

toxicity, and the small molecule inhibitors specific for LIF protein have not been reported yet. Only one antibody drug targeting LIF protein is currently in clinical development stage, and its relevant safety and efficacy data have not yet been published.

Therefore, more researches are needed to develop drugs and combination therapies for LIF targets.

Summary of Invention

The invention provides an isolated antibody or antigen-binding fragment specifically binding to LIF and the use thereof in the treatment of diseases.

In one ~~aspect~~respect, the ~~invention~~present disclosure provides an isolated antibody or antigen-binding fragment thereof that binds at an epitope represented by an amino acid sequence TYGPDTSKGKDVQKK(SEQ ID NO: 61) of human LIF protein or at an epitope of the corresponding amino acid sequence of a different mammalian species.

In another aspect, the present disclosure provides an isolated antibody or antigen-binding fragment thereof, comprising:

1) (a) LCDR1 comprising SEQ ID NO: 1, (b) LCDR2 comprising SEQ ID NO: 2, (c) LCDR3 comprising SEQ ID NO: 3, (d) HCDR1 comprising SEQ ID NO: 4, (e) HCDR2 comprising SEQ ID NO: 5, and (f) HCDR3 comprising SEQ ID NO: 6;

2) (a) LCDR1 comprising SEQ ID NO: 1, (b) LCDR2 comprising SEQ ID NO: 2, (c) LCDR3 comprising SEQ ID NO: 3, (d) HCDR1 comprising SEQ ID NO: 4, (e) HCDR2 comprising SEQ ID NO: 45, and (f) HCDR3 comprising SEQ ID NO: 6; or

3) (a) LCDR1 comprising SEQ ID NO: 66, (b) LCDR2 comprising SEQ ID NO: 67, (c) LCDR3 comprising SEQ ID NO: 68, (d) HCDR1 comprising SEQ ID NO: 69, (e) HCDR2 comprising SEQ ID NO: 70, and (f) HCDR3 comprising SEQ ID NO: 71.

In another aspect, the present disclosure provides a nucleotide composition comprising a nucleotide molecule encoding the isolated antibody or antigen-binding fragment thereof as disclosed herein.

In another aspect, the present disclosure provides a vector, comprising the nucleotide composition as disclosed herein.

In another aspect, the present disclosure provides a host cell comprising the vector as disclosed herein.

In another aspect, the present disclosure provides a method of preparing the isolated antibody or antigen-binding fragment thereof as disclosed herein, comprising expressing the antibody or antigen-binding fragment thereof in the host cell as disclosed herein and isolating the antibody or antigen-binding fragment thereof.

In another aspect, the present disclosure provides a pharmaceutical composition comprising a therapeutically effective amount of the isolated antibody or antigen-binding fragment thereof as disclosed herein, and a pharmaceutical acceptable excipient.

In another aspect, the present disclosure provides a reagent for detecting LIF in biological samples comprising the isolated antibody or antigen-binding fragment thereof as disclosed herein.

In another aspect, the present disclosure provides the use of the isolated antibody or antigen-binding fragment thereof as disclosed herein, and/or the pharmaceutical composition as disclosed herein in manufacture of a medicament for inhibiting the expression of LIF and/or blocking the activity of LIF.

In another aspect, the present disclosure provides an *ex vivo* method for detecting the LIF in biological samples comprising (i) obtaining a subject's tissue or liquid sample, (ii) exposing the tissue or liquid sample to the isolated antibody or antigen-binding fragment thereof as disclosed herein or the reagent as disclosed herein; and (iii) comparing the LIF binding to the tissue or liquid sample of (ii) with the LIF binding to a control sample, wherein the increase in the amount of the bound LIF compared with the control sample shows the abnormal level of LIF production, expression or activation.

In another aspect, the present disclosure provides the use of the isolated antibody or antigen-binding fragment thereof as disclosed herein, and/or the pharmaceutical composition as disclosed herein in manufacture of a medicament for treating a disease or condition related to LIF.

