

We claim:

1. An immuno-suppression refractory protein or polypeptide comprising the amino acid residue sequence of SEQ ID NO: 3, wherein one, two, or three amino acid residues in said sequence are substituted with an amino acid residue different than shown in SEQ ID NO: 3, wherein the one, two, or three substituted amino acid residues reduce or eliminate binding of the immuno-suppression refractory protein or polypeptide to an immuno-suppressive protein, relative to the immuno-suppression refractory protein or polypeptide without the one, two, or three amino acid substitutions.
2. The immuno-suppression refractory protein or polypeptide of claim 1 which is a full-length antibody.
3. The immuno-suppression refractory protein or polypeptide of claim 1 which is a bispecific antibody.
4. The immuno-suppression refractory protein or polypeptide of claim 1 wherein the immuno-suppressive protein is CA125/MUC16.
5. The immuno-suppression refractory protein or polypeptide of claim 1 selected from the group consisting of:
 - a. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 5;
 - b. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 8;
 - c. T an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 10;
 - d. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 12;
 - e. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 14;
 - f. comprises an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 16;
 - g. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 18;
 - h. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 20;

- i. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 22;
 - j. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 24;
 - k. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 26;
 - l. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 28;
 - m. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 30;
 - n. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 32;
 - o. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 34;
 - p. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 36;
 - q. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 38; and
 - r. an antibody containing a light chain according to SEQ ID NO: 6 and a heavy chain comprising SEQ ID: 40.
6. The immuno-suppression refractory protein or polypeptide of claim 1 which is a protein that consists of an immunoglobulin light chain and an immunoglobulin heavy chain of an IgG isotype antibody.
 7. The immuno-suppression refractory protein or polypeptide of claim 1 which is a full length IgG isotype antibody.
 8. The immuno-suppression refractory protein or polypeptide of claim 1 which is an antigen-binding fragment or Fab domain of an IgG isotype antibody.
 9. The immuno-suppression refractory protein or polypeptide of claim 1 wherein the amino acid residues are selected from positions 102, 103, 107, 108, 109, 122, 130, 131, 134, 136, 151, 161, 167, 169, 189, 196, 201, and 214 of rituximab IgG1 heavy chain as shown in SEQ ID NO: 47.
 10. The immuno-suppression refractory protein or polypeptide of claim 1 which binds to CD20 with an affinity/Kd that is > 1 nM or < 400 nM.
 11. The immuno-suppression refractory protein or polypeptide of claim 1 which binds to CD20 with an affinity/Kd that is > 10 nM or < 50 nM.

12. The immuno-suppression refractory protein or polypeptide of claim 1 which binds to CD20 with an affinity that is $\pm 50\%$ of the affinity/ K_d of the immuno-suppression refractory protein or polypeptide comprising the amino acid residue sequence of SEQ ID NO: 3 for CD20.
13. The immuno-suppression refractory protein or polypeptide of claim 1 wherein the amino acid residues are selected from positions in region CDR3 of rituximab heavy chain as shown in SEQ ID NO: 47.
14. The immune-suppression refractory protein or polypeptide of claim 1 wherein the amino acid residues are selected from positions in framework region 4 of rituximab as shown in SEQ ID NO: 47.
15. A nucleic acid vector encoding the immuno-suppression refractory protein or polypeptide of claim 1.
16. A polynucleotide encoding the immuno-suppression refractory protein or polypeptide of claim 1.
17. A stable cell line comprising the nucleic acid vector of claim 15 and expressing the immuno-suppression refractory protein or polypeptide.
18. A method to treat a patient with a disease who expresses an elevated level of CA125 compared to a population of healthy humans, comprising:
 - administering to the patient the immuno-suppression refractory protein or polypeptide of claim 1.
19. The method of claim 18 wherein the disease is cancer.
20. The method of claim 18 wherein the disease is an inflammatory disease.
21. The method of claim 19 wherein the cancer is selected from the group consisting of Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, Follicular Lymphoma, Large Cell Lymphoma, Diffuse Large B-cell Lymphoma, Chronic Lymphocytic Leukemia, and multiple myeloma.
22. A method of treating a cancer patient or a patient with an inflammatory disease, comprising:
 - administering to the cancer patient or the patient with an inflammatory disease a polypeptide selected from the group consisting of:

