

CLAIMS

What is claimed is:

1. An isolated antibody that binds to CD40L and that comprises a light chain and a heavy chain, wherein
 - (i) the light chain comprises a light chain variable region comprising an amino acid sequence having at least 95% sequence identity with SEQ ID NO:1;
 - (ii) the heavy chain comprises a variable heavy chain region and an Fc region wherein
 - a) the heavy chain variable region comprises an amino acid sequence having at least 95% sequence identity with SEQ ID NO:2; and
 - b) the Fc region comprises an amino acid sequence having at least 95% sequence identity with SEQ ID NO:3 wherein the Fc region comprises one or a combination of substitutions selected from the group consisting of C11S, C14S, and P23S.
2. The isolated antibody according to claim 1, wherein the Fc region further comprises the amino acid substitution C5S.
3. The isolated antibody according to claim 1 or claim 2, wherein the light chain variable region comprises an amino acid sequence having at least 98% sequence identity with SEQ ID NO:1 .
4. The isolated antibody according to any one of claims 1-3, wherein the light chain variable region does not comprise the substitution T33W, S26D, or Q27E.
5. The isolated antibody according to any one of claims 1-4, wherein the light chain variable region comprises the substitution R28K.
6. The isolated antibody according to any one of claims 1-3, wherein the light chain variable region comprises the amino acid sequences ISCRASQRVSSSTYSYMH (SEQ ID NO:15), YASNLES (SEQ ID NO:16) , and QHSWEIPPT (SEQ ID NO:17).
7. The isolated antibody according to claim 1 or claim 2, wherein the light chain variable region comprises the amino acid sequence of SEQ ID NO:1.
8. The isolated antibody according to any one of claims 1-7, wherein the heavy chain variable region comprises an amino acid sequence having at least 98% sequence identity with SEQ ID NO:2.
9. The isolated antibody according to any one of claims 1-8, wherein the heavy chain variable region does not comprise the substitution T30H, Y33W, or S54N.
10. The isolated antibody according to any one of claims 1-9, wherein the heavy chain variable region comprises the substitution K74R.
11. The isolated antibody according to any one of claims 1-9, wherein the heavy chain variable region comprises the amino acid sequences SYMY (SEQ ID NO:18), EINPSNGDTNFNEKFKS (SEQ ID NO:19), and SDGRNDMDS (SEQ ID NO:20).

12. The isolated antibody according to any one of claims 1, 2 or 7, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:2.
13. The isolated antibody according to claim 1, wherein
 - the light chain variable region comprises the amino acid sequence of SEQ ID NO:1.
 - the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:2; and
 - the Fc region comprises the amino acid sequence of SEQ ID NO:4.
14. The isolated antibody according to claim 1, wherein
 - the light chain variable region consists of the amino acid sequence of SEQ ID NO:1;
 - the heavy chain variable region consists of the amino acid sequence of SEQ ID NO:6;and
 - the Fc region consists of the amino acid sequence of SEQ ID NO:4.
15. The isolated antibody according to claim 1 wherein
 - the light chain variable region comprises the amino acid sequence of SEQ ID NO:5;
 - the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:2; and
 - the Fc region comprises the amino acid sequence of SEQ ID NO: 4.
16. The isolated antibody according to claim 1 wherein
 - the light chain variable region comprises the amino acid sequence of SEQ ID NO:5;
 - the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 6;and
 - the Fc region comprises the amino acid sequence of SEQ ID NO:4.
17. The isolated antibody according to claim 1, wherein the light chain consists of the amino acid sequence of SEQ ID NO:7 and the heavy chain consists of the amino acid sequence of SEQ ID NO:9.
18. The isolated antibody according to claim 1, wherein the light chain consists of the amino acid sequence of SEQ ID NO:7 and the heavy chain consists of the amino acid sequence of SEQ ID NO:13.
19. The isolated antibody according to claim 1, wherein the light chain consists of the amino acid sequence of SEQ ID NO: 11 and the heavy chain consists of the amino acid sequence of SEQ ID NO:9.
20. The isolated antibody according to claim 1, wherein the light chain consists of the amino acid sequence of SEQ ID NO:11 and the heavy chain consists of the amino acid sequence of SEQ ID NO:13.
21. The isolated antibody according to any one of claim 1-20, wherein the antibody is stable at 37°C for a period of at least 12 hours.

22. The isolated antibody according to any one of claim 1-21, wherein the antibody is modified to reduce immunogenicity.
23. A method for treating a subject with a CD40L-associated disease or disorder comprising administering to the subject a therapeutically effective amount of an antibody according to any one of claims 1-22.
24. A method for treating a subject with a neurodegenerative or neuromuscular disease or disorder; an inflammatory or immune disease or disorder; or an autoimmune disease, comprising administering to the subject a therapeutically effective amount of an antibody according to any one of claims 1-22.
25. The method according to claim 24, wherein the disease or disorder is an autoimmune disease, selected from the group consisting of systemic lupus erythematosus, type-1 diabetes, myasthenia gravis, inflammatory bowel disease, immune thrombocytopenic purpura and rheumatoid arthritis.
26. The method according to claim 24, wherein the disease or disorder is an inflammatory or immune disease or disorder selected from the group consisting of colitis, drug induced lupus nephritis, graft versus host disease, transplant rejection and atherosclerosis.
27. The method according to claim 24, wherein the disease or disorder is a neurodegenerative disorder, a neuromuscular disorder selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, Amyotrophic Lateral Sclerosis, Multifocal Motor Neuropathy, Primary Lateral Sclerosis, Spinal Muscular Atrophy, Kennedy's Disease, or Spinocerebellar Ataxia.
28. The method according to claim 27, wherein the disorder is Amyotrophic Lateral Sclerosis.
29. A method of inhibiting an immune response in a subject comprising administering to the subject a therapeutically effective amount of an antibody according to any one of claims 1-22.
30. The method of claim 25, wherein the immune response is graft vs. host disease, or organ transplant rejection.
31. The method according to any one of claim 23-30, wherein the antibody is administered in combination with another therapeutic agent.
32. The method according to claim 31, wherein the antibody is administered in combination with a compound that blocks the interaction between CD28 and CD86 or between CD28 and CD80.
33. The method according to claim 32, wherein the compound that blocks the interaction between CD28 and CD86 or between CD28 and CD80 is a CTLA4-Ig fusion protein.
34. The method according to claim 33, wherein the compound that blocks the interaction between CD28 and CD86 or between CD28 and CD80 is abatacept or belatacept or galiximab.