In another respect, the invention provides an isolated antibody or antigen-binding fragment thereof, which comprises:

- (a) LCDR1 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 1 or 66, and conservative modifications thereof;
- (b) LCDR2 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 2 or 67, and conservative modifications thereof;
- (c) LCDR3 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 3 or 68, and conservative modifications thereof;
- (d) HCDR1 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 4 or 69, and conservative modifications thereof;
- (e) HCDR2 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 5, 45, or 70, and conservative modifications thereof; and
- (f) HCDR3 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 6 or 71, and conservative modifications thereof.

Optionally, the LCDR1, LCDR2, LCDR3, HCDR1, HCDR2 or HCDR3 has additions, substitutions, deletions and/or insertions of 17 or less amino acids.

In some embodiments, the isolated antibody or antigen-binding fragment thereof comprises:

- (a) LCDR1 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 1, and conservative modifications thereof;
- (b) LCDR2 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 2, and conservative modifications thereof;
- (c) LCDR3 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 3, and conservative modifications thereof;
- (d) HCDR1 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 4, and conservative modifications thereof;
- (e) HCDR2 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 5 or 45, and conservative modifications thereof;
- (f) HCDR3 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 6, and conservative modifications thereof.

Optionally, the LCDR1, LCDR2, LCDR3, HCDR1, HCDR2 or HCDR3 has additions, substitutions, deletions and/or insertions of 17 or less amino acids.

In some embodiments, optionally, the LCDR1, LCDR2, LCDR3, HCDR1, HCDR2 or HCDR3 has additions, substitutions, deletions and/or insertions of 9 or less amino acids.

In some embodiments, optionally, the LCDR1, LCDR2, LCDR3, HCDR1, HCDR2 or HCDR3 has additions, substitutions, deletions and/or insertions of 5 or less amino acids.

In some embodiments, the isolated antibody or antigen-binding fragment thereof comprises:

- 1) (a) LCDR1 comprising SEQ ID NO: 1, (b) LCDR2 comprising SEQ ID NO: 2, (c) LCDR3 comprising SEQ ID NO: 3, (d) HCDR1 comprising SEQ ID NO: 4, (e) HCDR2 comprising SEQ ID NO: 5, and (f) HCDR3 comprising SEQ ID NO: 6;
- 2) (a) LCDR1 comprising SEQ ID NO: 1, (b) LCDR2 comprising SEQ ID NO: 2, (c) LCDR3 comprising SEQ ID NO: 3, (d) HCDR1 comprising SEQ ID NO: 4, (e) HCDR2 comprising SEQ ID NO: 45, and (f) HCDR3 comprising SEQ ID NO: 6; or

In one respect, the invention provides an isolated antibody or antigen-binding fragment thereof comprising a combination of a heavy and a light chain variable region selected from any one of the following (ai) to (eii):

- (ai) a light chain variable region (VL) comprising LCDR1, LCDR2 and LCDR3 that have the same sequence as any one of SEQ ID NO: 7, 11, 15, 19, 46 or 82; and
- (ii) a heavy chain variable region (VH) comprising HCDR1, HCDR2 and HCDR3 that have the same sequence as any one of SEQ ID NO: 23, 27, 31, 48 or 83.

In some embodiments, the isolated antibody or antigen-binding fragment thereof comprises a light and a heavy chain, wherein:

- (I) the light chain comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 9, 13, 17, 21, 37, 39, 50 or 54, and conservative modifications thereof; and
- (II) the heavy chain comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 25, 29, 33, 35, 52 or 56, and conservative modifications thereof.

In some embodiments, the isolated antibody or antigen-binding fragment thereof comprises a light and a heavy chain, wherein:

- (I) the light chain comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 9, 13, 17, 21, 37, 39 or 50, and conservative modifications thereof; and
- (II) the heavy chain comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 25, 29, 33, 35 or 52, and conservative modifications thereof.

