

CLAIMS

What is claimed is:

1. An isolated antibody or fragment thereof, wherein the antibody or fragment thereof has specificity to a human Lymphocyte Activation Gene-3 (LAG-3) protein, wherein the antibody or fragment thereof comprises a heavy chain variable region comprising heavy chain complementarity determining regions CDRH1, CDRH2, and CDRH3, and a light chain variable region comprising light chain complementarity determining regions CDRL1, CDRL2, and CDRL3, wherein
 - the CDRH1 comprises an amino acid sequence of SEQ ID NO:240;
 - the CDRH2 comprises an amino acid sequence of SEQ ID NO:241;
 - the CDRH3 comprises an amino acid sequence of SEQ ID NO:242;
 - the CDRL1 comprises an amino acid sequence selected from the group consisting of SEQ ID NO:243, SEQ ID NO: 376, and amino acid residues 24-39 of SEQ ID NO: 330;
 - the CDRL2 comprises an amino acid sequence of SEQ ID NO:244; and
 - the CDRL3 comprises an amino acid sequence of SEQ ID NO:245 or 374.
2. The antibody or fragment thereof of claim 1, wherein:
 - the CDRH1 has the amino acid sequence of SEQ ID NO:240;
 - the CDRH2 has the amino acid sequence of SEQ ID NO:241;
 - the CDRH3 has the amino acid sequence of SEQ ID NO:242;
 - the CDRL1 has the amino acid sequence of SEQ ID NO:243;
 - the CDRL2 has the amino acid sequence of SEQ ID NO:244; and
 - the CDRL3 has the amino acid sequence of SEQ ID NO:245.
3. The antibody or fragment thereof of claim 2, wherein the heavy chain variable region comprising an amino acid sequence of SEQ ID NO:238, and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 239.
4. The antibody or fragment thereof of claim 2, wherein the heavy chain variable region comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 251, 252, 258 and 259, and the light chain variable region comprising the amino acid sequence of SEQ ID NO: 260.

5. The antibody or fragment thereof of claim 1, wherein
the CDRH1 comprises the amino acid sequence of SEQ ID NO:240;
the CDRH2 comprises the amino acid sequence of SEQ ID NO:347;
the CDRH3 comprises the amino acid sequence of SEQ ID NO:354;
the CDRL1 comprises the amino acid sequence of amino acid residues 24-39 of SEQ ID NO:330;
the CDRL2 comprises the amino acid sequence of SEQ ID NO:244; and
the CDRL3 comprises the amino acid sequence of SEQ ID NO:374.
6. The antibody or fragment thereof of claim 5, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:329, and the light chain variable region comprises the amino acid sequences of SEQ ID NO:330.
7. The antibody or fragment thereof of claim 1, wherein:
the CDRH1 has the amino acid sequence of SEQ ID NO:240;
the CDRH2 has the amino acid sequence of SEQ ID NO:347;
the CDRH3 has the amino acid sequence of SEQ ID NO:354;
the CDRL1 has the amino acid sequence of SEQ ID NO:376;
the CDRL2 has the amino acid sequence of SEQ ID NO:244; and
the CDRL3 has the amino acid sequence of SEQ ID NO:374.
8. The antibody or fragment thereof of claim 1, wherein the heavy chain variable region comprises one or more amino acid residues selected from the group consisting of:
 - (a) Ala (A) at position 71,
 - (b) Leu (L) at position 69,
 - (c) Lys (K) at position 66,
 - (d) Ala (A) at position 67,
 - (e) Ile (I) at position 48,
 - (f) Ile (I) at position 37,
 - (g) Lys (K) at position 38,
 - (h) Phe (F) at position 91, and
 - (i) Glu (E) at position 1, according to Kabat numbering, and combinations thereof.

9. The antibody or fragment thereof of any one of claims 1-8, wherein the antibody or fragment thereof is for use in a method of treating cancer in a patient in need thereof, comprising administering to the patient the antibody or fragment thereof.

10. The antibody or fragment thereof of claim 9, wherein the cancer is selected from the group consisting of a leukemia, a lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer (colorectal cancer), rectal cancer, bladder cancer, urothelial cancer, lung cancer (non-small cell lung cancer, adenocarcinoma of the lung, squamous cell carcinoma of the lung), bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, gastric cancer, hepatocellular carcinoma, gall bladder cancer, bile duct cancer, esophageal cancer, renal cell carcinoma, thyroid cancer, squamous cell carcinoma of the head and neck (head and neck cancer), testicular cancer, cancer of the endocrine gland, cancer of the adrenal gland, cancer of the pituitary gland, cancer of the skin, cancer of soft tissues, cancer of blood vessels, cancer of brain, cancer of nerves, cancer of eyes, cancer of meninges, cancer of oropharynx, cancer of hypopharynx, cancer of cervix, and cancer of uterus, glioblastoma, meduloblastoma, astrocytoma, glioma, meningioma, gastrinoma, neuroblastoma, melanoma, myelodysplastic syndrome, and a sarcoma.

11. The antibody or fragment thereof of claim 10, wherein the leukemia is selected from the group consisting of systemic mastocytosis, acute lymphocytic (lymphoblastic) leukemia (ALL), T cell – ALL, acute myeloid leukemia (AML), myelogenous leukemia, chronic lymphocytic leukemia (CLL), multiple myeloma (MM), chronic myeloid leukemia (CML), myeloproliferative disorder / neoplasm, myelodysplastic syndrome, monocytic cell leukemia, and plasma cell leukemia; wherein said lymphoma is selected from the group consisting of histiocytic lymphoma and T cell lymphoma, B cell lymphomas, including Hodgkin's lymphoma and non-Hodgkin's lymphoma, low grade/follicular non-Hodgkin's lymphoma (NHL), cell lymphoma (FCC), mantle cell lymphoma (MCL), diffuse large cell lymphoma (DLCL), small lymphocytic (SL) NHL, intermediate grade/follicular NHL, intermediate grade diffuse NHL, high grade immunoblastic NHL, high grade lymphoblastic NHL, high grade small non-cleaved cell NHL, bulky disease NHL, and Waldenstrom's Macroglobulinemia; and wherein said sarcoma is selected from the group consisting of osteosarcoma, Ewing's sarcoma, leiomyosarcoma, synovial sarcoma, alveolar soft part sarcoma, angiosarcoma, liposarcoma, fibrosarcoma, rhabdomyosarcoma, and chondrosarcoma.

12. The antibody or fragment thereof of any one of claims 1-8, wherein the antibody or fragment thereof is for use in a method of treating cancer in a patient in need thereof, comprising:

- (a) treating a T cell, in vitro, with the antibody or fragment thereof; and
- (b) administering the treated T cell to the patient.

13. The antibody or fragment thereof of any one of claims 1-8, wherein the antibody or fragment thereof is for use in a method of treating or inhibiting infection in a patient in need thereof, comprising administering to the patient the antibody or fragment thereof.

14. The antibody or fragment thereof of any one of claims 1-8, wherein the antibody or fragment thereof is for use in a method of detecting expression of LAG3 in a sample, comprising contacting the sample with the antibody or fragment thereof under conditions for the antibody or fragment thereof to bind to the LAG3, and detecting the binding which indicates expression of LAG3 in the sample.