Claims

1. An isolated antibody that binds to CD47, wherein the antibody has a modified IgG constant region comprising one or more substitutions compared to SEQ ID NO: 1 that results in a reduced FcγR binding affinity as compared to a corresponding anti-CD47 antibody with a wildtype IgG1 isotype, wherein the antibody causes a reduced level of platelet depletion after administration compared to the corresponding anti-CD47 antibody with a wildtype IgG1 isotype platelet depletion after administration.

2. The antibody of claim 1, and wherein the antibody is an IgG isotype selected from the group consisting of IgG1 isotype, IgG2 isotype, IgG3 isotype, andor IgG4 isotype.

32. The antibody of claim 21, wherein the IgG isotype is a human IgG isotype.

43. The antibody of claim 32, wherein the antibody comprises a N297A mutation.

54. The antibody of any one of claims 21-43, wherein the antibody is a human IgG1 isotype.

65. The antibody of claim 54, wherein the antibody comprises L235E, L235A, and/or L234A.

7. The antibody of any one of claims 2-4, wherein the antibody is a human IgG2 isotype.

8. The antibody of any one of claims 2-4, wherein the antibody is a human IgG3 isotype.

9. The antibody of claim 8, wherein the antibody comprises a R435H mutation.

106. The antibody of any one of claims 21-43, wherein the antibody is a human IgG4 isotype.

117. The antibody of claim 106, wherein the antibody comprises a S228P mutation (IgG4P).

128. The antibody of claim 10 6 or 117, wherein the antibody comprises a L235E mutation.

139. The antibody of claim 128, wherein the antibody comprises a S228P and a L235E mutation (IgG4PE).

1410. The antibody of any one of claims 1-139, wherein the antibody does not cause a significant level of agglutination of red blood cells.

~~15~~11. The antibody of any one of claims 1-~~14~~10, wherein the antibody prevents CD47 from interacting with signal-regulatory-protein α (SIRPα).

~~16~~12. The antibody of any one of claims 1-~~15~~11, wherein the antibody promotes macrophage-mediated phagocytosis of a CD47-expressing cell.

~~17~~13. The antibody of any one of claims 1-~~16~~12, wherein the antibody is chimeric or humanized.

~~18~~14. The antibody of any one of claims 1-~~17~~13, wherein the CD47 is human CD47.

~~19~~15. The antibody of any one of claims 1-~~18~~14, wherein the corresponding anti-CD47 antibody with a wildtype IgG1 isotype has a wildtype human IgG1 isotype.

~~20. The antibody of any one of claims 1-19, wherein the antibody binds to CD47 in a head to side orientation, wherein a VH chain of the antibody is positioned near the membrane of a CD47 expressing cell, and wherein a VL chain of the antibody occludes a SIRPα binding site on CD47.~~

~~21. The antibody of any one of claims 1-19, wherein the antibody binds to CD47 in a head to side orientation, wherein a VL chain of the antibody is positioned near the membrane of a CD47 expressing cell, and wherein a VH chain of the antibody occludes a SIRPα binding site on CD47.~~

~~22~~16. A pharmaceutical composition comprising the antibody of any one of claims 1-~~21~~15 and a carrier.

~~23~~17. Use of the antibody of any one of claims 1-~~21~~15, or the pharmaceutical composition of claim ~~22~~16, in the manufacture of a medicament for the treatment of cancer in a subject.

~~24~~18. The use of claim ~~23~~17, wherein the subject is a human.

~~25~~19. The use of claim ~~23~~17 or claim ~~24~~18, wherein the use is in combination with a second therapy comprising chemotherapy.

~~26~~20. The use of any one of claim ~~23~~17-~~25~~19, wherein the antibody is to be administered to the subject at a dose of at least 10 mg/kg.

~~27~~21. The use of any one of claims ~~23~~17-~~26~~20, wherein the antibody is to be administered to the subject at a dose of at least 30 mg/kg.

~~28~~22. The antibody of any one of claims 1-~~21~~15, or the pharmaceutical composition of claim ~~22~~16, for use in therapy.