

CLAIMS

1. An isolated antibody having a binding specificity for human PDL1 comprising an HCDR1, HCDR2, HCDR3 sequences of SEQ ID NOs: 1, 2 and 3, respectively, and an LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NOs: 17, 18 and 19, respectively.
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2. The antibody of claim 1, wherein the antibody comprises a heavy chain variable region (VH), wherein said VH is VH3 or VH4, preferably VH3.
3. The antibody of claim 1 or claim 2, wherein the antibody comprises a light chain variable region (VL), wherein said VL comprises V κ frameworks FR1, FR2 and FR3, particularly V κ 1 or V κ 3 FR1 to FR3, preferably V κ 1 FR1 to FR3, and a framework FR4, which is selected from a V κ FR4, particularly V κ 1 FR4, V κ 3 FR4, and V λ FR4, particularly V λ FR4 comprising the amino acid sequence having at least 60, 70, 80, 90 percent identity to an amino acid sequence selected from any of SEQ ID NO: 64 to
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SEQ ID NO: 70, preferably V λ FR4 as set forth in any of SEQ ID NO: 64 to SEQ ID NO: 70, preferably V λ FR4 as set forth in SEQ ID NO: 64 or 65, more preferably V λ FR4 as set forth in SEQ ID NO: 64.
4. The antibody of any one of the preceding claims, wherein the antibody comprises a
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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: 14, 15, 16, preferably SEQ ID NO: 14 or 16, more preferably SEQ ID NO: 16; 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
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consisting of SEQ ID NOs: 26 and 27, preferably SEQ ID NO: 27.
5. The antibody of any of the preceding claims, comprising: (a) a VH sequence of SEQ ID NO: 14 and a VL sequence of SEQ ID NO: 26; or (b) a VH sequence of SEQ ID NO: 15 and a VL sequence of SEQ ID NO: 26; or (c) a VH sequence of SEQ ID NO:
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16 and a VL sequence of SEQ ID NO: 27.

6. The antibody of any of the preceding claims, wherein said antibody:
- (i) binds to human PDL1 with a dissociation constant (KD) of less than 5 nM, particularly less than 1 nM, particularly less than 500 pM, more particularly less than 100 pM, preferably less than 50 pM, more preferably less than 10 pM as measured by surface plasmon resonance (SPR);
 - (ii) binds to human PDL1 with a K_{off} rate of 10^{-3} s^{-1} or less, or 10^{-4} s^{-1} or less, or 10^{-5} s^{-1} or less as measured by SPR;
 - (iii) binds to human PDL1 with a K_{on} rate of at least $10^3 \text{ M}^{-1} \text{ s}^{-1}$ or greater, at least $10^4 \text{ M}^{-1} \text{ s}^{-1}$ or greater, at least $10^5 \text{ M}^{-1} \text{ s}^{-1}$ or greater, at least $10^6 \text{ M}^{-1} \text{ s}^{-1}$ or greater as measured by SPR;
 - (iv) is cross-reactive with *Macaca fascicularis* (Cynomolgus) PDL1, in particular binds to Cynomolgus PDL1 with a KD of less than 5 nM, particularly less than 1 nM, particularly less than 500 pM, more particularly less than 100 pM, preferably less than 50 pM, more preferably less than 10 pM as measured by surface plasmon resonance;
 - (v) is non-cross-reactive to *Mus musculus* PDL1, in particular as measured by SPR;
 - (vi) does not bind to human PDL2, in particular as measured by SPR;
 - (vii) has the ability to neutralize PDL1/PD-1 interaction with a potency relative to that of avelumab (relative potency), determined in ELISA assay, greater than 2, preferably greater than 3, more preferably greater than 4, and wherein said relative potency is the ratio of the IC_{50} value in ng/mL of avelumab as measured in the ELISA assay to the IC_{50} value in ng/mL of said antibody, in particular wherein said antibody is an scFv, as measured in the ELISA assay;
 - (viii) has the ability to neutralize PDL1/PD-1 interaction with a potency relative to that of avelumab (relative potency), determined in NFAT reporter gene assay, greater 2, preferably greater than 3, more preferably greater than 4, and wherein said relative potency is the ratio of the IC_{50} value in ng/mL of avelumab as measured in the NFAT reporter gene assay to the IC_{50} value in

ng/mL of said antibody, in particular wherein said antibody is an scFv, as measured in the NFAT reporter gene assay; and/or

(ix) has the ability to neutralize PDL1/B7-1 interaction with a potency relative to that of avelumab (relative potency), determined in ELISA assay, greater than 2, preferably greater than 3, more preferably greater than 4, and wherein said relative potency is the ratio of the IC₅₀ value in ng/mL of avelumab as measured in the ELISA assay to the IC₅₀ value in ng/mL of said antibody, in particular wherein said antibody is an scFv, as measured in the ELISA assay.

7. The antibody of any of the preceding items, wherein said antibody:
- (i) when in scFv format, has a melting temperature (T_m), determined by differential scanning fluorimetry, of at least 60°C, preferably at least 65°C, more preferably at least 70°C, in particular wherein said antibody is formulated in 50 mM phosphate-citrate buffer at pH 6.4, 150 mM NaCl;
 - (ii) when in scFv format, has a loss in monomer content, after five consecutive freeze-thaw cycles, of less than 5%, preferably less than 3%, more preferably less than 1%, when the antibody of the invention is at a starting concentration of 10 mg/ml, and in particular wherein the antibody of the invention is formulated 50 mM phosphate citrate buffer with 150 mM NaCl at pH 6.4; and/or
 - (iii) when in scFv format, has a loss in monomer content, after storage for at least two weeks, particularly for at least four weeks, at 4°C, of less than 15%, e.g. less than 12%, less than 10%, less than 7%, less than 5%, less than 4%, less than 3%, less than 2%, preferably less than 1%, when the antibody of the invention is at a starting concentration of 10 mg/ml, and in particular wherein said antibody is formulated in 50 mM phosphate citrate buffer with 150 mM NaCl at pH 6.4.
8. The antibody of any one of the preceding claims, wherein the antibody is selected from the group consisting of: a monoclonal antibody, a chimeric antibody, a Fab, an

Fv, an scFv, dsFv, a 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 scFv.

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9. The antibody of claim 8, which is an scFv, wherein said scFv has an amino acid sequence selected from the group consisting of SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, preferably SEQ ID NO: 31.

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10. The antibody of any one of claims 1 to 7, wherein said antibody is a multispecific molecule, in particular wherein said multispecific molecule comprises at least a second functional molecule.

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11. A pharmaceutical composition comprising the isolated antibody of any one of claims 1 to 10, and a pharmaceutically acceptable carrier.

12. The antibody of any one of claims 1 to 10, or the composition of claim 11 for use as a medicament.

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13. The antibody of any one of claims 1 to 10, or the pharmaceutical composition of claim 11 for use in the treatment of a cancer.

14. A nucleic acid encoding the antibody of any one of claims 1-10.

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15. A method of producing the antibody of any one of claims 1- 10, the method comprising the step of culturing a host cell comprising the nucleic acid of claim 14.