a constant region of a heavy chain at positions 152 and 375, wherein said positions are numbered according to EU system;
   b. on a constant region of a heavy chain at positions 327 and 375, wherein said positions are numbered according to the EU system;
   c. on a constant region at position 107 of a light chain and position 360 of a heavy chain, wherein said light chain is a kappa chain, and wherein said positions are numbered according to the EU system;
   d. on a constant region at position 375 of a heavy chain and position 165 of a light chain, wherein said light chain is a kappa chain, and wherein said positions are numbered according to the EU system; or
   e. on a constant region at position 334 of a heavy chain and at position 165 of a light chain, wherein said light chain is a kappa chain, and wherein said positions are numbered according to the EU system.

4. The immunoconjugate of any one of claims 1 to 3, comprising a modified antibody or antibody fragment thereof, wherein said modified antibody or antibody fragment thereof comprises a combination of substitution of three or more amino acids with cysteine on its

constant regions wherein the combinations comprise substitutions selected from the group consisting of:

a. positions 375 and 392 of an antibody heavy chain and position 165 of an antibody light chain;
b. positions 334 and 375 of an antibody heavy chain and position 165 of an antibody light chain;
c. positions 334 and 392 of an antibody heavy chain and position 165 of an antibody light chain;
d. positions 152, 375 and 392 of the an antibody heavy chain,
e. positions 152, 334 and 375 of an antibody heavy chain, and
f. positions 152, 334 and 392 of an antibody heavy chain,

wherein said light chain is a kappa chain, and wherein said positions are numbered according to the EU system.

5. The immunoconjugate of any one of claims 1 to 4. comprising a modified antibody or antibody fragment thereof, wherein said modified antibody or antibody fragment thereof comprises a combination of substitution of four or more amino acids with cysteine:

a. on its constant region at positions 334, 375, and 392 of a heavy chain and position 165 of a light chain;
b. on its constant region at positions 333, 375, and 392 of a heavy chain and at position 165 of a light chain;
c. on its constant region at positions 152, 334, 375, and 392 of a heavy chain; or
d. on its constant region at positions 152, 333, 375, and 392 of a heavy chain;

wherein said light chain is a kappa chain, and wherein said positions are numbered according to the EU system.

6. The immunoconjugates of any one of claims 1 to 5, wherein the drug antibody ratio is about 4, about 6 or about 8.

7. The immunoconjugate of any one of claims 1 to 6, further comprising a drug moiety.

8. The immunoconjugate of claim 7, wherein a drug moiety is attached to the modified antibody or antibody fragment through the sulfur of said cysteine and an optional linker.

9. The immunoconjugate of claim 8, wherein said drug moiety is connected to said sulfur of said cysteine through a cleavable or non-cleavable linker.

10. The immunoconjugate of claim 8 or claim 9, wherein said immunoconjugate comprises a thiol-maleimide linkage. a -S-CH_2-C(=O)- linkage or a disulfide linkage.

11. The immunoconjugate of any one of claims 7 to 10, wherein said drug moiety is a cytotoxic agent.

12. The immunoconjugate of claim 11, wherein said drug moiety is selected from the group consisting of taxanes, DNA-alkylating agent, anthracyclines, tubulysin analogs, duocarmycin analogs, auristatins, and maytansinoids.

13. The immunoconjugate of any one of claims 1 to 12, wherein said antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, a fully humanized antibody, a bispecific antibody, or a multi-specific antibody.

14. The immunoconjugate of any one of claims 1 to 13, wherein said antibody or antibody fragment specifically binds to a cell surface marker characteristic of a tumor.

15. A pharmaceutical composition comprising the immunoconjugate of any one of claims 1 to 14.

16. A modified antibody or antibody fragment thereof comprising a substitution of one or more amino acids with cysteine on its constant region selected from positions 124, 152, 164, 174, and 189 of a heavy chain of said antibody or antibody fragment, and wherein said positions are numbered according to the EU system.

17. The modified antibody or antibody fragment of claim 16, wherein substitution is selected from the group consisting of:

a. positions 152 and 375 of a heavy chain;
b. positions 327 and 375 of a heavy chain;
c. position 107 of a light chain and position 360 of a heavy chain;
d. position 375 of a heavy chain and position 165 of a light chain;
e. at position 334 of a heavy chain and position 165 of a light chain;
f. positions 375 and 392 of a heavy chain and position 165 of a light chain;
g. positions 334 and 375 of a heavy chain and position 165 of a light chain;
h. positions 334 and 392 of a heavy chain and position 165 of a light chain;
i. positions 152, 375 and 392 of a heavy chain;
j. positions 152, 334 and 375 of a heavy chain;
k. positions 152, 334 and 392 of an antibody heavy chain;
l. positions 334, 375, and 392 of a heavy chain and position 165 of a light chain;
m. positions 333, 375, and 392 of a heavy chain and at position 165 of a light chain;
n. positions 152, 334, 375, and 392 of a heavy chain; and
o. positions 152, 333, 375, and 392 of a heavy chain;

wherein said light chain is a kappa chain, and wherein said positions are numbered according to the EU system.

18. A nucleic acid encoding the modified antibody or antibody fragment of any one of claims 1 to 17.

19. A host cell comprising the nucleic acid of claim 18.

20. A method of producing a modified antibody or antibody fragment comprising incubating the host cell of claim 19 under suitable conditions for expressing the antibody or antibody fragment, and isolating said antibody or antibody fragment.

21. Use of the immunoconjugate of any one of claims 1 to 14 in the manufacture of a medicament for treating or preventing cancer in a subject in need thereof.

22. A modified antibody or antibody fragment produced by the method of claim 20.