

CLAIMS

1. An isolated antibody, or antigen-binding portion thereof, that specifically binds each of the following TGF β 1 complexes:
a GARP-TGF β 1 complex,
a LTBP1-TGF β 1 complex,
a LTBP3-TGF β 1 complex, and
a LRRC33-TGF β 1 complex;
wherein the antibody does not bind free mature TGF β 1, and,
wherein the antibody, or antigen-binding portion thereof is a humanized or fully human antibody or antigen-binding portion thereof.
2. An anti-TGF β 1 antibody, or antigen-binding portion thereof, that competes for binding with the antibody, or antigen binding portion thereof, according to claim 1.
3. A pharmaceutical composition comprising the antibody or the antigen-binding portion thereof according to claim 1 or 2, and an excipient.
4. Use of an isoform-specific inhibitor of TGF β 1 for the manufacture of a medicament for treating a subject diagnosed with a TGF β -related indication, wherein the indication is:
i) associated with expression of one or more of the following markers: plasminogen activator inhibitor-1 (PAI-1), connective tissue growth factor (CTGF), TGF β 1, fibronectin-1, α -smooth muscle actin (α SMA), monocyte chemotactic protein 1 (MCP-1), collagen type I alpha 1 (Colla1), and collagen type III alpha 1 chain (Col3a1); and/or,
ii) cancer; and,
wherein the isoform-specific inhibitor of TGF β 1 does not inhibit TGF β 2.
5. Use of an isoform-specific inhibitor of TGF β 1 for the manufacture of a medicament for treating a TGF β -related indication, wherein, when administered at a therapeutically effective dose to a subject, the inhibitor does not cause a cardiovascular toxicity associated with TGF β inhibition in the subject.
6. The use according to claim 4, wherein the subject has cancer comprising a solid tumor, and, wherein the medicament inhibits or decreases the growth of the solid tumor.
7. The use according to claim 4, wherein the subject has or is at risk of a fibrotic indication, wherein optionally the fibrotic indication is a liver fibrosis, kidney fibrosis, or lung fibrosis, wherein further optionally the lung fibrosis is idiopathic pulmonary fibrosis.

8. The use according to any one of claims 4-7, wherein the subject has or is at risk of a condition related to fibrosis selected from Marfan's syndrome, stiff skin syndrome, scleroderma, rheumatoid arthritis, bone marrow fibrosis, Crohn's disease, ulcerative colitis, systemic lupus erythematosus, muscular dystrophy, including Duchenne muscular dystrophy, Dupuytren's contracture, Camurati-Engelmann disease, neural scarring, dementia, proliferative vitreoretinopathy, corneal injury, complications after glaucoma drainage surgery, and multiple sclerosis.
9. The use according to any one of claims 4-8, wherein the isoform-specific inhibitor of $TGF\beta 1$ is a biologic or a small molecule agent.
10. The use according to claim 9, wherein the biologic is an antibody or an antigen-binding fragment thereof.
11. The use according to claim 10, wherein the antibody or antigen-binding fragment thereof specifically binds a pro/latent $TGF\beta 1$ complex.
12. The use according to claim 11, wherein the pro/latent $TGF\beta 1$ complex comprises LTBP1, LTBP3, GARP or LRRC33.
13. The use according to any one of claims 10-12, wherein the therapeutically effective dose is from about 0.1 $\mu\text{g/kg}$ to about 30 mg/kg .
14. The use according to any one of claims 10-13, wherein the antibody or antigen-binding fragment thereof is to be administered in combination with an additional agent or therapy.
15. The use according to claim 14, wherein the additional agent is a checkpoint inhibitor.
16. The use according to any one of claims 4-15, wherein the isoform-specific inhibitor of $TGF\beta 1$ does not inhibit $TGF\beta 2$ or $TGF\beta 3$.
17. A method for selecting an isoform specific inhibitor of $TGF\beta 1$ for use as medicament, the method comprising the steps of:
 - i) providing one or more agents that inhibit signaling of at least one isoform of $TGF\beta$ selected from the group consisting of $TGF\beta 1$, $TGF\beta 2$ and $TGF\beta 3$;
 - ii) measuring activities of the one or more agents towards all isoforms of $TGF\beta$;

iii) selecting an agent for specific activity against the of TGF β 1 isoform for formulating into a pharmaceutical composition.

18. The method of claim 17, wherein the isoform-specific TGF β 1 inhibitor is an antibody or an antigen-binding fragment thereof.

19. The method of claim 17 or 18, wherein the antibody or fragment thereof specifically binds a pro/latent complex of TGF β 1 but does not bind free mature TGF β 1 which is not associated with a pro/latent complex, wherein optionally the pro/latent complex comprises GARP, LRRC33, LTBP1, or LTBP3.

20. A pharmaceutical composition produced by the method according to any one of claims 17-19.