SEQ ID NO: 30 or sequences at least 90% identical thereto; and/or the heavy chain variable region comprises at least a CDR1 selected from SEQ ID NO: 25 or sequences at least 90% identical thereto, a CDR2 selected from SEQ ID NO: 26 or sequences at least 90% identical thereto, and a CDR3 selected from SEQ ID NO: 27 or sequences at least 90% identical thereto.

~~**[0022a]** In one aspect, the present disclosure refers to an antibody that binds transforming growth factor beta (TGFβ)1, TGFβ2 and TGFβ3 comprising:~~

~~A. (a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 25, or a variant thereof in which one or two amino acids have been changed;~~

~~(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 26, or a variant thereof in which one or two amino acids have been changed;~~

~~(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 27, or a variant thereof in which one or two amino acids have been changed;~~

~~(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 28, or a variant thereof in which one or two amino acids have been changed;~~

~~(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 29, or a variant thereof in which one or two amino acids have been changed; and~~

~~(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 30, or a variant thereof in which one or two amino acids have been changed; or~~

~~B. (a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 25, or a variant thereof in which one or two amino acids have been changed;~~

~~(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 26, or a variant thereof in which one or two amino acids have been changed;~~

~~(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 27, or a variant thereof in which one or two amino acids have been changed;~~

~~(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 16, or a variant thereof in which one or two amino acids have been changed;~~

~~(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 17, or a variant thereof in which one or two amino acids have been changed; and~~

~~(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 18, or a variant thereof in which one or two amino acids have been changed.~~

[0023] It is contemplated that the percent identity of any one of the above antibody sequences can be at least 70%, 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96% , 97%, 98%, 99% or more identical to a heavy or light chain variable region or any of HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 or LCDR3 disclosed herein.

[0024] In some examples, an antibody of the disclosure further comprises a heavy chain constant region, wherein the heavy chain constant region is a modified or unmodified IgG, IgM, IgA, IgD, IgE, a fragment thereof, or combinations thereof.

[0025] In certain examples, an antibody is provided in which one or more light chain framework amino acids have been replaced with corresponding amino acid(s) from another human antibody amino acid sequence.

[0026] In one example, the antibody of the disclosure is selected from the group consisting of XPA.42.089, XPA.42.068 and XPA.42.681. Heavy and light chain amino acid sequences of XPA.42.089 are set out in SEQ ID NOs: 6 and 8, respectively. Heavy and light chain amino acid sequences of XPA.42.068 are set out in SEQ ID NOs: 2 and 4, respectively, and heavy and light chain amino acid sequences of XPA.42.681 are set out in SEQ ID NOs: 10 and 12, respectively.

[0027] In one example, an antibody described herein further comprises a human light chain constant region attached to said light chain variable region. In some examples, the light chain constant region is a modified or unmodified lambda light chain constant region, a kappa light chain constant region, a fragment thereof, or combinations thereof.

[0028] In a preferred example, the disclosure provides an antibody specific for TGFβ1, TGFβ2 and TGFβ3 with an affinity Kd of 10^{-6} M or less. In some examples, an anti-TGFβ antibody described herein binds at least one isoform of TGFβ with an affinity of 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M or less, or optionally binds two TGFβ isoforms, or all of TGFβ1, 2, or 3 with an affinity of 10^{-6} M. 10^{-7} M, 10^{-8} M, 10^{-9} M, 10^{-10} M, 10^{-11} M, or 10^{-12} M

or less for one or more of the isoforms. In other examples, an antibody described herein binds to TGFβ1 and TGFβ2 with at least 2-50 fold, 10-100 fold, 2-fold, 5-fold, 10-fold, 25-fold, 50-fold or 100-fold, or 20-50%, 50-100%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 100% higher affinity (e.g., preferentially binds to TGFβ1 and TGFβ2) compared to binding to TGFβ3. Alternatively, an antibody described herein, binds each of TGFβ isoforms TGFβ1, TGFβ2 and TGFβ3 with an affinity within 3-fold, 5-fold or 10-fold of each other. In certain examples, the antibody binds to TGFβ1 and TGFβ2 with greater affinity than TGFβ3. In certain examples, the affinity is measured by surface plasmon resonance or KINEXA assay.

