

CLAIMS

What is claimed is:

1. An isolated anti-TNFR2 (tumor necrosis factor receptor 2) antibody comprising a set of three complementarity determining regions (CDRs) on a heavy chain (HCDR1, HCDR2, and HCDR3) and a set of three CDRs on a light chain (LCDR1, LCDR2, and LCDR3), wherein
 - (i) the set of HCDR1, HCDR2, HCDR3, and the set of LCDR1, LCDR2, LCDR3 on a corresponding light chain comprise the amino acid sequences as shown in Table 9; or
 - (ii) the set of HCDR1, HCDR2, and HCDR3 comprise the amino acid sequences as shown in Table 7, and the set of LCDR1, LCDR2, and LCDR3 on a corresponding light chain comprise the amino acid sequences as shown in Table 8.
2. The anti-TNFR2 antibody of claim 1, wherein the antibody comprises a heavy chain variable region and a light chain variable region, said heavy chain variable region and light chain variable region comprise the amino acid sequences selected from the group consisting of SEQ ID NOs:289-290, SEQ ID NOs:3-4, SEQ ID NOs:7-8, SEQ ID NOs:11-12, SEQ ID NOs:15-16, SEQ ID NOs:19-20, SEQ ID NOs:23-24, SEQ ID NOs:27-28, SEQ ID NOs:31-32, SEQ ID NOs:35-36, SEQ ID NOs:39-40, SEQ ID NOs:43-44, SEQ ID NOs:47-48, SEQ ID NOs:51-52, SEQ ID NOs:55-56, SEQ ID NOs:59-60, SEQ ID NOs:63-64, SEQ ID NOs:67-68, SEQ ID NOs:71-72, SEQ ID NOs:75-76, SEQ ID NOs:79-80, SEQ ID NOs:83-84, SEQ ID NOs:87-88, SEQ ID NOs:91-92, SEQ ID NOs:95-96, SEQ ID NOs:99-100, SEQ ID NOs:103-104, SEQ ID NOs:107-108, SEQ ID NOs:111-112, SEQ ID NOs:115-116, SEQ ID NOs:119-120, SEQ ID NOs:123-124, SEQ ID NOs:127-128, SEQ ID NOs:131-132, SEQ ID NOs:135-136, SEQ ID NOs:139-140, SEQ ID NOs:143-144, SEQ ID NOs:147-148, SEQ ID NOs:151-152, SEQ ID NOs:157-158, SEQ ID NOs:163-164, SEQ ID NOs:169-170, SEQ ID NOs:175-176, SEQ ID NOs:181-182, SEQ ID NOs:193-194, SEQ ID NOs:199-200, SEQ ID NOs:205-206, SEQ ID NOs:211-212, SEQ ID NOs:217-218, SEQ ID NOs:223-224, SEQ ID NOs:229-230, SEQ ID NOs:233-234, SEQ ID NOs:237-238, SEQ ID NOs:241-242, SEQ ID NOs:245-246, SEQ ID NOs:249-250, SEQ ID NOs:253-254, SEQ ID NOs:257-258, SEQ ID NOs:261-262, SEQ ID NOs:265-266, SEQ ID NOs:269-270, SEQ ID NOs:273-274, SEQ

ID NOs:277-278, SEQ ID NOs:281-282, SEQ ID NOs:285-286, SEQ ID NOs:293-294, SEQ ID NOs:297-298, SEQ ID NOs:301-302, SEQ ID NOs:305-306, SEQ ID NOs:309-310, SEQ ID NOs:313-314, SEQ ID NOs:317-318, SEQ ID NOs:321-322, SEQ ID NOs:325-326, and SEQ ID NOs:329-330.

