CLAIMS

1. Use of an isolated fully human monoclonal CD3 antibody or fragment thereof in the manufacture of a medicament for treating an immune-related disorder that may be modulated by the CD3 pathway, wherein said antibody or fragment thereof comprises a heavy chain amino acid sequence comprising three complementarity determining regions (CDRs) and a light chain amino acid sequence comprising three CDRs, where the three heavy chain CDRs and the three light chain CDRS are selected from:

   a. a variable heavy chain CDR1 (VH CDR1) comprising the amino acid sequence GYGMH (SEQ ID NO:27), a variable heavy chain CDR2 (VH CDR2) comprising the amino acid sequence VIWYDGSKKYYVDSVKG (SEQ ID NO:28), a variable heavy chain CDR3 (VH CDR3) comprising the amino acid sequence QMGYWHFDL (SEQ ID NO:29), a variable light chain CDR1 (VL CDR1) comprising the amino acid sequence RASQSVSSYLA (SEQ ID NO:30), a variable light chain CDR2 (VL CDR2) comprising the amino acid sequence DASNRAT (SEQ ID NO:31), and a variable light chain CDR3 (VL CDR3) comprising the amino acid sequence QQRSNWPPLT (SEQ ID NO:32;

   b. a VH CDR1 comprising the amino acid sequence SYGMH (SEQ ID NO:33), a VH CDR2 comprising the amino acid sequence IIWYDGSKKNYADSVKG (SEQ ID NO:34), a VH CDR3 comprising the amino acid sequence GTGYNWFDP (SEQ ID NO:35), a VL CDR1 comprising the amino acid sequence (SEQ ID NO:36), RASQGISSALA (SEQ ID NO:39) or WASQGISSYLA (SEQ ID NO:43), a VL CDR2 comprising the amino acid sequence GASSRAT (SEQ ID NO:37), YASSLQS (SEQ ID NO:40) or DASSLGS (SEQ ID NO:42), and a VL CDR3 comprising the amino acid sequence QQYGSSPIT (SEQ ID NO:38) or QQYYSTLT (SEQ ID NO:41); and

   c. a VH CDR1 comprising the amino acid SYGMH (SEQ ID NO:33); a VH CDR2 comprising the amino acid sequence AIWYNGRKQDYADSVKG (SEQ ID NO:44); and a VH CDR3 comprising the amino acid sequence GTGYNWFDP (SEQ ID NO:35); a VL CDR1 comprising the amino acid sequence RASQSVSSYLA (SEQ ID NO:30) or RASQGISSALA (SEQ ID NO:39); a VL CDR2 comprising the amino

acid sequence DASNRAT (SEQ ID NO:31) or DASSLES (SEQ ID NO:46); and a VL CDR3 comprising the amino acid sequence QQRSNWPWT (SEQ ID NO:45) or QQFNSYPIT (SEQ ID NO:47).

2. Use of an isolated fully human monoclonal CD3 antibody or fragment thereof in the manufacture of a medicament for preventing rejection of an organ or tissue transplant, wherein said antibody or fragment thereof comprises a heavy chain amino acid sequence comprising three complementarity determining regions (CDRs) and a light chain amino acid sequence comprising three CDRs, where the three heavy chain CDRs and the three light chain CDRS are selected from:

   a. a variable heavy chain CDR1 (VH CDR1) comprising the amino acid sequence GYGMH (SEQ ID NO:27), a variable heavy chain CDR2 (VH CDR2) comprising the amino acid sequence VIWYDGSKKYYVDSVKG (SEQ ID NO:28), a variable heavy chain CDR3 (VH CDR3) comprising the amino acid sequence QMGYWHFDL (SEQ ID NO:29), a variable light chain CDR1 (VL CDR1) comprising the amino acid sequence RASQSVSSYLA (SEQ ID NO:30), a variable light chain CDR2 (VL CDR2) comprising the amino acid sequence DASNRAT (SEQ ID NO:31), and a variable light chain CDR3 (VL CDR3) comprising the amino acid sequence QQRSNWPPLT (SEQ ID NO:32);

   b. a VH CDR1 comprising the amino acid sequence SYGMH (SEQ ID NO:33), a VH CDR2 comprising the amino acid sequence IIWYDGSKKNYADSVKG (SEQ ID NO:34), a VH CDR3 comprising the amino acid sequence GTGYNWFDP (SEQ ID NO:35), a VL CDR1 comprising the amino acid sequence (SEQ ID NO:36), RASQGISSALA (SEQ ID NO:39) or WASQGISSYLA (SEQ ID NO:43), a VL CDR2 comprising the amino acid sequence GASSRAT (SEQ ID NO:37), YASSLQS (SEQ ID NO:40) or DASSLGS (SEQ ID NO:42), and a VL CDR3 comprising the amino acid sequence QQYGSSPIT (SEQ ID NO:38) or QQYYSTLT (SEQ ID NO:41); and

   c. a VH CDR1 comprising the amino acid SYGMH (SEQ ID NO:33); a VH CDR2 comprising the amino acid sequence AIWYNGRKQDYADSVKG (SEQ ID NO:44); and a VH CDR3 comprising the amino acid sequence GTGYNWFDP (SEQ ID NO:35); a VL CDR1 comprising the amino acid sequence RASQSVSSYLA (SEQ ID