[0029] In some examples, the antibody neutralizes activity of TGFβ1 and TGFβ2 to a greater extent than TGFβ3. In some examples, antibody neutralization of TGFβ1 and TGFβ2 is at least 2-50 fold, 10-100 fold, 2-fold, 5-fold, 10-fold, 25-fold, 50-fold or 100-fold, or 20-50%, 50-100%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 100% more potent that neutralization of TGFβ3. Exemplary neutralization assays contemplated herein include, but are not limited to, an interleukin-11 release assay and an HT-2 cell proliferation assay. In addtion, a TGFβ activity assay can be carried out to determine if an antibody disclosed herein inhibits one TGFβ isoform preferentially, including a pSMAD phosphorylation assay or an rhLAP binding assay. In a further example, the antibody has a lower IC50 (i.e., better binding, greater potency) for TGFβ1 and TGFβ2 compared to TGFβ3.

[0030] In another example, the disclosure provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain and/or light chain as described herein. ~~In one aspect, the present disclosure refers to an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain or light chain as described herein.~~

[0031] In a further example, the disclosure provides an expression vector comprising a nucleic acid molecule contemplated herein operably linked to an expression control sequence. ~~In one aspect, the present disclosure refers to an expression vector comprising the nucleic acid molecule as described herein operably linked to an expression control sequence.~~ Also contemplated is a host cell comprising an expression vector or a nucleic acid molecule of the disclosure. In certain examples, the disclosure provides a host cell comprising a nucleic acid molecule encoding a heavy chain and a light chain variable region, wherein the heavy chain and light chain nucleic acids are expressed by different nucleic acids or on the same nucleic acid. ~~In one aspect, the present disclosure refers to a recombinant host cell comprising the vector as described herein or a nucleic acid molecule as described herein, excluding cells within a human.~~

[0032] In a related example, the disclosure provides a method of using the host cell as described herein to produce an antibody, the method comprising culturing the host cell under

suitable conditions and recovering said antibody. ~~In one aspect, the present disclosure refers to a method of using the host cell as described herein to produce an antibody, comprising culturing the host cell as described herein under suitable conditions and recovering said antibody.~~ Also provided is an antibody produced by the method disclosed herein.

[0033] In one example~~aspect~~, the present disclosure further refers to a sterile pharmaceutical composition comprising the antibody as disclosed herein and a pharmaceutically acceptable carrier.

[0034] In another example, the disclosure provides a method for treating a disease, condition or disorder associated with TGFβ expression comprising the step of administering to a subject in need thereof a therapeutically effective amount of an antibody or a pharmaceutical composition contemplated herein. ~~In one aspect, the present disclosure refers to use of an antibody as described herein or a pharmaceutical composition as described herein in the preparation of a medicament for treating a disease, condition or disorder associated with TGFβ expression.~~ In certain examples, the disease, condition or disorder is selected from the group consisting of a cancer, an eye (e.g., ocular, optic, ophthalmic or ophthalmological) disease, condition or disorder, a disease condition or disorder associated with fibrosis, e.g., fibroproliferative diseases, conditions or disorders, or disease, conditions or disorders having an associated fibrosis.

[0035] Fibroproliferative diseases, conditions or disorders or diseases having an associated fibrosis include those that affect any organ or tissue in the body, including, but not limited to the skin, lung, kidney, heart, brain and eye. Fibroproliferative diseases, conditions or disorders or diseases having an associated fibrosis include, but are not limited to pulmonary fibrosis, idiopathic pulmonary fibrosis, peribronchiolar fibrosis, interstitial lung disease, chronic obstructive pulmonary disease (COPD), small airway disease (e.g., obstructive bronchiolitis), emphysema, adult or acute respiratory distress syndrome (ARDS), acute lung injury (ALI), pulmonary fibrosis due to infectious or toxic agents, kidney fibrosis, glomerulonephritis (GN) of all etiologies, mesangial proliferative GN, immune GN, crescentic GN, glomerulosclerosis, tubulointerstitial injury, renal interstitial fibrosis, renal fibrosis and all causes of renal interstitial fibrosis, renal fibrosis resulting from complications of drug exposure, including cyclosporin treatment of transplant recipients, HIV-associated nephropathy, transplant necropathy, diabetic kidney disease, diabetic nephropathy, nephrogenic systemic fibrosis, diabetes, idiopathic retroperitoneal fibrosis, scleroderma, liver fibrosis, hepatic diseases associated with excessive scarring and progressive sclerosis, liver cirrhosis due to all etiologies, disorders of the biliary tree, hepatic dysfunction attributable to infections, fibrocystic diseases, cardiovascular diseases, congestive heart failure, dilated cardiomyopathy, myocarditis, vascular stenosis cardiac fibrosis, post-infarction cardiac fibrosis, post myocardial infarction, left ventricular hypertrophy, veno-occlusive disease, restenosis, post-angioplasty restenosis, arteriovenous graft failure, atherosclerosis, hypertension, hypertensive heart disease, cardiac hypertrophy, hypertrophic cardiomyopathy,

