CLAIMS

We claim:

1. A method for producing an antibody that binds to KIR2DLI, KIR2DL2, and/or KIR2DL3 and potentiates the cytotoxic activity of, and thereby activates, natural killer 244 (NK) cells by blocking or neutralizing NK cell inhibition mediated by a KIR2DL1, KIR2DL2, and/or KIR2DL3 polypeptide expressed on NK cells for the treatment of an inflammatory disorder mediated by T cells or an autoimmune disorder mediated by T cells, said method comprising the steps of: (a) immunizing a non-human mammal with an immunogen comprising a KIR2DL 1, KIR2DL2, and/or KIR2DL3 polypeptide; (b) selecting antibodies from said immunized mammal, wherein said antibodies bind to said KIR2DL1, KIR2DL2 and/or KIR2DL3 polypeptide, and (c) selecting antibodies of (b) that potentiate NK cell-mediated elimination of T cells.

2. A method for producing an antibody that binds to KIR2DL1, KIR2DL2, and/or KIR2DL3 and potentiates the cytotoxic activity of, and thereby activates, natural killer (NK) cells by blocking or neutralizing NK cell inhibition mediated by a KIR 2 DL 1, KIR2DL2, and/or KIR2DL3 polypeptide expressed on NK cells for the treatment of an inflammatory disorder mediated by T cells or an autoimmune disorder mediated by T cells comprising providing a library of antibodies by phage display technology, wherein said antibodies bind to said KIR2DL1, KIR2DL2, and/or KIR2DL3 polypeptide, and selecting antibodies that potentiate the elimination or depletion of T cells by NK cells.

3. Use of an antibody or an antigen-binding fragment thereof that binds to KIR2DL1, KIR2DL2, and/or KIR2DL3, and potentiates the cytotoxic activity of, and thereby activates, natural killer (NK) cells by blocking or neutralizing NK cell inhibition mediated by a KIR2DL1, KIR2DL2, and/or KIR2DL3 polypeptide expressed on NK cells, in the manufacture of a pharmaceutical composition for the treatment of an autoimmune disorder mediated by T cells in an individual, wherein the activated NK cells reduce the number of T cells involved in mediating the autoimmune disorder.

4. The use according to claim 3, wherein the autoimmune disorder is selected from acute sinusitis, chronic sinusitis, Addison's disease, autoimmune hepatitis, Behget's disease, celiac disease, chronic active hepatitis, contact dermatitis, ulcerative colitis, Crohn's disease, dermatomyositis, eczema, Goodpasture's syndrome, Guillain-Barre syndrome, Hashimoto's encephalitis, Hashimoto's thyroiditis, juvenile diabetes, juvenile onset (Type I) diabetes mellitus, multiple sclerosis (MS), spino-optical MS, opsoclonus myoclonus syndrome (OMS), paraneoplastic cerebellar degeneration, pernicious anemia, polymyositis, primary biliary cirrhosis, rheumatoid arthritis, sarcoidosis, scleroderma, lupus erythematosus, and temporal arteritis/giant cell arteritis.

5. The use according to claim 3 or 4, wherein the antibody or antigen-binding fragment thereof:

   (i) comprises a light chain CDR1 having the amino acid sequence corresponding to residues 24-34 of SEQ ID NO:1; a light chain CDR2 having the amino acid sequence corresponding to residues 50-56 of SEQ ID NO:1; a light chain CDR3 having the amino acid sequence corresponding to residues 89-97 of SEQ ID NO:1; a heavy chain CDR1 having the amino acid sequence corresponding to residues 31-35 of SEQ ID NO:2; a heavy chain CDR2 having the amino acid sequence corresponding to residues 50-65 of SEQ ID NO:2; and a heavy chain CDR3 having the amino acid sequence corresponding to residues 99-112 of SEQ ID NO:2;

   (ii) comprises a light chain CDR1 having the amino acid sequence corresponding to residues 24-34 of SEQ ID NO:3; a light chain CDR2 having the amino acid sequence corresponding to residues 50-56 of SEQ ID NO:3; a light chain CDR3 having the amino acid sequence corresponding to residues 89-97 of SEQ ID NO:3; a heavy chain CDR1 having the amino acid sequence corresponding to residues 31-35 of SEQ ID NO:4; a heavy chain CDR2 having the amino acid sequence corresponding to residues 50-66 of

SEQ ID NO:4; and a heavy chain CDR3 having the amino acid sequence corresponding to residues 99-113 of SEQ ID NO:4;

(iii) comprises a variable light chain region having the amino acid sequence set forth in SEQ ID NO:1, and a variable heavy chain region having the amino acid sequence set forth in SEQ ID NO:2;

(iv) comprises a variable light chain region having the amino acid sequence set forth in SEQ ID NO:3, and a variable heavy chain region having the amino acid sequence set forth in SEQ ID NO:4;

(v) comprises a light chain having the amino acid sequence set forth in SEQ ID NO:5, and a heavy chain having the amino acid sequence set forth in SEQ ID NO:6;

(vi) binds to an epitope within a region of KIR2DL1 and/or KIR2DL2/3 having the amino acid sequence set forth in SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, or SEQ ID NO:24;

(vii) binds to KIR2DL1 within a region defined by at least one of the amino acid residues selected from the group consisting of residues 105, 106, 107, 108, 109, 110, 111, 127, 129, 130, 131, 132, 133, 134, 135, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 181, and 192 of SEQ ID NO:7;

(viii) binds to KIR2DL2/3 within a region defined by at least one of the amino acid residues selected from the group consisting of residues 105, 106, 107, 108, 109, 110, 111, 127, 129, 130, 131, 132, 133, 134, 135, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 181, and 192 of SEQ ID NO:8 or SEQ ID NO:9;

(ix) has an affinity for KIR2DL1, KIR2DL2 and/or KIR2DL3 of at least about 10^7 to about 10^{10} M^{-1}, preferably of at least about 10^8 to about 10^9 M^{-1};

(x) binds to KIR2DL1, KIR2DL2 and/or KIR2DL3 with a disassociation constant of less than about 100 nM;

(xi) cross-reacts with KIR2DL1 and KIR2DL2/3; KIR2DL1, KIR2DL2/3 and KIR2DS4; or KIR2DL1 and KIR2DL2/3 but not KIR2DS4;

(xii) is selected from DF200, 1-7F9, and NKVSF1;

(xiii) is to be administered as a monotherapy; or

(xiv) is to be administered in combination with a second therapeutic agent.