NO:30) or RASQGISSALA (SEQ ID NO:39); a VL CDR2 comprising the amino acid sequence DASNRAT (SEQ ID NO:31) or DASSLES (SEQ ID NO:46); and a VL CDR3 comprising the amino acid sequence QQRSNWPWT (SEQ ID NO:45) or QQFNSYPIT (SEQ ID NO:47).

3. The use of claim 1 or claim 2, wherein said antibody or fragment thereof inhibits binding of the murine anti-human OKT3 monoclonal antibody to a T-lymphocyte.

4. The use of claim 1 or claim 2, wherein said antibody or fragment thereof binds an epitope that wholly or partially includes the amino acid sequence EMGGITQTPYKVSISGT (SEQ ID NO:67).

5. The use of claim 1, wherein said immune-related disorder that may be modulated by the CD3 pathway is an autoimmune disease or an inflammatory disorder.

6. The use of claim 5, wherein said autoimmune disease is selected from the group consisting of: ankylosing spondylitis, asthma, Behcet's disease, glomerular nephritis, graft-versus-host disease, grave's disease, Hashimoto's thyroiditis, juvenile rheumatoid arthritis, luminal and fistulizing Crohn's disease, polyarticular juvenile arthritis, polymyositis/myositis/giant cell myocarditis and dermatomyositis, psoriasis, psoriatic arthritis, rheumatoid arthritis, systemic lupus erythematosus, ulcerative colitis, and uveitis.

7. The use of claim 5, wherein said inflammatory disorder is selected from the group consisting of: Alzheimer's disease, asthma, atopic allergy, allergy, atherosclerosis, bronchial asthma, eczema, glomerulonephritis, graft vs. host disease, hemolytic anemias, osteoarthritis, sepsis, stroke, transplantation of tissue and organs, vasculitis, diabetic retinopathy and ventilator induced lung injury.

8. The use of claim 1, wherein said immune-related disorder is rheumatoid arthritis.

9. The use of claim 1, wherein said immune-related disorder is Crohn's disease.

10. The use of any one of claims 1-9, wherein said antibody or antigen-binding fragment thereof comprises a VH CDR1 comprising the amino acid sequence of GYGMH (SEQ ID NO:27); a VH CDR2 comprising the amino acid sequence of VIWYDGSKKYYVDSVKG (SEQ ID NO:28); a VH CDR3 comprising the amino acid sequence of QMGYWHFDL (SEQ ID NO:29) a VL CDR1 comprising the amino acid sequence of RASQSVSSYLA (SEQ ID NO:30); a VL CDR2 comprising the amino acid sequence of DASNRAT (SEQ ID NO:31); and a VL CDR3 comprising the amino acid sequence of QQRSNWPPLT (SEQ ID NO:32), and wherein the antibody or antigen-binding fragment thereof further comprises a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 2 and a variable light chain comprising the amino acid sequence of SEQ ID NO: 4

11. The use of any one of claims 1-10, wherein said antibody or fragment thereof includes a mutation in the heavy chain at an amino acid residue at position 234, 235, 265, or 297 or combinations thereof, and wherein the release of cytokines from a T-cell in the presence of said antibody is reduced as compared to the release of cytokines from a T-cell in the presence of an antibody that does not include a mutation in the heavy chain at position 234, and 235, 265 or 297 or combinations thereof.

12. The use of claim 11, wherein said mutation results in an alanine or glutamic acid residue at said position.

13. The use of any one of claims 1-12, wherein said antibody is an IgG1 isotype and contains at least a first mutation at position 234 and a second mutation at position 235, wherein said first mutation results in an alanine residue at position 234 and said second mutation results in a glutamic acid residue at position 235.

14. The use of any one of claims 1-9, wherein said antibody or fragment thereof has a heavy chain with three CDRs, comprising a VH CDR1 comprising the amino acid sequence of GYGMH (SEQ ID NO:27); a VH CDR2 comprising the amino acid sequence of VIWYDGSKKYYVDSVKG (SEQ TD NO:28); a VH CDR3 comprising the amino acid sequence of QMGYWHFDL (SEQ ID NO:29)and a light chain with three CDRs, comprising a VL CDR1 comprising the amino acid sequence of RASQSVSSYLA (SEQ

ID NO:30); a VL CDR2 comprising the amino acid sequence of DASNRAT (SEQ ID NO:31); and a VL CDR3 comprising the amino acid sequence of QQRSNWPPLT (SEQ ID NO:32), and wherein the antibody or antigen-binding fragment thereof further comprises a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 6 and a variable light chain comprising the amino acid sequence of SEQ ID NO: 8.

