

CLAIMS:

1. An antibody, or a fragment thereof, having a variable region which binds a target molecule, and a constant region, wherein the constant region comprises a mutation at position 180 of the light chain wherein the mutated residue at light chain position 180 is cysteine, and one or more further mutations introducing a site specific conjugation site selected so as to permit conjugation of the antibody or fragment to a payload, wherein the fragment retains the specific binding properties of the antibody.
2. The antibody of claim 1 wherein the wild type residue at position 180 is T.
3. The antibody of claim 1 or 2, wherein the one or more further mutations is selected from a mutation in the heavy chain and light chain (LC) S208, LC S171, LC S182, LC A184, LC V191, LC S202, LC S203 and LC T206 according to a positional numbering convention.
4. The antibody of any preceding claim, wherein the one or more further mutations is a mutation in the heavy chain.
5. The antibody of any preceding claim wherein the one or more further mutations is selected from light chain (LC) S208, LC S171, LC S182, LC A184, LC V191, LC S202, LC S203, LC T206, heavy chain (HC) S160, HC T190, HC S443, HC S447, HC S139, HC S168, HC V170, HC V176, HC T200 and HC S445 according to a positional numbering convention.
6. The antibody of claim 1, wherein the further mutation is HC S160.
7. The antibody of any preceding claim, wherein the antibody is selected from the group comprising IgG1, IgG2, IgG3, and IgG4, wherein preferably the antibody is human, humanised or chimeric.
8. The antibody of any preceding claim wherein the constant region comprises at least a portion of an IgG1 constant region; wherein preferably the constant region comprises one or more, preferably all, of the Ck, CH1 and CH3 domains of the IgG1 constant region.
9. The antibody of any preceding claim wherein the antibody is selected from the group consisting of Fabs, bi specific antibody fragments (tandem scFv-Fc, scFv-Fc knobs-into-

holes, scFv-Fc-scFv, F(ab')₂, Fab-scFv, (Fab'scFv)₂, scDiabody-Fc, or scDiabody-CH₃), IgG- based bispecific antibodies (Hybrid hybridoma, Knobs-into-holes with common light chain, Two-in-one IgG, Dual V domain IgG, IgG-scFv, scFv-IgG, IgG-V, V-IgG), minibody, tribi-minibody, nanobodies, and di-diabody.

10. The antibody of any preceding claim wherein the antibody is selected from Abciximab; Rituximab; Basiliximab ;Daclizumab; Palivizumab; Infliximab; Trastuzumab; Alemtuzumab; Adalimumab; Efalizumab; Cetuximab; Ibritumomab; Omalizumab; Bevacizumab; Ranibizumab; Golimumab; Canakinumab; Ustekinumab; Tocilizumab; Ofatumumab; Belimumab; Ipilimumab; Brentuximab; Pertuzumab; Raxibacumab; Vedolizumab; Ramucirumab; Obinutuzumab; Siltuximab; Secukinumab; Dinutuximab.

11. The antibody of any preceding claim further comprising a linker.

12. An immunoconjugate comprising an antibody according to any of claims 1 to 11, a payload, and a linker joining the payload to the antibody.

13. The antibody of claim 11, or the immunoconjugate of claim 12, wherein the linker is selected from 6-maleimidocaproyl (MC), maleimidopropanoyl (MP), valine-citrulline (val-cit), alanine-phenylalanine (ala-phe), p-aminobenzyloxycarbonyl (PAB), N-Succinimidyl 4-(2-pyridylthio) pentanoate (SPP), N-succinimidyl 4-(N-maleimidomethyl) cyclohexane-1 carboxylate (SMCC), N-Succinimidyl, (4-iodo-acetyl) aminobenzoate (SIAB),), SPDB, hydrazone, maleimidocaproyl and 6-maleimidocaproyl-valine-citrulline-p-aminobenzyloxycarbonyl (MC-vc-PAB); or is a branched linker which comprises a peptide chain and is derived from o-hydroxy p-amino benzylic alcohol, wherein the peptide chain is connected to the phenyl ring via the p-amino group, the payload is connected to the phenyl ring via the benzylic alcohol moiety, and the antibody is connected to the phenyl ring via the o-hydroxy group.

14. The immunoconjugate of claim 12 or 13, wherein the payload is selected from the group consisting of a radionuclide, a chemotherapeutic agent, a cytotoxic agent, a microbial toxin, a plant toxin, a polymer, a carbohydrate, a cytokine, a fluorescent label, a luminescent label, an enzyme-substrate label, an enzyme, a peptide, a peptidomimetic, a nucleotide, an siRNA, a microRNA, an RNA mimetic, and an aptamer; wherein preferably the payload is selected from the group consisting of ⁹⁰Y, ¹³¹I, ⁶⁷Cu, ¹⁷⁷Lu, ²¹³Bi, ²¹¹At, dolastatin, vedotin, monomethyl auristatin F(MMAF), monomethyl auristatin E (MMAE); maytansinoids including

DM1 and DM4, duocarmycin, duocarmycin analogs, calicheamicin, pyrrolobenzodiazepines (PBD), centanamycin, irinotecan, and doxorubicin, alpha-amanitin, melatonin, membrane disrupting peptide, Pseudomonas exotoxin A, Diphtheria toxin, ricin, polyethylene glycol, hydroxyethyl starch, and a mannosyl residue; or wherein the payload is a microtubule disrupting agent, or a DNA modifying agent.

15. A pharmaceutical composition comprising an antibody or an immunoconjugate according to any preceding claim, and a pharmaceutically acceptable diluent, carrier or excipient.

16. A method for generating an immunoconjugate, the method comprising conjugating an antibody according to any of claims 1 to 11 to a payload.

17. The antibody of any of claims 1 to 11 prepared by a process comprising:

(i) mutagenizing a nucleic acid sequence of a parent antibody by replacing one or more amino acid residues with a mutant residue to encode the antibody;

(ii) expressing the mutant antibody; preferably in a prokaryotic or a eukaryotic cell; preferably a mammalian or an insect cell; and

(iii) isolating the mutant antibody,

and wherein preferably the process further comprises:

(i) reacting the mutant antibody with a thiol-reactive affinity reagent to generate an affinity labelled, antibody; and

(ii) measuring the binding of the affinity labelled antibody to a capture media.

18. An isolated or recombinant polynucleotide encoding the antibody of any of claims 1 to 11 or a vector comprising the polynucleotide, wherein preferably the vector further comprises an inducible promoter operably linked to the polynucleotide or a host cell comprising the vector.

19. A method of producing an antibody comprising:

(a) providing a culture medium comprising the host cell of claim 18; and

(b) placing the culture medium in conditions under which the antibody is expressed, and optionally (c) isolating the antibody.