WHAT IS CLAIMED:

1. Use of an antibody that binds transforming growth factor beta (TGFβ)1, TGFβ2 and TGFβ3, wherein the antibody comprises:

(a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 19;

(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 20;

(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 21;

(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 22;

(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 23; and

(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 24;

in the preparation of a medicament for the treatment of colorectal cancer, hepatocellular carcinoma, breast cancer, prostate cancer, pancreatic cancer, renal cancer, lung cancer, fibrotic cancer, idiopathic pulmonary fibrosis (IPF) or fibroproliferative diseases,

wherein the medicament is capable of administration with one or more second agents.

2. Use of an antibody that binds transforming growth factor beta (TGFβ)1, TGFβ2 and TGFβ3, wherein the antibody comprises:

(a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 19;

(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 20;

(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 21;

(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 22;

(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 23; and

(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 24;

in the preparation of a medicament for the treatment of colorectal cancer, hepatocellular carcinoma, breast cancer, prostate cancer, pancreatic cancer, renal cancer, lung cancer, fibrotic cancer, idiopathic pulmonary fibrosis (IPF) or fibroproliferative diseases,

wherein the antibody comprises an amino acid sequence at least 90% identical to a heavy chain variable region amino acid sequence set out in SEQ ID NO: 6 and an amino acid sequence at least 90% identical to a light chain variable region amino acid sequence set out in SEQ ID NO: 8.

3. Use of an antibody that binds transforming growth factor beta (TGFβ)1, TGFβ2 and TGFβ3, wherein the antibody comprises:

(a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 19;

(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 20;

(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 21;

(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 22;

(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 23; and

(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 24;

in the preparation of a medicament for the treatment of colorectal cancer, hepatocellular carcinoma, breast cancer, prostate cancer, pancreatic cancer, renal cancer, lung cancer, fibrotic cancer, idiopathic pulmonary fibrosis (IPF) or fibroproliferative diseases,

wherein the antibody is capable of being administered at a dose of about 1 mg/kg, about 3 mg/kg or about 10 mg/kg.

4. Use of an antibody that binds transforming growth factor beta (TGFβ)1, TGFβ2 and TGFβ3, wherein the antibody comprises:

(a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 19;

(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 20;

(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 21;

(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 22;

(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 23; and

(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 24;

in the preparation of a medicament for the treatment of colorectal cancer, hepatocellular carcinoma, breast cancer, prostate cancer, pancreatic cancer, renal cancer, lung cancer, fibrotic cancer, idiopathic pulmonary fibrosis (IPF) or fibroproliferative diseases,

wherein the antibody is capable of being administered at a dose of approximately 100 mg/day or 150 mg/day.

5. Use of an antibody that binds transforming growth factor beta (TGFβ)1, TGFβ2 and TGFβ3, wherein the antibody comprises:

(a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 19;

(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 20;

(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 21;

(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 22;

(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 23; and

(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 24;

in the preparation of a medicament for the treatment of colorectal cancer, hepatocellular carcinoma, breast cancer, prostate cancer, pancreatic cancer, renal cancer, lung cancer, fibrotic cancer, idiopathic pulmonary fibrosis (IPF) or fibroproliferative diseases,

wherein the antibody is capable of being administered weekly, every 2 weeks, every 3 weeks, or monthly.

