

Claims

1. An antibody or antigen-binding fragment thereof which binds specifically to human CD127, which comprises a VH chain comprising the following amino acid sequences:
 - VHCDR1 SEQ ID No:10;
 - VHCDR2 SEQ ID No:12; and
 - VHCDR3 SEQ ID No:14 or SEQ ID No:48;
 and a VL chain comprising the following amino acid sequences:
 - VLCDR1 SEQ ID No:16 or SEQ ID No:50;
 - VLCDR2 SEQ ID No:18 or SEQ ID No:52; and
 - VLCDR3 SEQ ID No:20.
2. An antibody or antigen-binding fragment according to claim 1, wherein said antibody, antigen-binding fragment or antigen-binding antibody mimetic is an antagonist of IL-7R signaling induced by IL-7.
3. An antibody or antigen-binding fragment according to claim 1 or 2, which does not increase the maturation of dendritic cells induced by Thymic Stromal Lymphopoietin (TSLP).
4. An antibody or antigen-binding fragment according to any one of claims 1 to 3, which specifically binds to the epitope sequences from domain D1 and from the 2b site of human CD127 comprising or consisting of the sequence of SEQ ID No: 86 or SEQ ID No:116 and the sequence of SEQ ID No:110 or SEQ ID No:115 and the sequence of SEQ ID No:111 or SEQ ID No:117,
 - i. wherein the epitope sequence of human CD127 comprising SEQ ID No:110 does not extend to comprise the amino acids adjacent to said sequence in the sequence of human CD127 by more than 1 N-terminal amino acid or by more than 7 C-terminal amino acids; and/or
 - ii. wherein the epitope sequence of human CD127 comprising SEQ ID No:111 does not extend to comprise the amino acids adjacent to said sequence in the sequence of human CD127 by more than 30 N-terminal amino acid or by more than 30 C-terminal amino acids.
5. An antibody or antigen-binding fragment according to claim 4, which specifically binds to the epitope sequences from domain D1 and from the 2b site of human CD127 wherein

the epitope sequences comprise or consist of the sequence of SEQ ID No:116 and the sequence of SEQ ID No:115 and the sequence of SEQ ID No:117.

6. An antibody or antigen-binding fragment according to any one of claims 1 to 5, which comprises:
 - a heavy chain with the sequence of SEQ ID No:2 or of SEQ ID No:6 or of SEQ ID No:54, or which comprises the sequence of SEQ ID No:22 or of SEQ ID No:36 or of SEQ ID No:38 or of SEQ ID No:40; and
 - a light chain with the sequence of SEQ ID No:4 or of SEQ ID No:56, or which comprises the sequence of SEQ ID No:24 or of SEQ ID No:42 or of SEQ ID No:44 or of SEQ ID No:46.
7. An antibody or antigen-binding fragment according to any one of claims 1 to 6 which is a chimeric antibody or a humanized antibody or a deimmunized antibody.
8. A macromolecule which is a chimeric molecule comprising an antibody or antigen-binding fragment according to any one of claims 1 to 7, said chimeric molecule being a fusion chimeric protein or a conjugate with a chemical or biological group or molecule.
9. A macromolecule according to claim 8, wherein said chemical or biological group is a PEG polymer, or is suitable for protection against protease cleavage *in vivo*, or is suitable for improving the stability and/or half-life of the antibody, antigen-binding fragment or antigen-binding antibody mimetic, or is a toxin, or is a therapeutic active ingredient, or is a vector suitable for targeting the antibody, the antigen-binding fragment or antigen-binding antibody mimetic to specific cells or tissues of the human body, or is a label, or is a linker.
10. A nucleic acid molecule encoding an antibody or antigen-binding fragment according to any one of claims 1 to 7.
11. A nucleic acid molecule according to claim 10, wherein the nucleic acid molecule encodes an amino acid chosen from the group consisting of SEQ ID No:2; SEQ ID No:4; SEQ ID No:6; SEQ ID No:8; SEQ ID No:10; SEQ ID No:12; SEQ ID No:14; SEQ ID No:16; SEQ ID No:18; SEQ ID No:20; SEQ ID No:22; SEQ ID No:24; SEQ ID No:36; SEQ ID No:38; SEQ ID No:40; SEQ ID No:42; SEQ ID No:44; SEQ ID No:46; SEQ ID No:48; SEQ ID No:50; SEQ ID No:52; SEQ ID No:54 and SEQ ID No:56, or wherein the nucleic acid molecule comprises or consists of a nucleotide sequence chosen from the group consisting of SEQ ID No:1; SEQ ID No:3; SEQ ID No:5; SEQ ID No:7; SEQ ID No:9; SEQ ID No:11; SEQ ID No:13; SEQ ID No:15; SEQ ID No:17; SEQ ID No:19; SEQ ID No:21; SEQ ID No:23; ; SEQ ID No:35; SEQ ID No:37; SEQ ID No:39; SEQ ID No:41; SEQ ID No:43; SEQ ID No:45; SEQ ID No:47; SEQ ID No:49; SEQ ID No:51; SEQ ID No:53 and SEQ ID No:55.

12. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to any one of claims 1 to 7, a macromolecule according to claim 8 or 9, or a nucleic acid molecule according to claim 10 or 11, with a pharmaceutical vehicle.
13. A pharmaceutical composition according to claim 12, wherein said pharmaceutical composition further comprises an additional compound having a therapeutic immunomodulator effect on cells involved in an autoimmune disease or an allergic disease, leukemia such as acute lymphoblastic leukemia, lymphoma, a cancer, a chronic viral infection, an inflammatory disease, transplantation, a respiratory disease or autoimmunity.
14. An antibody or antigen-binding fragment according to any one of claims 1 to 7, a macromolecule according to claim 8 or 9, a nucleic acid molecule according to claim 10 or 11, or a pharmaceutical composition according to claim 12 or 13 for use as a therapeutically active ingredient in a combination or in an add-on therapeutic regimen in a patient in need thereof.
15. An antibody or antigen-binding fragment according to any one of claims 1 to 7, a macromolecule according to claim 8 or 9, a nucleic acid according to claim 10 or 11, or a pharmaceutical composition according to claim 12 or 13 for use in the treatment of a patient in need of transplantation, about to be transplanted, or having received a transplant, or a patient with or at risk of a disease.
16. The antibody, antigen-binding fragment, macromolecule, nucleic acid or pharmaceutical composition for use according to claim 15, wherein the disease is associated with IL-7 pathway, the disease being an autoimmune disease such as rheumatoid arthritis, multiple sclerosis, type I diabetes, autoimmune thyroiditis or lupus, an inflammatory disease such as inflammatory bowel disease (IBD) or encephalomyelitis, an allergic disease, a cancer, a respiratory disease, or a disease related to transplantation.
17. Use of an antibody or antigen-binding fragment according to any one of claims 1 to 7, a macromolecule according to claim 8 or 9, a nucleic acid molecule according to claim 10 or 11, or a pharmaceutical composition according to claim 12 or 13 in the manufacture of a medicament for administration to a patient in need of transplantation, about to be transplanted, or having received a transplant.
18. Use of an antibody or antigen-binding fragment according to any one of claims 1 to 7, a macromolecule according to claim 8 or 9, a nucleic acid molecule according to claim 10 or 11, or a pharmaceutical composition according to claim 12 or 13 in the manufacture of a medicament for administration to a patient having, or at risk of developing, a disease associated with an IL-7 pathway, the disease being selected from an autoimmune

disease, an inflammatory disease, an allergic disease, a cancer, a respiratory disease or a disease related to transplantation.

19. A method of manufacturing an antibody according to any one of claims 1 to 7, wherein said antibody is raised against an antigen, said antigen consisting of a fragment of the polypeptide of sequence SEQ ID No: 114 wherein the fragment comprises epitope sequence(s) from domain D1 and from the site 2b of human CD127, the epitope sequences comprising or consisting of non-contiguous sequences of SEQ ID No:86 (or SEQ ID No:116) and of SEQ ID No:110 (or SEQ ID No:115) and of SEQ ID No:111 (or SEQ ID No:117),
 - (i) wherein the epitope sequence of human CD127 comprising SEQ ID No:110 does not extend to comprise the amino acids adjacent to said sequence in the sequence of human CD127 by more than 1 N-terminal amino acid or by more than 7 C-terminal amino acids; and/or
 - (ii) wherein the epitope sequence of human CD127 comprising SEQ ID No:111 does not extend to comprise the amino acids adjacent to said sequence in the sequence of human CD127 by more than 30 N-terminal amino acid or by more than 30 C-terminal amino acids.
20. A method according to claim 19, wherein the epitope sequences comprise or consist of the sequences of SEQ ID No:116, SEQ ID No:115 and SEQ ID No:117.
21. A method of selecting an antibody obtained according to claim 19 or 20, an antigen-binding fragment of said antibody or a macromolecule comprising said antibody or antigen-binding fragment, comprising or consisting of at least one of the following steps:
 - a. testing the binding capacity of said antibody, antigen-binding fragment or macromolecule to CD127;
 - b. testing the internalization of CD127 in CD127-expressing cells induced by the presence of said antibody, antigen-binding fragment or macromolecule;
 - c. testing the inhibition by said antibody, antigen-binding fragment or macromolecule of IL7-induced internalization of CD127 in CD127-expressing cells; and
 - d. testing the increase of the maturation of DCs induced by TSLP in the presence of said antibody, antigen-binding fragment or macromolecule.
22. A method according to claim 21, further comprising one or more of the following steps:
 - e. testing the inhibition by said antibody, antigen-binding fragment or macromolecule of IL-7 induced signalling, in particular STAT5 phosphorylation;

- f. testing the inhibition by said antibody, antigen-binding fragment or macromolecule of TSLP-induced production of Thymus and Activation-Regulated Chemokine (TARC);
 - g. testing the inhibition by said antibody, antigen-binding fragment or macromolecule of the expression of $\alpha 4$, $\beta 7$ and/or $\alpha 4/\beta 7$ integrin expression, in particular cell surface expression on T-lymphocytes.
23. An antibody or an antigen-binding fragment according to any one of claims 1 to 3, which recognizes an epitope comprising a sequence taken from domain D1 and from the 2b site of human CD127.