CLAIMS

1. An isolated antibody having a binding specificity for human CD137, which comprises: HCDR1, HCDR2, and HCDR3 sequences of SEQ ID NOs: 1, 2, and 3, respectively, and LCDR1, LCDR 2 and LCDR3 sequences of SEQ ID NOs: 16, 17 and 18, respectively, wherein said antibody binds human CD137 extracellular domain at an epitope located in the distal part of the extracellular domain of CD137 within amino acid residues 24-86 of SEQ ID NO: 32, wherein said epitope is characterized by a set of critical residues, determined in accordance with Example 13, comprising the residues Ala33, Asn40, Arg 41, Gln43, Cys45, Cys48, Pro49, Ser52, and Ser80; provided that amino acid residue Asn42 of CD137 is not a critical residue for binding.

2. The antibody of claim 1 , wherein the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 90 percent identical to the amino acid sequence selected from the group consisting of SEQ ID NOs: 13, 14, and 15; and a light chain variable region comprising an amino acid sequence that is at least 90 percent identical to the amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 26, and 27.

3. The antibody of claim 2, comprising: (a) a VH sequence of SEQ ID NO: 13 and a VL sequence of SEQ ID NO: 25; (b) a VH sequence of SEQ ID NO: 14 and a VL sequence of SEQ ID NO: 26; or (c) a VH sequence of SEQ ID NO: 15 and a VL sequence of SEQ ID NO: 27.

4. The antibody of claim 1, wherein said antibody does not inhibit the interaction between CD137 and its ligand CD137L as measured by the competition ELISA.

5. The antibody of claim 1, wherein said antibody
   (i) binds to human CD137 with a dissociation constant (KD) of less than 50 nM, as measured by surface plasmon resonance;
   (ii) optionally, binds to Cynomolgus CD137 with a KD of less than 50 nM, as measured by surface plasmon resonance;
   (iii) optionally, does not bind to human CD40 and/or does not bind to human OX40 as measured by SPR;

(iv) when in scFv format, has a melting temperature (Tm), determined by differential scanning fluorimetry, of at least 50°C wherein said antibody is formulated in 50 mM phosphate-citrate buffer at pH 6.4, 150 mM NaCl;

(v) when in scFv format, has a loss in monomer content, after storage for at least two weeks at 4°C, of less than 7%, when the antibody ~~of the invention~~ is at a starting concentration of 10 mg/ml, and wherein the antibody in scFv format is formulated in 50 mM phosphate citrate buffer with 150 mM NaCl at pH 6.4; and/or

(vi) when in scFv format, has a loss in monomer content, after five consecutive freeze-thaw cycles of less than 5%, when the antibody ~~of the invention~~ is at a starting concentration of 10 mg/ml, and wherein the antibody in scFv format is formulated in 50 mM phosphate citrate buffer with 150 mM NaCl at pH 6.4.

6. The antibody of claim 1, wherein the isolated antibody is selected from the group consisting of: a monoclonal antibody, a chimeric antibody, a Fab, an Fv, an scFv, dsFv, an scAb, STAB, and binding domains based on alternative scaffolds including but limited to ankyrin-based domains, fynomers, avimers, anticalins, fibronectins, and binding sites being built into constant regions of antibodies (e.g. F-star's Modular Antibody Technology), preferably Fv or scFv.

7. The antibody of claim 6, wherein said antibody is an scFv having an amino acid sequence selected from the group consisting of SEQ ID NO: 29, SEQ ID NO: 30, and SEQ ID NO: 31.

8. The isolated antibody of claim 1, wherein said epitope characterized by a set of critical residues, determined in accordance with Example 13, further comprises the residues Pro32, Gly34, Thr35, Ser46, Pro47, Pro50, Cys78, and Ser79.

9. The antibody of claim 1, wherein the antibody is a multispecific molecule having at least a second functional molecule.

10. A pharmaceutical composition comprising the antibody of claim 1 and a pharmaceutically acceptable carrier.

11. The antibody of claim 1 or the composition of claim 10 for use as a medicament.

12. Use of the antibody of claim 1, or the composition of claim 10 in the manufacture of a medicament for the treatment of a cancer.

13. A nucleic acid encoding the antibody of claim 1.

14. A method of producing the antibody of claim 1, the method comprising the step of culturing a host cell comprising a nucleic acid or a vector encoding the antibody of claim 1.