

CLAIMS

1. An antagonistic antibody, or an antigen-binding fragment thereof, which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3 comprising a heavy chain, wherein the variable domain of the heavy chain comprises the sequence given in SEQ ID NO:4 for CDR-H1, the sequence given in SEQ ID NO:5 for CDR-H2 and the sequence given in SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:9 for CDR-H3 and

additionally comprising a light chain, wherein the variable domain of the light chain comprises the sequence given in SEQ ID NO:1 for CDR-L1, the sequence given in SEQ ID NO:2 for CDR-L2 and the sequence given in SEQ ID NO:3 for CDR-L3.

2. The antagonistic antibody, or an antigen-binding fragment thereof, according to claim 1, wherein the antibody comprises a heavy chain comprising the sequence given in SEQ ID NO:52, SEQ ID NO:66, SEQ ID NO:80 or SEQ ID NO:94.

3. The antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 or 2, wherein the antibody comprises a light chain comprising the sequence given in SEQ ID NO:38.

4. The antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 3, wherein the antibody molecule is selected from: a complete antibody molecule having full length heavy and light chains or an antigen-binding fragment thereof, a Fab, modified Fab, modified Fab', Fab', F(ab')₂, Fv and scFv fragment.

5. An antagonistic antibody, or an antigen-binding fragment thereof, which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3, having a heavy chain comprising the sequence given in SEQ ID NO:52, SEQ ID NO:66, SEQ ID NO:80 or SEQ ID NO:94 and a light chain comprising the sequence given in SEQ ID NO:38.

6. An antagonistic antibody, or an antigen-binding fragment thereof, which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3, having a heavy chain comprising the sequence given in SEQ ID NO:59, SEQ ID NO:73, SEQ ID NO:87 or SEQ ID NO:101 and a light chain comprising the sequence given in SEQ ID NO:45.

7. The antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 6, having an effector or a reporter molecule attached to it.

8. The antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 7, having a binding affinity for human TGF-beta 1 of 200pM or better, a binding affinity for human TGF-beta 2 of 300pM or better and a binding affinity for human TGF-beta 3 of 2500pM or better.

9. The antagonistic antibody, or an antigen-binding fragment thereof, according to any preceding claim, wherein said antibody or binding fragment thereof is a monoclonal humanized antibody.

10. An isolated DNA molecule encoding the heavy and light chain of an antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 9, or a pair of isolated DNA molecules wherein a first DNA molecule encodes the heavy chain of an antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 9 and a second DNA molecule encodes the light chain of an antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 9.

11. A cloning or expression vector encoding the heavy and light chains of an antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 9, or a pair of cloning or expression vectors wherein a first vector encodes the heavy chain of an antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 9 and a second vector encodes the light chain of an antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 9.

12. A vector or pair of vectors according to claim 11, comprising a light chain DNA sequence given in SEQ ID NO:46 or SEQ ID NO:47 and/or a heavy chain DNA sequence given in SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:102 or SEQ ID NO:103.

13. A host cell comprising one or more cloning or expression vectors according to any one of claims 11 or 12.

14. A process for the production of the antibody, or an antigen-binding fragment thereof, of any one of claims 1 to 9, comprising culturing the host cell of claim 13 and isolating the antibody, or an antigen-binding fragment thereof.

15. A pharmaceutical composition comprising an antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 9 in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier.

16. A pharmaceutical composition according to claim 15, additionally comprising other active ingredients.

17. A pharmaceutical composition of claim 15 or 16, wherein said pharmaceutical composition is suitable for inhaled administration, for example by nebulisation, aerosol and/or dry powder.

18. The antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 9 or the composition according to any one of claims 15 to 17 for use in the treatment or prophylaxis of a pathological disorder that is mediated by TGF-beta 1, 2 or 3 or that is associated with an increased level of TGF-beta 1, 2 or 3, wherein the pathological disorder is fibrosis.

19. The use of the antagonistic antibody, or an antigen-binding fragment thereof, according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment or prophylaxis of a pathological disorder that is mediated by TGF-beta 1, 2 or 3 or that is associated with an increased level of TGF-beta 1, 2 or 3, wherein the pathological disorder is fibrosis.

20. An antagonistic antibody Fab or Fab' fragment according to any one of claims 1 to 9 which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3 for use in the treatment or prophylaxis of a pathological disorder that is mediated by TGF-beta 1, 2 or 3 or that is associated with an increased level of TGF-beta 1, 2 or 3 by inhaled administration, for example by nebulisation, aerosol and/or dry powder, wherein the pathological disorder is fibrosis and/or pulmonary hypertension.

21. The use of an antagonistic antibody Fab or Fab' fragment according to any one of claims 1 to 9 which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3 in the manufacture of a medicament for the treatment or prophylaxis of a pathological disorder that is mediated by TGF-beta 1, 2 or 3 or that is associated with an increased level of TGF-beta 1, 2 or 3 by inhaled administration, for example by nebulisation, aerosol and/or dry powder, wherein the pathological disorder is fibrosis and/or pulmonary hypertension.

22. The antagonistic antibody Fab or Fab' fragment according to claim 20 or the use according to claim 21, wherein the antagonistic antibody Fab or Fab' fragment is as defined in any one of claims 1 to 9.

23. The antagonistic antibody Fab or Fab' fragment according to claim 20 or the use according to claim 21, wherein the fibrosis is selected from the group consisting of: pulmonary fibrosis such as idiopathic pulmonary fibrosis, cystic fibrosis or secondary to systemic sclerosis, and/or wherein the pulmonary hypertension is pulmonary arterial hypertension.