- (a) a full-length human complement proprotein C3B or C4B,
 - (b) a naturally occurring, proteolytic fragment of human complement proprotein C3B or C4B that is capable of binding IgG, or
 - (c) a portion of human complement proprotein C3B or C4B that is capable of binding IgG.
23. The method of claim 22 wherein the polypeptide comprises amino acid sequences shown in SEQ ID NO: 1 or SEQ ID NO: 2.
24. The method of claim 22 wherein the cancer patient or the patient with inflammatory disease expresses elevated CA125 levels compared with a control, normal human population.
25. The method of claim 22 wherein the polypeptide is administered in combination with an anti-CD20 antibody.
26. The method of claim 25 wherein the anti-CD20 antibody is rituximab.
27. The method of claim 22 wherein the patient is a cancer patient, and further comprising:
- administering to the cancer patient an antibody that targets a tumor, wherein humoral immune responses mediated by the antibody are suppressed by CA125 in the absence of the polypeptide.
28. The method of claim 22 wherein the patient is a cancer patient and the patient has a cancer selected from the group consisting of Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, Follicular Lymphoma, Large Cell Lymphoma, Diffuse Large B-cell Lymphoma, Chronic Lymphocytic Leukemia, and multiple myeloma.
29. A combination comprising (a) an anti-CD20 antibody and (b) full-length complement proprotein C3B or C4B, a naturally occurring, proteolytic fragment of complement proprotein C3B or C4B that is capable of binding IgG, or a portion of complement proprotein C3B or C4B that is capable of binding IgG.
30. The combination of claim 29 wherein the anti-CD20 antibody is rituximab.
31. The combination of claim 29 which comprises the naturally occurring, proteolytic fragment of complement proprotein C3B or C4B, wherein the naturally occurring, proteolytic fragment of complement proprotein C3B or C4B is selected from the group

consisting of C3B residues 23-1663, C3B residues 23-667, C3B residues 569-667, C3B residues 672-1663, C3B residues 672-748, C3B residues 672-747, C3B residues 749-1663, C3B residues 749-954, C3B residues 955-1303, C3B residues 955-1001, C3B residues 1002-1303, C3B residues 1304-1320, C3B residues 1321-1663, C4B residues 20-675, C4B residues 676-679, C4B residues 680-1446, C4B residues 680-756, C4B residues 757-1446, C4B residues 957-1336, C4B residues 1447-1453, and C4B residues 1454-1744.

32. A human cancer cell line that expresses human proteins CA125 and CD20.
33. The human cancer cell line of claim 32 that is a human ovarian cancer cell line.
34. The human cancer cell line of claim 33 which is made by transducing cells of cell line OVCAR3 with an expression vector encoding CD20.
35. A method of screening candidate antibodies that bind to CD20, comprising:
 - a. contacting a candidate antibody with the human cancer cell line of claim 36; and
 - b. determining antibody dependent cellular cytotoxicity (ADCC) or complement dependent cytotoxicity (CDC) of the human cancer cell line initiated by the candidate antibody.
36. A method for testing and treating a tumor expressing CA125 in a patient, comprising:
 - contacting (a) a body fluid sample isolated from the patient; with
 - (b) an antibody comprising the amino acid sequence of SEQ ID NO: 3;
 - and contacting (a) with (c) an immuno-suppression refractory protein or polypeptide comprising the amino acid residue sequence of SEQ ID NO: 3, wherein one, two, or three amino acid residues in said sequence are substituted with an amino acid residue different than shown in SEQ ID NO: 3, wherein the one, two, or three substituted amino acid residues reduce or eliminate binding of the immuno-suppression refractory protein or polypeptide to an immuno-suppressive protein, relative to the immuno-suppression refractory protein or polypeptide without the one, two, or three amino acid substitutions;
 - and
 - determining that CA125 in the body fluid sample binds to (b) but not (c) and treating the patient with (c); or
 - determining that CA125 in the body fluid sample binds to (b) and/or (c) and treating the patient with full-length complement proprotein C3B or C4B, a naturally occurring,

proteolytic fragment of complement proprotein C3B or C4B that is capable of binding IgG, or a portion of complement proprotein C3B or C4B that is capable of binding IgG.

37. The method of claim 22 or 36 wherein the naturally occurring, proteolytic fragment of complement proprotein C3B or C4B is administered, wherein the naturally occurring, proteolytic fragment of complement protein C3B or C4B is selected from the group consisting of C3B residues 23-1663, C3B residues 23-667, C3B residues 569-667, C3B residues 672-1663, C3B residues 672-748, C3B residues 672-747, C3B residues 749-1663, C3B residues 749-954, C3B residues 955-1303, C3B residues 955-1001, C3B residues 1002-1303, C3B residues 1304-1320, C3B residues 1321-1663, C4B residues 20-675, C4B residues 676-679, C4B residues 680-1446, C4B residues 680-756, C4B residues 757-1446, C4B residues 957-1336, C4B residues 1447-1453, C4B residues 1454-1744.