In some embodiments, the isolated antibody or antigen-binding fragment thereof comprises a light and a heavy chain, wherein:

- (I) the light chain comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 9, 13, 17 or 21, and conservative modifications thereof; and

nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 75.

In some embodiments, the nucleotide composition comprises:
a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 82 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 83.

In some embodiments, the first nucleic acid sequence [and the second nucleic acid sequence](#) comprises a DNA sequence with at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% identity to the first nucleic acid sequence or the second nucleic acid sequence selected from 1)-15), respectively.

In some embodiments, DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 7 is shown as SEQ ID NO: 8.

In some embodiments, DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 11 is shown as SEQ ID NO: 12.

In some embodiments, DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 15 is shown as SEQ ID NO: 16.

In some embodiments, DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 19 is shown as SEQ ID NO: 20.

In some embodiments, DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 46 is shown as SEQ ID NO: 47.

In some embodiments, DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 74 is shown as SEQ ID NO: 76.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 depicts the binding ability of the LIF antibody of the invention to human LIF protein;

FIG. 2 depicts the binding ability of the LIF antibody of the invention to mouse LIF protein;

FIG. 3 depicts the binding ability of the LIF antibody of the invention to machin LIF protein;

FIG. 4 depicts the affinity of the 38E10E1C11 antibody of the invention binding to the antigen;

FIG. 5 depicts the ability of the 38E10E1C11 antibody of the invention competing with LIFR for binding to human LIF protein;

FIG. 6 depicts the ability of the P36-~~333~~-033 antibody competing with GP130 receptor for binding to human LIF protein;

FIG. 7 depicts the cross-reaction of the 38E10E1C11 antibody and the P36-~~333~~-033 antibody of the invention with the IL-6 family protein;

FIG. 8 depicts that the 38E10E1C11R antibody of the invention recognizes denatured human LIF protein;

Subfigure A in FIG. 9 depicts that the 38E10E1C11 antibody of the invention inhibits the phosphorylation of colon cancer cells (HCT116) induced by human LIF protein;

Subfigure B in FIG. 9 depicts that the 38E10E1C11 antibody of the invention inhibits the phosphorylation of STAT3 in pancreatic cancer cells (KP4) induced by human LIF protein;

FIG. 10 depicts that the 38E10E1C11 antibody of the invention blocks the activation of STAT3 in pancreatic cancer cells KP4 by human LIF secreted by CT26-hLIF cells;

FIG. 11 depicts that the P36-~~333~~-033 antibody of the invention inhibits the phosphorylation of STAT3 in colon cancer cells (HCT116) induced by human LIF protein;

FIG. 12 depicts that the 38E1E1C11 and P36-033 antibodies of the invention reverse the proliferation inhibition of M1 cells caused by LIF;

abbreviated as HCDR, that is, the three CDRs of the VH region can be abbreviated as HCDR1, HCDR2, and HCDR3; the CDRs of the VL region are abbreviated as LCDR, that is, the three CDRs of the VL region can be abbreviated as LCDR1, LCDR2, LCDR3. Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component of the classical complement system (C1q).

The heavy chain of an antibody may or may not contain a terminal lysine (K), or a terminal glycine and lysine (GK). Thus, any of the heavy chain sequences and heavy chain constant region sequences provided herein can end in either GK or ~~GK~~, or lack K or GK, regardless of what the last amino acid of the sequence provides. This is because the terminal lysine and sometimes glycine and lysine are cleaved during expression of the antibody.

Antibodies typically bind specifically to their cognate antigen with high affinity, reflected by a dissociation constant (K_D) of 10^{-7} to 10^{-11} M or less. Any K_D greater than about 10^{-6} M is generally considered to indicate binding nonspecifically. As used herein, an antibody that "binds specifically" to an antigen refers to an antibody that binds to the antigen and substantially identical antigens with high affinity, which means having a K_D of 10^{-7} M or less, preferably 10^{-8} M or less, even more preferably 5×10^{-9} M or less, and most preferably between 10^{-8} M and 10^{-10} M or less, but does not bind with high affinity to unrelated antigens. An antigen is "substantially identical" to a given antigen if it exhibits a high degree of sequence identity to the given antigen, for example, if it exhibits at least 80%, at least 90%, at least 95%, at least 97%, or at least 99% or greater sequence identity to the sequence of the given antigen.