6. Use of an antibody that binds transforming growth factor beta (TGFβ)1, TGFβ2 and TGFβ3, wherein the antibody comprises:

(a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 19;

(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 20;

(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 21;

(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 22;

(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 23; and

(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 24;

in the preparation of a medicament for the treatment of colorectal cancer, hepatocellular carcinoma, breast cancer, prostate cancer, pancreatic cancer, renal cancer, lung cancer, fibrotic cancer, idiopathic pulmonary fibrosis (IPF) or fibroproliferative diseases,

wherein the antibody is capable of being administered intravenously or subcutaneously.

7. The use of any one of claims 1 or 3-6, wherein the antibody comprises an amino acid sequence at least 90% identical to a heavy chain variable region amino acid sequence set out in SEQ ID NO: 6 and an amino acid sequence at least 90% identical to a light chain variable region amino acid sequence set out in SEQ ID NO: 8.

8**.** The use of any one of claims 1-7, wherein the antibody comprises a heavy chain variable region amino acid sequence set out in SEQ ID NO: 6 and a light chain variable region amino acid sequence set out in SEQ ID NO: 8.

9. The use of any one of claims 1-8, wherein the antibody further comprises a heavy chain constant region, wherein the heavy chain constant region is a modified or unmodified IgG, IgM, IgA, IgD, IgE, a fragment thereof, or combinations thereof.

10. The use of any one of claims 1-9, wherein the antibody further comprises a light chain constant region wherein the light chain constant region is a modified or

unmodified lambda light chain constant region, a kappa light chain constant region, a fragment thereof, or combinations thereof.

11. The use of any one of claims 1-10 in which one or more light chain framework amino acids of the antibody have been replaced with corresponding amino acid(s) from another human antibody amino acid sequence.

12. The use of any one of claims 1-11, wherein the antibody further comprises a human light chain constant region attached to said light chain variable region.

13. The use of any one of claims 1-12, wherein the antibody binds to TGFβ1 and TGFβ2 with greater affinity than TGFβ3.

14. The use of any one of claims 1-13, wherein the antibody neutralizes activity of TGFβ1 and TGFβ2 to a greater extent than TGFβ3.

15. The use of any one of claims 1-14, wherein the antibody is in a sterile pharmaceutical composition comprising the antibody and a pharmaceutically acceptable carrier.

16. The use of any one of claims 1-15, wherein the antibody or composition increases the number of natural killer (NK) cells in a tumor and/or improves NK cell cytolytic activity.

~~17. The use of any one of claims 1-15, wherein the antibody or composition decreases the number of regulatory T cells in a tumor and/or inhibits regulatory T cell function.~~

~~18. The use of any one of claims 1-15, wherein the antibody or composition increases the number of cytotoxic T cells (CTLs) in a tumor and/or enhances CTL function.~~

~~19~~17. The use of any one of claims 1-15, wherein the antibody decreases the number of myeloid-derived suppressor cells (MDSC) in a tumor ~~and/or inhibits MDSC function~~.

~~20~~18. The use of any one of claims 1-15, wherein the antibody decreases the number of dendritic cells (DC) in a tumor and/or inhibits the tolerogenic function of dendritic cells.

~~21~~19. The use of any one of claims 2-6, further ~~comprises~~comprising use of one or more second agents.

~~22~~20. The use of claim 1 or claim 19~~21~~, wherein the second agent is selected from the group consisting of a chemotherapeutic agent, a cytotoxic agent, and azacitidine.

~~23~~21. The use of claim 20~~22~~, wherein the chemotherapeutic agent is selected from the group consisting of 5-fluorouracil, oxaliplatin, irinotecan, and combinations thereof.

~~24~~22. The use according to any one of claims 1-~~23~~21, wherein the antibody is in lyophilized form or liquid form.

~~25~~23. The use according to any one of claims 1, 2, 5 or 6, wherein the antibody is capable of being administered at a dose of about 1 mg/kg, about 3 mg/kg or about 10 mg/kg.

~~26~~24. The use according to any one of claims 1, 2, 5 or 6, wherein the antibody is capable of being administered at a dose of approximately 100 mg/day or 150 mg/day.

