

of SEQ ID NOs: 146-156. In some examples, the Fc region comprises an amino acid substitution at positions E430G, L243A, L235A, and P331S, wherein the numbering of the residue position is according to EU numbering. In some examples, the Fc region comprises an amino acid substitution at positions E430G and P331S, wherein the numbering of the residue position is according to EU numbering. In some examples, the Fc region comprises an amino acid substitution at positions E430G and K322A, wherein the numbering of the residue position is according to EU numbering. In some examples, the Fc region comprises an amino acid substitution at positions E430G, A330S, and P331S, wherein the numbering of the residue position is according to EU numbering. In some examples, the Fc region comprises an amino acid substitution at positions E430G, K322A, A330S, and P331S, wherein the numbering of the residue position is according to EU numbering. In some examples, the Fc region comprises an amino acid substitution at positions E430G, K322A, and A330S, wherein the numbering of the residue position is according to EU numbering. In some examples, the Fc region comprises an amino acid substitution at positions E430G, K322A, and P331S, wherein the numbering of the residue position is according to EU numbering. In some examples, the Fc region increases clustering without activating complement as compared to a corresponding antibody comprising an Fc region that does not comprise the amino acid substitutions. In some examples, the antibody induces one or more activities of a target specifically bound by the antibody. In some examples, the antibody binds to TREM2.

[0028a] In one aspect, the present disclosure refers to an antibody comprising an Fc region, wherein the antibody comprises an amino acid substitution at position E430G and one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: L234F, L235A, L235E, S267E, K322A, L328F, A330S, P331S, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering.

[0029] It is to be understood that one, some, or all of the properties of the various examples described herein may be combined to form other examples of the present disclosure. These and other examples of the disclosure will become apparent to one of skill in the art. These and other examples of the disclosure are further described by the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0030] **FIG. 1A** shows increased agonistic activity of Fc variant anti-TREM2 antibodies.

Luciferase activity after 6h culture with Fc variants of an anti-TREM2 antibody. **FIG. 1B** shows increased agonistic activity of Fc variant anti-TREM2 antibodies. Luciferase activity after 6hr co-culture of Fc variant antibodies with BWZ reporter cells and THP-1 cells in 1:1 ratio.

[0031] **FIG. 2A** shows C3b deposition induced by Fc variant anti-TREM2 antibodies. Fold change of C3b deposition on HEK expressing TREM2 cell line by AL2p Fc variants over human IgG1 isotype control antibody at 10 µg/mL. **FIG. 2B** shows C3b deposition induced by Fc variant anti-TREM2 antibodies. Fold change of C3b deposition by AL2p affinity matured variants with the listed Fc mutations over their parental IgG1 Fc variant.

[0032] **FIG. 3A** shows increased activity of soluble anti-TREM2 antibodies. **FIG. 3B** shows increased activity of plate bound anti-TREM2 antibodies. **FIG. 3C** shows reporter activity of affinity matured anti-TREM2 antibodies plate bound at 5 µg/ml (grey bars) compared to parental humanized