What is claimed is:

1. An isolated antibody or antigen-binding fragment thereof that binds at an epitope represented by an amino acid sequence TYGPDTSGKDVFQKK (SEQ ID NO: 61) of human LIF protein or at an epitope of the corresponding amino acid sequence of a different mammalian species.

2. An isolated antibody or antigen-binding fragment thereof, comprising:

~~(a) LCDR1 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 1 or 66, and conservative modifications thereof;~~

~~(b) LCDR2 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 2 or 67, and conservative modifications thereof;~~

~~(c) LCDR3 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 3 or 68, and conservative modifications thereof;~~

~~(d) HCDR1 comprising an amino acid sequence selected from a group consisting of SEQ ID NOs: 4 or 69, and conservative modifications thereof;~~

~~(e) HCDR2 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 5, 45, or 70, and conservative modifications thereof; and~~

~~(f) HCDR3 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 6 or 71, and conservative modifications thereof.~~

3. The isolated antibody or antigen binding fragment thereof of claim 2, comprising:

~~(a) LCDR1 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 1, and conservative modifications thereof;~~

~~(b) LCDR2 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 2, and conservative modifications thereof;~~

~~(c) LCDR3 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 3, and conservative modifications thereof;~~

~~(d) HCDR1 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 4, and conservative modifications thereof;~~

~~(e) HCDR2 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 5 or 45, and conservative modifications thereof;—~~

~~(f) HCDR3 comprising an amino acid sequence selected from a group consisting of SEQ ID NO: 6, and conservative modifications thereof.~~

~~4. The isolated antibody or antigen binding fragment thereof of claim 2 or 3, comprising:~~

1) (a) LCDR1 comprising SEQ ID NO: 1, (b) LCDR2 comprising SEQ ID NO: 2, (c) LCDR3 comprising SEQ ID NO: 3, (d) HCDR1 comprising SEQ ID NO: 4, (e) HCDR2 comprising SEQ ID NO: 5, and (f) HCDR3 comprising SEQ ID NO: 6;

2) (a) LCDR1 comprising SEQ ID NO: 1, (b) LCDR2 comprising SEQ ID NO: 2, (c) LCDR3 comprising SEQ ID NO: 3, (d) HCDR1 comprising SEQ ID NO: 4, (e) HCDR2 comprising SEQ ID NO: 45, and (f) HCDR3 comprising SEQ ID NO: 6; or

3) (a) LCDR1 comprising SEQ ID NO: 66, (b) LCDR2 comprising SEQ ID NO: 67, (c) LCDR3 comprising SEQ ID NO: 68, (d) HCDR1 comprising SEQ ID NO: 69, (e) HCDR2 comprising SEQ ID NO: 70, and (f) HCDR3 comprising SEQ ID NO: 71.

~~5. The isolated antibody or antigen binding fragment thereof of claim 4, comprising:~~

~~(a) LCDR1 comprising SEQ ID NO: 1, (b) LCDR2 comprising SEQ ID NO: 2, (c) LCDR3 comprising SEQ ID NO: 3, (d) HCDR1 comprising SEQ ID NO: 4, (e) HCDR2 comprising SEQ ID NO: 5, and (f) HCDR3 comprising SEQ ID NO: 6.~~

~~6. The isolated antibody or antigen binding fragment thereof of claim 4, comprising:~~

