

CLAIMS

1. An antibody comprising a TNF α -binding domain and an FcRn-binding site, having a high affinity to human FcRn at pH 6, said high affinity being characterized by a dissociation equilibrium constant (K_D) of less than 500 nM, and further having no affinity or a low affinity to human FcRn at pH 7.4, said low affinity being characterized by a K_D of greater than 10 μ M, wherein the amino acid sequence of the antibody comprises the amino acids 380A (EU numbering) and 434A (EU numbering) and wherein the antibody comprises (i) a V_L domain comprising a CDR1 region having the amino acid sequence as shown in SEQ ID NO:3, a CDR2 region having the amino acid sequence as shown in SEQ ID NO:4, and a CDR3 region having the amino acid sequence as shown in SEQ ID NO:5, and (ii) a V_H domain comprising a CDR1 region having the amino acid sequence as shown in SEQ ID NO:6, a CDR2 region having the amino acid sequence as shown in SEQ ID NO:7, and a CDR3 region having the amino acid sequence as shown in SEQ ID NO:8.
2. The antibody of claim 1, wherein the amino acid sequence of the antibody further comprises the amino acid 307T (EU numbering).
3. The antibody of any one of the preceding claims, having an affinity to human FcRn at pH 6 that is greater than that of infliximab.
4. The antibody of any one of the preceding claims, wherein said high affinity to human FcRn is characterized by a dissociation constant K_D of less than 300 nM.
5. The antibody of any one of the preceding claims, which binds to human TNF α with a K_D of less than 100 pM.
6. The antibody of any one of the preceding claims, which is transported across a polarized cell monolayer from the apical side to the basolateral side in greater amount than infliximab.
7. The antibody of claim 6, wherein the amount of antibody transported across the polarized cell monolayer is greater than two times the amount of a parent immunoglobulin transported across the polarized cell monolayer, wherein said parent immunoglobulin differs from said antibody only in that it comprises the amino acids 380E (EU numbering) and 434N (EU numbering).

8. The antibody of any one of the preceding claims, wherein a greater percentage of the antibody than that of infliximab is transported across a polarized cell monolayer from the apical side to the basolateral side in the presence of a tenfold excess of competing immunoglobulins, wherein the percentage refers to the total mass of immunoglobulins transported across the polarized cell monolayer.
9. The antibody of any one of the preceding claims, which is a non-fucosylated antibody.
10. A nucleic acid encoding the antibody of any one of the preceding claims.
11. Use of the antibody as defined in any one of claims 1 to 9 for the manufacturing of a medicament for the treatment of an inflammatory condition.
- 10 12. Use of the antibody according to claim 11, wherein the inflammatory condition is an inflammatory disorder of the gastrointestinal tract.
13. Use of the antibody according to claim 11, wherein an effective amount of said antibody is to be orally administered~~said treatment comprises orally administering an effective amount of said antibody.~~
- 15 14. Use of the antibody according to claim 11 or 12, wherein said antibody is to be applied topically.
15. A pharmaceutical composition comprising the antibody of any one of claims 1 to 9.
16. A method for improving the transcytosis of an antibody directed against TNF α as defined in any one of claims 1-9, comprising introducing the substitutions E380A (EU numbering) and N434A (EU numbering) in the amino acid sequence of the antibody.
- 20 17. A method for extending the plasma half life of an antibody directed against TNF α as defined in any one of claims 1-9, comprising introducing the substitutions E380A (EU numbering) and N434A (EU numbering) in the amino acid sequence of the antibody.