

CLAIMS

1. A fusion protein that is capable of binding both CD137 and PD-L1, wherein the fusion protein comprises two subunits, wherein the first subunit comprises a full-length immunoglobulin that is specific for PD-L1, and wherein the second subunit comprises a lipocalin mutein that is specific for CD137,
wherein the fusion protein comprises amino acid sequences having at least 90% sequence identity to the amino acid sequences shown in SEQ ID NOs: 90 and 87,
wherein the heavy chain of the immunoglobulin comprises the following set of CDR sequences: GFSLSNYD (HCDR1, SEQ ID NO: 60), IWTGGAT (HCDR2, SEQ ID NO: 61), and VRDSNYRYDEPFTY (HCDR3, SEQ ID NO: 62), and the light chain of the immunoglobulin comprises the following set of CDR sequences: QSIGTN (LCDR1, SEQ ID NO: 63), YAS (LCDR2), and QQSNSWPYT (LCDR3, SEQ ID NO: 64), and
wherein the amino acid sequence of the lipocalin mutein comprises the following set of mutated amino acid residues in comparison with the linear polypeptide sequence of mature hNGAL as shown in SEQ ID NO: 2: Gln 28 → His; Leu 36 → Gln; Ala 40 → Ile; Ile 41 → Arg; Gln 49 → Ile; Tyr 52 → Met; Asn 65 → Asp; Ser 68 → Met; Leu 70 → Lys; Arg 72 → Asp; Lys 73 → Asp; Asp 77 → Met; Trp 79 → Asp; Arg 81 → Trp; Cys 87 → Ser; Asn 96 → Lys; Tyr 100 → Phe; Leu 103 → His; Tyr 106 → Ser; Lys 125 → Phe; Ser 127 → Phe; Tyr 132 → Glu; and Lys 134 → Tyr.
2. The fusion protein of claim 1, wherein the amino acid sequence of the lipocalin mutein has at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 42.
3. The fusion protein of claim 1 or 2, wherein the amino acid sequence of the lipocalin mutein comprises the amino acid sequence of SEQ ID NO: 42.
4. The fusion protein of any one of claims 1-3, wherein the second subunit is linked at the N-terminus via a linker to the C-terminus of each heavy chain constant region (CH) of the first subunit, wherein the linker is preferably the linker of SEQ ID NO: 13.
5. The fusion protein of any one of claims 1-4, wherein the immunoglobulin comprises a heavy chain variable region and a light chain variable region comprising the amino acid sequences as shown in SEQ ID NOs: 77 and 82.
6. The fusion protein of any one of claims 1-5, wherein the immunoglobulin comprises a heavy chain and a light chain comprising the amino acid sequences as shown in SEQ

ID NOs: 86 and 87.

7. The fusion protein of any one of claims 1-5, wherein the immunoglobulin has an IgG4 backbone, wherein the IgG4 backbone preferably has one or more of the following mutations: S228P, N297A, F234A, L235A, M428L, N434S, M252Y, S254T, and T256E, according to the EU index of Kabat.
8. The fusion protein of any one of claims 1-5 or 7, wherein the fusion protein comprises amino acid sequences having at least 92%, at least 95%, at least 97%, at least 98%, or higher sequence identity to the amino acid sequences shown in SEQ ID NOs: 90 and 87.
9. The fusion protein of any one of claims 1-8, wherein the fusion protein comprises the amino acid sequences shown in SEQ ID NOs: 90 and 87.
10. A nucleic acid molecule comprising a nucleotide sequence encoding the fusion protein of any one of claims 1-9, wherein preferably
 - (i) the nucleic acid molecule is operably linked to a regulatory sequence to allow expression of said nucleic acid molecule; or
 - (ii) the nucleic acid molecule is comprised in a vector or in a phagemid vector.
11. A host cell containing a nucleic acid molecule of claim 10.
12. A method of producing the fusion protein of any one of claims 1-9, wherein the fusion protein is produced starting from the nucleic acid coding for the fusion protein, wherein the fusion protein is preferably produced in a bacterial or eukaryotic host organism and is isolated from this host organism or its culture.
13. A pharmaceutical composition comprising a fusion protein of any one of claims 1-9.
14. A fusion protein of any one of claims 1-9 for use in therapy.
15. The fusion protein for the use of claim 14, wherein the use is in the treatment of cancer.