~~(a) LCDR1 comprising SEQ ID NO: 1, (b) LCDR2 comprising SEQ ID NO: 2, (c) LCDR3 comprising SEQ ID NO: 3, (d) HCDR1 comprising SEQ ID NO: 4, (e) HCDR2 comprising SEQ ID NO: 45, and (f) HCDR3 comprising SEQ ID NO: 6.~~

~~7. The isolated antibody or antigen binding fragment thereof of claim 4, comprising:~~

~~(a) LCDR1 comprising SEQ ID NO: 66, (b) LCDR2 comprising SEQ ID NO: 67, (c) LCDR3 comprising SEQ ID NO: 68, (d) HCDR1 comprising SEQ ID NO: 69, (e) HCDR2 comprising SEQ ID NO: 70, and (f) HCDR3 comprising SEQ ID NO: 71.~~

~~8. The isolated antibody or antigen binding fragment thereof of any one of claims 2 to 7, comprising:~~

~~(i) a light chain variable region (VL) comprising an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 7, 11, 15, 19, 46, 74 or 82, and conservative modifications thereof; and~~

~~(ii) a heavy chain variable region (VH) comprising an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 23, 27, 31, 48, 75 or 83, and conservative modifications thereof.~~

~~9. The isolated antibody or antigen binding fragment thereof of any one of claims 2 to 8, comprising:~~

~~(i) a light chain variable region (VL) comprising an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NOs: 7, 11, 15, 19 or 46, and conservative modifications thereof; and~~

~~(ii) a heavy chain variable region (VH) comprising an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 23, 27, 31 or 48, and conservative modifications thereof.~~

~~10. The isolated antibody or antigen binding fragment thereof of any one of claims 2 to 9, wherein the isolated antibody comprises a light chain variable region comprising an amino acid sequence with at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to the light chain variable region selected from (i) in claim 8 or 9, and a heavy chain variable region comprising an amino acid sequence with at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to the heavy chain variable region selected from (ii) in claim 8 or 9.~~

~~11. The isolated antibody or antigen-binding fragment thereof of any one of claims 2 to 10~~claim 2, comprising:

1) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 7, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 23;

- 2) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 7, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 27;
- 3) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 7, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 31;
- 4) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 11, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 23;
- 5) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 11, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 27;
- 6) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 11, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 31;
- 7) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 15, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 23;
- 8) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 15, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 27;

- 9) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 15, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 31;
- 10) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 19, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 23;
- 11) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 19, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 27;
- 12) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 19, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 31;
- 13) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 46, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 48;
- 14) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 74, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 75; or
- 15) a light chain variable region (VL) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 82, and a heavy chain variable region (VH) that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 83.

~~12. The isolated antibody or antigen-binding fragment thereof of any one of claims 2 to 11, comprising a light chain variable region and a heavy chain variable region, which comprise an amino acid sequence with at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to the light chain variable region and the heavy chain variable region selected from 1) 15) in claim 11, respectively.~~

~~13. The isolated antibody or antigen-binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 7, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 23.~~

~~14. The isolated antibody or antigen-binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 7, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 27.~~

~~15. The isolated antibody or antigen-binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 7, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 31.~~

~~16. The isolated antibody or antigen-binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 11, and a heavy chain~~

~~variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 23.~~

~~17. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 11, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 27.~~

~~18. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 11, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 31.~~

~~19. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 15, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 23.~~

~~20. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 15, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 27.~~

~~21. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 15, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 31.~~

~~22. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 19, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 23.~~

~~23. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 19, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 27.~~

~~24. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 19, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 31.~~

~~25. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 46, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 48.~~

~~26. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 74, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 75.~~

~~27. The isolated antibody or antigen binding fragment thereof of claim 11, comprising:—~~

~~a light chain variable region (VL) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 82, and a heavy chain variable region (VH) that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 83.~~

~~28. The isolated antibody or antigen binding fragment thereof of any one of claims 2 to 27, comprising a light and a heavy chain, wherein:~~

~~(I) the light chain comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 9, 13, 17, 21, 37, 39, 50 or 54, and conservative modifications thereof; and~~