15. The use of any one of claims 1-9, wherein said antibody or fragment thereof has a heavy chain with three CDRs, comprising a VH CDR1 comprising the amino acid sequence SYGMH (SEQ ID NO:33); a VH CDR2 comprising the amino acid sequence of IIWYDGSKKNYADSVKG (SEQ ID NO:34); a VH CDR3 comprising the amino acid sequence of GTGYNWFDP (SEQ ID NO:35); and a light chain with three CDRs, comprising a VL CDR1 comprising the amino acid sequence of RASQSVSSSYLA (SEQ ID NO:36), RASQGISSALA (SEQ ID NO:39) or WASQGISSYLA (SEQ ID NO:43); a VL CDR2 comprising the amino acid sequence of GASSRAT (SEQ ID NO:37), YASSLQS (SEQ ID NO:40), or DASSLGS (SEQ ID NO:42); and a VL CDR3 comprising the amino acid sequence of QQYGSSPIT (SEQ ID NO:38) or QQYYSTLT (SEQ ID NO:41), and wherein the antibody or antigen-binding fragment thereof further comprises a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 10 and a variable light chain comprising the amino acid sequence of SEQ ID NO: 16, 17, 18, 19 or 20.

16. The use of any one of claims 1-9, wherein said antibody or fragment thereof has a heavy chain with three CDRs, comprising a VH CDR1 comprising the amino acid sequence SYGMH (SEQ ID NO:33); a VH CDR2 comprising the amino acid sequence of AIWYNGRKQDYADSVKG (SEQ ID NO:44); a VH CDR3 comprising the amino acid sequence of GTGYNWFDP (SEQ ID NO:35); and a light chain with three CDRs, comprising a VL CDR1 comprising the amino acid sequence of RASQSVSSYLA (SEQ ID NO:30) or RASQGISSALA (SEQ ID NO:39); a VL CDR2 comprising the amino acid sequence of DASNRAT (SEQ ID NO:31) or DASSLES (SEQ ID NO:46); and a VL CDR3 comprising the amino acid sequence of QQRSNWPWT (SEQ ID NO:45) or QQFNSYPIT (SEQ ID NO:47), and wherein said antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of

SEQ ID NO: 22, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 25 or 26.

17. The use of any one of claims 1 to 16, antibody or fragment thereof, wherein said antibody comprises a framework 2 region (FWR2) comprising the amino acid sequence WVRQAPGKGLEWV (SEQ ID NO:73).

18. The use of any one of claims 1 to 17, wherein said antibody comprises a framework 3 region (FRW3) comprising the amino acid sequence RFTISRDNSKNTLYLQMNSLRAEDTAVYYCA (SEQ ID NO:74).

19. The use of any one of claims 1 to 18, wherein said antibody comprises a variable region located C-terminal to the CDR3 region, wherein said variable region comprises the amino acid sequence VTVSS (SEQ ID NO:64) at a position that is C-terminal to the CDR3 region.

20. The use of claim 19, wherein said antibody comprises a variable region located C-terminal to the CDR3 region, wherein said variable region comprises the amino acid sequence GTLVTVSS (SEQ ID NO:65) at a position that is C-terminal to the CDR3 region.

21. The use of claim 19, wherein said antibody comprises a variable region located C-terminal to the CDR3 region, wherein said variable region comprises the amino acid sequence WGRGTLVTVSS (SEQ ID NO:66) at a position that is C-terminal to the CDR3 region.

22. The use of any one of claims 14-21, wherein said antibody includes a mutation in the heavy chain at an amino acid residue at position 234, 235, 265, or 297 or combinations thereof, and wherein the release of cytokines from a T-cell in the presence of said antibody is reduced as compared to the release of cytokines from a T-cell in the presence of an antibody that does not include a mutation in the heavy chain at position 234, 235, 265 or 297 or combinations thereof.

23. The use of claim 22, wherein said mutation results in an alanine or glutamic acid residue at said position.

24. The use of claim 22, wherein said antibody contains at least a first mutation is at position 234 and a second mutation is at position 235, and wherein said first mutation results in an alanine residue at position 234 and said second mutation results in a glutamic acid residue at position 235.

25. The use of any one of claims 1 to 24, wherein the subject is a human.

26. The use of claim 25, wherein said antibody is to be co-administered with a second agent selected from an anti-inflammatory compound and an immunosuppressive compound.

27. The use of claim 26, wherein the second agent to be co-administered is GLP-1, a beta cell resting compound, methotrexate, cyclosporin A, tacrolimus, corticosteroids, statins, interferon beta, glatiramer acetate, mitoxantrone, dexamethasone, methylprednisolone, prednisone, Infliximab, Etanercept or Adalimumab.

28. The use of claim 27, wherein the second agent to be co-administered is an anti-TNF antibody.