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3. The anti-TNFR2 antibody of claim 1, wherein the antibody comprises a heavy chain and a light chain, said heavy chain and a light chain comprise the amino acid sequences selected from the group consisting of SEQ ID NOs: 438 and 292, SEQ ID NOs: 291-292, SEQ ID NOs:235-236, SEQ ID NOs:239-240, SEQ ID NOs:243-244, SEQ ID NOs:247-248, SEQ ID NOs:251-252, SEQ ID NOs:255-256, SEQ ID NOs:259-260, SEQ ID NOs:263-264, SEQ ID NOs:267-268, SEQ ID NOs:271-272, SEQ ID NOs:275-276, SEQ ID NOs:279-280, SEQ ID NOs:283-284, SEQ ID NOs:287-288, SEQ ID NOs:295-296, SEQ ID NOs:299-300, SEQ ID NOs:303-304, SEQ ID NOs:307-308, SEQ ID NOs:311-312, SEQ ID NOs:315-316, SEQ ID NOs:319-320, SEQ ID NOs:323-324, SEQ ID NOs:327-328, SEQ ID NOs:331-332, SEQ ID NOs 432 and 260, SEQ ID NOs: 433 and 304, SEQ ID NOs: 434 and 308, SEQ ID NOs: 434 and 308, SEQ ID NOs: 435 and 236, SEQ ID NOs: 436 and 244, SEQ ID NOs: 437 and 284, and SEQ ID NOs: 439 and 296.
4. The anti-TNFR2 antibody of any of claims 1, 2, or 3, wherein the antibody is an IgG, a Fv, a scFv, a Fab, a F(ab')₂, a minibody, a diabody, a triabody, a nanobody, a bispecific antibody, or a single domain antibody.
5. The anti-TNFR2 antibody of claim 4, wherein said IgG is IgG1, IgG2, IgG3, or IgG4.
6. The anti-TNFR2 antibody of claim 1, wherein the antibody agonizes TNFR2.
7. The anti-TNFR2 antibody of claim 6, wherein the antibody agonizes TNFR2 in an Fc independent manner.
8. The anti-TNFR2 antibody of claim 1, wherein the antibody has an EC₅₀ binding measurement of about 0.05-100 nM.
9. The anti-TNFR2 antibody of claim 1, wherein the antibody has an EC₅₀ functional agonism

measurement of about 0.05-100 nM.

10. The anti-TNFR2 antibody of claim 1, wherein the antibody activates signaling through TNFR2 at a level of at least 80% as compared to signaling activated by TNF.
- 5 11. The anti-TNFR2 antibody of claim 1, wherein the antibody activates signaling through TNFR2 at a level of at least 95% as compared to signaling activated by TNF.
- 10 12. A composition comprising the anti-TNFR2 antibody of any one of claims 1-3 and a pharmaceutically acceptable carrier.
13. An isolated polynucleotide sequence encoding the anti-TNFR2 antibody of any of claims 1-3.
- 15 14. A vector comprising the polynucleotide sequence of claim 13.
15. A host cell comprising the vector of claim 14.
- 20 16. A method of modulating activities or functions of regulatory T cells in a subject, comprising the step of administering to the subject a composition comprising an effective amount of the anti-TNFR2 antibody of any one of claims 1-3.
17. The method of claim 16, wherein the regulatory T cells are CD4⁺CD25⁺Foxp3⁺.
- 25 18. The method of claim 16, wherein the method stimulates proliferation of the regulatory T cells.
19. The method of claim 16, wherein the method activates said regulatory T cells.
- 30 20. The method of claim 16, wherein the method modulates immune responses mediated by said regulatory T cells.
21. A method of modulating activities or functions of myeloid-derived suppressor cells

(MDSCs) in a subject, comprising the step of administering to the subject a composition comprising an effective amount of the anti-TNFR2 antibody of claim 1-3.

22. The method of claim 21, wherein the method stimulates proliferation of the MDSCs.
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23. The method of claim 21, wherein the method activates said MDSCs.
24. A method of treating a disease in a subject, comprising the step of administering to the subject a composition comprising an effective amount of the anti-TNFR2 antibody of any
- 10 of claims 1-3.
25. The method of claim 24, wherein the disease is a cancer, an autoimmune disease, GvHD, a viral infection, or a bacterial infection.