~~(II) the heavy chain comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 25, 29, 33, 35, 52 or 56, and conservative modifications thereof.~~

~~29. The isolated antibody or antigen binding fragment thereof of any one of claims 2 to 28, comprising a light and a heavy chain, wherein:~~

~~(I) the light chain comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 9, 13, 17, 21, 37, 39 or 50, and conservative modifications thereof; and~~

~~(II) the heavy chain comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from a group consisting of SEQ ID NO: 25, 29, 33, 35 or 52, and conservative modifications thereof.~~

~~30. The isolated antibody or antigen-binding fragment thereof of any one of claims 2 to 29, comprising a light chain comprising an amino acid sequence with at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to the light chain selected from (I) in claim 28 or 29, and a heavy chain comprising an amino acid sequence with at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to the heavy chain selected from (II) in claim 28 or 29.~~

~~314.~~ The isolated antibody or antigen-binding fragment thereof of any one of claims 2 to 30, comprising:

- 1) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 9, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 25;
- 2) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 9, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 29;
- 3) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 9, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 33;
- 4) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 13, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 25;
- 5) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 13, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 29;

- 6) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 13, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 33;
- 7) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 17, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 25;
- 8) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 17, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 29;
- 9) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 17, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 33;
- 10) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 21, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 25;
- 11) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 21, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 29;
- 12) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 21, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 33;

13) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 37, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 35;

14) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 39, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 35;

15) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 50, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 52; or

16) a light chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 54, and a heavy chain that comprises an amino acid sequence with at least 85% identity to an amino acid sequence of SEQ ID NO: 56.

~~32. The isolated antibody or antigen binding fragment thereof of any one of claims 2 to 31, comprising a light and a heavy chain, wherein the light and heavy chain comprise an amino acid sequence with at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identity to the light and heavy chain variable regions selected from 1) 16) in claim 31, respectively.~~

~~33. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 9, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 25.~~

~~34. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 9, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 29.~~

~~35. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:—~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 9, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 33.~~

~~36. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:—~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 13, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 25.~~

~~37. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:—~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 13, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 29.~~

~~38. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:—~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 13, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 33.~~

~~39. The isolated antibody or antigen-binding fragment thereof of claim 31,
comprising:—~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the
amino acid sequence of SEQ ID NO: 17, and a heavy chain that comprises the amino
acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO:
25.~~

~~40. The isolated antibody or antigen-binding fragment thereof of claim 31,
comprising:—~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the
amino acid sequence of SEQ ID NO: 17, and a heavy chain that comprises the amino
acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO:
29.~~

~~41. The isolated antibody or antigen-binding fragment thereof of claim 31,
comprising:—~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the
amino acid sequence of SEQ ID NO: 17, and a heavy chain that comprises an amino
acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO:
33.~~

~~42. The isolated antibody or antigen-binding fragment thereof of claim 31,
comprising:—~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the
amino acid sequence of SEQ ID NO: 21, and a heavy chain that comprises the amino
acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO:
25.~~

~~43. The isolated antibody or antigen-binding fragment thereof of claim 31,
comprising:—~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the
amino acid sequence of SEQ ID NO: 21, and a heavy chain that comprises the amino~~

~~acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 29.~~

~~44. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 21, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 33.~~

~~45. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 37, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 35.~~

~~46. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 39, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 35.~~

~~47. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 50, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 52.~~

~~48. The isolated antibody or antigen binding fragment thereof of claim 31, comprising:~~

~~a light chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 54, and a heavy chain that comprises the amino acid sequence with at least 85% identity to the amino acid sequence of SEQ ID NO: 56.~~

~~49. An isolated antibody or antigen-binding fragment thereof comprising: (a) L_{CDR1} comprising SEQ ID NO: 1, (b) L_{CDR2} comprising SEQ ID NO: 2, (c) L_{CDR3} comprising SEQ ID NO: 3, (d) H_{CDR1} comprising SEQ ID NO: 4, (e) H_{CDR2} comprising SEQ ID NO: 5, and (f) H_{CDR3} comprising SEQ ID NO: 6.~~

