

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a therapeutic anti-leukemia inhibitory factor (LIF) antibody in the manufacture of a medicament for treating cancer in an individual, comprising determining that a level of LIF exceeds a reference level in a biological sample from the individual and determining a protein level of an immunomodulatory molecule exceeds a reference level of the immunomodulatory molecule, wherein the immunomodulatory molecule is selected from CCL7, CCL2, CCL3, and CCL22, and a therapeutic amount of the therapeutic anti-LIF antibody is to be administered to the individual when the level of LIF is greater than the reference level of LIF and the protein level of the immunomodulatory molecule exceeds a reference level of the immunomodulatory molecule, and wherein the therapeutic anti-LIF antibody comprises:
 - a. an immunoglobulin heavy chain complementarity determining region 1 (VH-CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 2 (GFTFSHAW);
 - b. an immunoglobulin heavy chain complementarity determining region 2 (VH-CDR2) comprising the amino acid sequence set forth in SEQ ID NO: 5 (IKAKSDDYAT);
 - c. an immunoglobulin heavy chain complementarity determining region 3 (VH-CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 6 (TCWEWDLDF);
 - d. an immunoglobulin light chain complementarity determining region 1 (VL-CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 10 (QSLLDSDGHTY);
 - e. an immunoglobulin light chain complementarity determining region 2 (VL-CDR2) comprising the amino acid sequence set forth in SEQ ID NO: 12 (SVS); and
 - f. an immunoglobulin light chain complementarity determining region 3 (VL-CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 13 (MQATHAPPYT).
2. The use of claim 1, wherein the therapeutic anti-LIF antibody comprises an immunoglobulin heavy chain variable region comprising at least 85%, 90%, 95%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 15 and an immunoglobulin light chain variable region comprising at least 85%, 90%, 95%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 19.

3. The use of claim 2, wherein the therapeutic anti-LIF antibody comprises an immunoglobulin heavy chain region comprising at least 85%, 90%, 95%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 31, and an immunoglobulin light chain region comprising at least 85%, 90%, 95%, 97%, 98%, 99%, or 100% identity to SEQ ID NO:35.
4. The use of any one of the preceding claims, wherein the therapeutic anti-LIF antibody is an IgG antibody comprising two immunoglobulin heavy chains and two immunoglobulin light chains.
5. The use of any one of claims 1 to 3, wherein the therapeutic anti-LIF antibody is humanized.
6. The use of any one of the preceding claims, wherein determining the level of LIF comprises performing an immunohistochemistry assay.
7. The use of claim 6, wherein the reference level is an IHC-score of 10 to 100.
8. The use of claim 5, wherein determining the level of LIF comprises performing an enzyme linked immunosorbent assay (ELISA), and wherein the ELISA detects electrochemiluminescence.
9. The use of claim 8, wherein the reference level is 4 pg/mL of LIF in an undiluted biological sample from the individual.
10. The use of any one of claims 6 to 9, wherein the reference level of LIF corresponds to the 5th percentile, 10th percentile, 25th percentile, or the 50th percentile of LIF protein expression in human cancer.
11. The use of claim 10, wherein the human cancer is selected from the list consisting of lung cancer, ovarian cancer, kidney cancer, bladder cancer, pancreatic cancer, prostate cancer, genitourinary cancer, gynecologic cancer, gastrointestinal cancer, endocrine system cancer, glioblastoma multiforme, breast cancer, melanoma, colorectal cancer, bile duct cancer, cervical cancer, endometrial cancer, head and neck squamous cell carcinoma, and combinations thereof.
12. The use of claim 11, wherein the human cancer is selected from the list consisting of non-small cell lung cancer, glioblastoma multiforme, epithelial ovarian carcinoma, pancreatic adenocarcinoma, and combinations thereof.
13. The use of any one of the preceding claims, wherein the biological sample comprises plasma or serum.
14. The use of any one of the preceding claims, wherein the biological sample is a tumor biopsy.

15. The use of any one of the preceding claims, wherein a protein level of an immunomodulatory molecule that exceeds a reference level of the immunomodulatory molecule is to be further determined.
16. The use of claim 15, wherein the immunomodulatory molecule is selected from CCL7, CCL2, CCL3, and CCL22.
17. The use of any one of the preceding claims, wherein a protein level of an immunomodulatory molecule that is below a reference level of the immunomodulatory molecule is to be further determined.
18. The use of claim 17, wherein the immunomodulatory molecule is selected from MHCII, CXCL9, CXCL10, CXCR3, and PD-L1.
19. The use of any one of the preceding claims, wherein a level of a Type II macrophage (M2) marker that exceeds a reference level of protein of the Type II macrophage (M2) marker is to be further determined.
20. The use of claim 19, wherein the M2 marker is selected from the list consisting of CD206, CD163, PF4, CTSK, and ARG1.