

What is claimed is:

1. An antagonistic antibody 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 at least one of a CDR having the sequence given in SEQ ID NO:4 for CDR-H1, a CDR having the sequence given in SEQ ID NO:5 for CDR-H2 and a CDR having the sequence given in SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:9 for CDR-H3.
2. An antibody according to claim 1, 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.
3. An antagonistic antibody which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3, comprising a light chain, wherein the variable domain of the light chain comprises at least one of a CDR having the sequence given in SEQ ID NO:1 for CDR-L1, a CDR having the sequence given in SEQ ID NO:2 for CDR-L2 and a CDR having the sequence given in SEQ ID NO:3 for CDR-L3.
4. An antibody according to claim 1 or claim 2, additionally comprising a light chain, wherein the variable domain of the light chain comprises at least one of a CDR having the sequence given in SEQ ID NO:1 for CDR-L1, a CDR having the sequence given in SEQ ID NO:2 for CDR-L2 and a CDR having the sequence given in SEQ ID NO:3 for CDR-L3.
5. An antibody according to claim 3 or claim 4 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.

6. An antagonistic antibody which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3, wherein the variable domain of the heavy chain comprises three CDRs and the sequence of CDR-H1 has at least 80% identity or similarity to the sequence given in SEQ ID NO:4, the sequence of CDR-H2 has at least 80% identity or similarity to the sequence given in SEQ ID NO:5 and the sequence of CDR-H3 has at least 80% identity or similarity to the sequence given in SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:9.

7. An antibody, according to claim 6, additionally comprising a light chain, wherein the variable domain of the light chain comprises three CDRs and the sequence of CDR-L1 has at least 80% identity or similarity to the sequence given in SEQ ID NO:1, the sequence of CDR-L2 has at least 80% identity or similarity to the sequence given in SEQ ID NO:2 and the sequence of CDR-L3 has at least 80% identity or similarity to the sequence given in SEQ ID NO:3.

8. An antibody according to any one claims 1 to 7, 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.

9. An antibody according to any one of claims 1 to 8, wherein the antibody comprises a light chain comprising the sequence given in SEQ ID NO:38.

10. An antibody according to any one of claims 1 to 9, wherein the antibody molecule is selected from the group consisting of: a complete antibody molecule having full length heavy and light chains or a fragment thereof, for example selected from the group comprising a Fab, modified Fab', Fab', F(ab')₂, Fv, VH, VL and scFv fragment.

11. An antagonistic antibody 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.

12. An antagonistic antibody which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3, wherein the variable domain of the light chain comprises a sequence having at least 80% identity or similarity to the light chain variable domain of the antibody of claim 11 and wherein the variable domain of the heavy chain comprises a sequence having at least 80% identity or similarity to the heavy chain variable domain of the antibody of claim 11.

13. An antagonistic antibody 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.

14. An antagonistic antibody which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3, in which the heavy and light chains are at least 80% identical or similar to the corresponding heavy and light chains of the antibody of claim 13.

15. An antagonistic antibody which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3, wherein the antibody contacts a sequence 90% identical to amino acids 25-34 of SEQ ID NO:114 and optionally at least one of amino acids 90-95 of SEQ ID NO:114.

16. An antibody of claim 15, wherein the antibody further contacts at least one of amino acids 60, 97 and 101 of SEQ ID NO:114.

17. An antibody according to any one of claims 1 to 16, having an effector or a reporter molecule attached to it.

18. An antagonistic antibody which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3 which cross-blocks the binding of an antibody comprising the CDRs given in sequence SEQ ID NO:1 for CDR-L1, SEQ ID NO:2 for CDR-L2, SEQ ID NO:3 for CDR-L3, SEQ ID NO:4 for CDR-H1, SEQ ID NO:5 for CDR-H2 and SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:9 for CDR-H3.

19. An antibody according to claim 18, wherein the antibody cross-blocks the binding by binding the same epitope as the antibody which it blocks.

20. An antibody according to any one of claims 1 to 19, 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.

21. An antibody according to any preceding claim, wherein said antibody or binding fragment thereof is a monoclonal humanized antibody.

22. An isolated DNA sequence encoding the heavy and/or light chain(s) of an antibody according to any one of claims 1 to 21.

23. A cloning or expression vector comprising one or more DNA sequences according to claim 22.

24. A vector according to claim 23, wherein the vector comprises a light chain DNA sequences given in SEQ ID NO:45 or SEQ ID NO:46 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.

25. A host cell comprising one or more cloning or expression vectors according to claim 24.

26. A process for the production of the antibody of any one of claims 1 to 21, comprising culturing the host cell of claim 25 and isolating the antibody.

27. A pharmaceutical composition comprising an antibody according to any one of claims 1 to 21 in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier.

28. A pharmaceutical composition according to claim 27, additionally comprising other active ingredients.

29. A pharmaceutical composition of claim 27 or 28, wherein said pharmaceutical composition is suitable for inhaled administration, for example by nebulisation, aerosol and/or dry powder.

30. An antibody according to any one of claims 1 to 21 or a composition according to claims 27 to 29 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.

31. The use of an antibody according to any one of claims 1 to 21 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.

32. An antagonistic antibody Fab or Fab' fragment which binds human TGF-beta 1, human TGF-beta 2 and human TGF-beta 3 for use in the treatment or prophylaxis of a pulmonary 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.

33. The use of an antagonistic antibody Fab or Fab' fragment 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 pulmonary 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.

34. The antibody according to claim 32 or the use according to claim 33, wherein the antibody is as defined in any one of claims 1 to 21.

35. The antibody according to claim 32 or the use according to claim 33, wherein the pulmonary disorder is selected from the group consisting of: pulmonary fibrosis such as idiopathic pulmonary fibrosis, cystic fibrosis or secondary to systemic sclerosis, and pulmonary hypertension such as pulmonary arterial hypertension.