~~50. An isolated antibody or antigen-binding fragment thereof comprising: (a) L_{CDR1} comprising SEQ ID NO: 1, (b) L_{CDR2} comprising SEQ ID NO: 2, (c) L_{CDR3} comprising SEQ ID NO: 3, (d) H_{CDR1} comprising SEQ ID NO: 4, (e) H_{CDR2} comprising SEQ ID NO: 45, and (f) H_{CDR3} comprising SEQ ID NO: 6.~~

~~51. An~~ The isolated antibody or antigen-binding fragment thereof of claim 2 comprising

a a light chain variable region (VL) represented by SEQ ID NO: 7, and a heavy chain variable region (VH) represented by SEQ ID NO: 23; or

~~52. An isolated antibody or antigen-binding fragment thereof comprising~~ b a light chain variable region (VL) represented by SEQ ID NO: 11, and a heavy chain variable region (VH) represented by SEQ ID NO: 31; or

~~53. An isolated antibody or antigen-binding fragment thereof comprising~~ c a light chain variable region (VL) represented by SEQ ID NO: 19, and a heavy chain variable region (VH) represented by SEQ ID NO: 31.

~~546.~~ The isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~53~~, wherein the isolated antibody is an IgG.

~~557.~~ The isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~546~~, wherein the isolated antibody is an IgG1, IgG2 or IgG4.

~~568.~~ The isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~557~~, wherein the isolated antibody is a monoclonal antibody, a chimeric antibody, a

humanized antibody, a human engineered antibody, a human antibody, a bispecific antibody, Fv, a single chain antibody (scFv), a Fab, a Fab', a Fab'-SH or a F(ab')₂.

~~579~~. The isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~568~~, which is leukemia inhibitory factor (LIF) antagonist.

~~5810~~. The isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~568~~, which is capable of inhibiting the expression of LIF and/or blocking the activity of LIF.

~~5911~~. The isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~568~~, which is capable of competing or cross competing for binding to LIF.

~~6012~~. A nucleotide composition comprising a nucleotide molecule encoding the isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~5911~~.

~~61. The nucleotide composition of claim 60, comprising:~~

~~(i) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 7, 11, 15, 19, 46 or 82; and~~

~~(ii) a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 23, 27, 31, 48 or 83.~~

~~62. The nucleotide composition of claim 60 or 61, comprising:~~

~~(i) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 7, 11, 15, 19 or 46; and~~

~~(ii) a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 23, 27, 31 or 48.~~

~~63. The nucleotide composition of any one of claims 60 to 62, comprising:~~

~~(i) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 7, 11, 15, or 19; and~~

~~(ii) a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 23, 27 or 31.~~

~~6413.~~ The nucleotide composition of ~~any one of claims 60 to 63~~claim 12, comprising:

- 1) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 7 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 23;
- 2) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 7 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 27;
- 3) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 7 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 31;
- 4) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 11 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 23;
- 5) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 11 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 27;
- 6) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 11 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 31;
- 7) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 15 and a

second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 23;

8) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 15 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 27;

9) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 15 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 31;

10) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 19 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 23;

11) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 19 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 27;

12) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 19 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 31;

13) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 46 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 48;

14) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 74 and a

second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 75; or
15) a first nucleic acid molecule comprising DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 82 and a second nucleic acid molecule comprising DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 83.