~~27~~25. The use according to any one of claims 1-4, wherein the antibody is capable of being administered weekly, every 2 weeks, every 3 weeks, or monthly.

~~28~~26. The use according to any one of claims 1-5, wherein the antibody is capable of being administered intravenously or subcutaneously.

~~29~~27. The use of any one of claims ~~or~~ 19~~21~~-21~~23~~, wherein the one or more second agents is capable of administration either simultaneously or sequentially.

~~30~~28. The use of any one of the preceding claims, wherein the disease is idiopathic pulmonary fibrosis (IPF).

~~31~~29. The use of any one of ~~the preceding~~ claims 1-27, wherein the disease is colorectal cancer.

~~32~~30. The use of any one of ~~the preceding~~ claims 1-27, wherein the disease is pancreatic cancer.

~~33. An antibody that binds transforming growth factor beta (TGFβ)1, TGFβ2 and TGFβ3 comprising:~~

~~A. (a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 25, or a variant thereof in which one or two amino acids have been changed;~~

~~(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 26, or a variant thereof in which one or two amino acids have been changed;~~

~~(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 27, or a variant thereof in which one or two amino acids have been changed;~~

~~(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 28, or a variant thereof in which one or two amino acids have been changed;~~

~~(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 29, or a variant thereof in which one or two amino acids have been changed; and~~

~~(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 30, or a variant thereof in which one or two amino acids have been changed; or~~

~~B. (a) a heavy chain CDR1 amino acid sequence set forth in SEQ ID NO: 25, or a variant thereof in which one or two amino acids have been changed;~~

~~(b) a heavy chain CDR2 amino acid sequence set forth in SEQ ID NO: 26, or a variant thereof in which one or two amino acids have been changed;~~

~~(c) a heavy chain CDR3 amino acid sequence set forth in SEQ ID NO: 27, or a variant thereof in which one or two amino acids have been changed;~~

~~(d) a light chain CDR1 amino acid sequence set forth in SEQ ID NO: 16, or a variant thereof in which one or two amino acids have been changed;~~

~~(e) a light chain CDR2 amino acid sequence set forth in SEQ ID NO: 17, or a variant thereof in which one or two amino acids have been changed; and~~

~~(f) a light chain CDR3 amino acid sequence set forth in SEQ ID NO: 18, or a variant thereof in which one or two amino acids have been changed.~~

~~34. The antibody of claim 33, that comprises~~

~~A. an amino acid sequence at least 90% identical to a heavy chain variable region amino acid sequence set forth in SEQ ID NO: 10 and an amino acid sequence at least 90% identical to a light chain variable region amino acid sequence set forth in SEQ ID NO: 12; or~~

~~B. an amino acid sequence at least 90% identical to a heavy chain variable region amino acid sequence set forth in SEQ ID NO: 10 and an amino acid sequence at least 90% identical to a light chain variable region amino acid sequence set forth in SEQ ID NO: 4.~~

~~35. The antibody of any one of claims 33 or 34, further comprising a heavy chain constant region, wherein the heavy chain constant region is a modified or unmodified IgG, IgM, IgA, IgD, IgE, a fragment thereof, or combinations thereof.~~

~~36. The antibody of any one of claims 33 to 35, in which one or more light chain framework amino acids have been replaced with corresponding amino acid(s) from another human antibody amino acid sequence.~~

~~37. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain or light chain of any one of claims 33 to 36.~~

~~38. An expression vector comprising the nucleic acid molecule of claim 37 operably linked to an expression control sequence.~~

~~39. A recombinant host cell comprising the vector of claim 38 or a nucleic acid molecule of claim 37, excluding cells within a human.~~

~~40. A method of using the host cell of claim 39 to produce an antibody, comprising culturing the host cell of claim 39 under suitable conditions and recovering said antibody.~~

~~41. A sterile pharmaceutical composition comprising the antibody of any one of claims 33-36 and a pharmaceutically acceptable carrier.~~

~~42. Use of an antibody of any one of claims 33-36 or a pharmaceutical composition of claim 41 in the preparation of a medicament for treating a disease, condition or disorder associated with TGFβ expression.~~