ENGINEERED PD-1 ANTIBODIES AND USES THEREOF

CROSS REFERENCE

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/281,404, filed November 19, 2021, which is incorporated herein by reference in its entirety.

REFERENCE TO A SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on November 7, 2022, is named 56270_718601_SL.xml and is 19,479 bytes in size.

SUMMARY

[0003] Disclosed herein, in some aspects, is a method of suppressing an immune cell that expresses Programmed death 1 (PD-1), comprising contacting the immune cell with an antibody that specifically binds to PD-1 and agonizes PD-1 signaling in the immune cell, wherein the antibody comprises an Fc region that comprises an amino acid substitution, and wherein the amino acid substitution results in reduced antibody-dependent cellular cytotoxicity (ADCC) against a PD-1 expressing regulatory T cell in the subject compared to a parent molecule that lacks the amino acid substitution, and wherein the antibody has the same or higher agonistic effect on PD-1 signaling in the immune cell compared to the parent molecule.

[0004] Disclosed herein, in some aspects, is a method of suppressing an ımmune cell that expresses Programmed death 1 (PD-1), comprising contacting the immune cell with an antibody that specifically binds to PD-1 and that enhances interaction of the PD-1 on the surface of the immune cell with PD-L1. In some cases, the antibody comprises an Fc region, and wherein the Fc region comprises an amino acid substitution. In some cases, the amino acid substitution results in reduced antibody-dependent cellular cytotoxicity (ADCC) against a PD-1 expressing regulatory T cell in the subject compared to a parent molecule that lacks the amino acid substitution, and wherein the antibody has the same or higher agonistic effect on PD-1 signaling in the immune cell compared to the parent molecule.

[0005] In some embodiments of the method, the ADCC against the PD-1 expressing regulatory T cell is reduced as determined by a natural killer cell activation assay as described in Example 7.

[0006] In some embodiments of the method, the antibody does not lead to significant ADCC against the PD-1 expressing regulatory T cell, as determined by a natural killer cell activation assay as described in Example 7.