

CLAIMS

1. An antibody or a functional fragment thereof capable of binding to human tumor necrosis factor alpha (TNF α), wherein said antibody or functional fragment comprises (i) a V_L domain comprising a CDR1 region consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, and SEQ ID NO:22, a CDR2 region consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:8, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25 and SEQ ID NO:26, and a CDR3 region consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:9, SEQ ID NO:27, SEQ ID NO: 28, SEQ ID NO:29, SEQ ID NO: 30, SEQ ID NO:31 and SEQ ID NO:32 and
 - (ii) a V_H domain comprising a CDR1 region consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35 and SEQ ID NO:36, a CDR2 region consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:11, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40 and SEQ ID NO:41 and a CDR3 region consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:12, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46 and SEQ ID NO: 48, and wherein said antibody or functional fragment
 - (i) binds to human TNF α with a dissociation constant (K_D) of less than 125 pM;
 - (ii) is cross-reactive with *Macaca mulatta* (Rhesus) TNF α and with *Macaca fascicularis* (Cynomolgus) TNF α ;
 - (iii) has a greater potency to inhibit TNF α -induced apoptosis than infliximab, as determined by an L929 assay;
 - (iv) comprises a variable domain having a melting temperature, determined by differential scanning fluorimetry, of at least 70°C and
 - (v) is capable of binding to human TNF α _{Trimer} in a stoichiometry (antibody: TNF α _{Trimer}) of at least 2.
2. The antibody or functional fragment of claim 1, wherein said antibody or functional fragment comprises (i) a V_L domain comprising a CDR1 region having the amino acid sequence as shown in SEQ ID NO:7, a CDR2 region having the amino acid sequence as shown in SEQ ID NO:8, and a CDR3 region having the amino acid sequence as shown in

SEQ ID NO:9, and (ii) a V_H domain comprising a CDR1 region having the amino acid sequence as shown in SEQ ID NO:10, a CDR2 region having the amino acid sequence as shown in SEQ ID NO:11, and a CDR3 region having the amino acid sequence as shown in SEQ ID NO:12.

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3. The antibody or functional fragment of any one of the preceding claims, which binds to human TNF α with a K_D of less than 50 pM.

4. The antibody or functional fragment of any one of the preceding claims, wherein said antibody or functional fragment comprises a V_H domain having the amino acid sequence as shown in SEQ ID NO:13.

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5. The antibody or functional fragment of any one of the preceding claims, wherein said antibody or functional fragment comprises a V_L domain having an amino acid sequence selected from SEQ ID NO:14 and SEQ ID NO:54.

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6. The functional fragment of any one of the preceding claims, which is a single-chain variable fragment (scFv).

7. The functional fragment of claim 6, wherein said scFv has the amino acid sequence as shown in SEQ ID NO:15 or SEQ ID NO:55.

8. The antibody of any one of claims 1 to 5, which is an immunoglobulin G (IgG).

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9. The antibody or functional fragment of any one of the preceding claims, wherein the sum of (i) the number of amino acids in framework regions I to III of the variable light domain of said antibody or functional fragment that are different from the respective human Vk1 consensus sequences with SEQ ID NOs: 56 to 58, and (ii) the number of amino acids in framework region IV of the variable light domain of said antibody or functional fragment that are different from the most similar human λ germline-based sequence selected from SEQ ID NOs: 59 to 62, is less than 7, preferably less than 4.

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10. The antibody or functional fragment of any one of the preceding claims, wherein the framework regions I to III of the variable light domain of said antibody or functional fragment consist of human Vk1 consensus sequences with SEQ ID NOs:56 to 58, respectively, and framework region IV consists of a λ germline-based sequence selected from SEQ ID NOs:59 to 62.

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11. A nucleic acid encoding the antibody or functional fragment of any one of the preceding claims.
12. A vector or plasmid comprising the nucleic acid of claim 11.
13. A cell comprising the nucleic acid of claim 11 or the vector or plasmid of claim 12.
- 5 14. A method of preparing the antibody or functional fragment of any one of claims 1 to 10, comprising culturing the cell of claim 13 in a medium under conditions that allow expression of the nucleic acid encoding the antibody or functional fragment, and recovering the antibody or functional fragment from the cells or from the medium.
- 10 15. A pharmaceutical composition comprising the antibody or functional fragment of any one of claims 1 to 10, and optionally a pharmaceutically acceptable carrier and/or excipient.
16. Use of the antibody or functional fragment as defined in any one of claims 1 to 10 for the manufacturing of a medicament for treating an inflammatory disorder or a TNF α -related disorder.
- 15 17. The use according to claim 16, wherein said inflammatory disorder is an inflammatory disorder of the gastrointestinal tract.
18. The use according to claim 17, wherein said inflammatory disorder of the gastrointestinal tract is inflammatory bowel disease.
19. The use according to claim 17 or 18, wherein said inflammatory disorder of the gastrointestinal tract is Crohn's disease or ulcerative colitis.