~~65~~14. The nucleotide composition of ~~any one of claims 60 to 64~~claim 13, wherein
1) DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 7 is shown as SEQ ID NO: 8-

~~66. The nucleotide composition of any one of claims 60 to 65, wherein;~~
2) DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 11 is shown as SEQ ID NO: 12-

~~67. The nucleotide composition of any one of claims 60 to 66, wherein;~~
3) DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 15 is shown as SEQ ID NO: 16-

~~68. The nucleotide composition of any one of claims 60 to 67, wherein;~~
4) DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 19 is shown as SEQ ID NO: 20-

~~69. The nucleotide composition of any one of claims 60 to 68, wherein;~~
5) DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 46 is shown as SEQ ID NO: 47-

~~70. The nucleotide composition of any one of claims 60 to 69, wherein;~~
6) DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 74 is shown as SEQ ID NO: 76-

~~71. The nucleotide composition of any one of claims 60 to 70, wherein;~~
7) DNA encoding a light chain variable region (VL) as represented by an amino acid sequence of SEQ ID NO: 82 is shown as SEQ ID NO: 72-

~~72. The nucleotide composition of any one of claims 60 to 71, wherein;~~

8) DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 23 is shown as SEQ ID NO: 24.

~~73. The nucleotide composition of any one of claims 60 to 72, wherein;~~

9) DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 27 is shown as SEQ ID NO: 28.

~~74. The nucleotide composition of any one of claims 60 to 73, wherein;~~

10) DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 31 is shown as SEQ ID NO: 32.

~~75. The nucleotide composition of any one of claims 60 to 74, wherein;~~

11) DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 48 is shown as SEQ ID NO: 49.

~~76. The nucleotide composition of any one of claims 60 to 75, wherein;~~

12) DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 75 is shown as SEQ ID NO: 77.

~~77. The nucleotide composition of any one of claims 60 to 76, wherein; and/or~~

13) DNA encoding a heavy chain variable region (VH) as represented by an amino acid sequence of SEQ ID NO: 83 is shown as SEQ ID NO: 73.

~~78. The nucleotide composition of any one of claims 60 to 77, comprising:~~

~~(I) a first nucleic acid sequence comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 9, 13, 17, 21, 37, 39, 50 or 54;~~
~~and~~

~~(II) a second nucleic acid sequence comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 25, 29, 33, 35, 52 or 56.~~

~~79. The nucleotide composition of any one of claims 60 to 78, comprising:~~

~~(I) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 9, 13, 17, 21, 37, 39 or 50;~~
~~and~~

~~(II) a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 25, 29, 33, 35 or 52.~~

~~80. The nucleotide composition of any one of claims 60 to 79, comprising:~~

~~(I) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 9, 13, 17 or 21; and~~

~~(II) a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 25, 29 or 33.~~

81~~15~~. The nucleotide composition of any one of claims ~~60-12~~ to ~~80~~14, comprising:

1) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 9 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 25;

2) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 9 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 29;

3) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 9 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 33;

4) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 13 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 25;

5) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 13 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 29;

6) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 13 and a second nucleic acid molecule

comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 33;

7) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 17 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 25;

8) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 17 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 29;

9) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 17 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 33;

10) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 21 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 25;

11) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 21 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 29;

12) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 21 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 33;

13) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 37 and a second nucleic acid

molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 35;

14) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 39 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 35;

15) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 50 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 52; or

16) a first nucleic acid molecule comprising DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 54 and a second nucleic acid molecule comprising DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 56.

~~82~~16. The nucleotide composition of ~~any one of claims 78 to 81~~claim 15, wherein 1) DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 13 is shown as SEQ ID NO: 14.

~~83. The nucleotide composition of any one of claims 78 to 82, wherein;~~
2) DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 17 is shown as SEQ ID NO: 18.

~~84. The nucleotide composition of any one of claims 78 to 83, wherein;~~
3) DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 21 is shown as SEQ ID NO: 22.

~~85. The nucleotide composition of any one of claims 78 to 84, wherein;~~
4) DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 37 is shown as SEQ ID NO: 38.

~~86. The nucleotide composition of any one of claims 78 to 85, wherein;~~
5) DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 39 is shown as SEQ ID NO: 40.

~~87. The nucleotide composition of any one of claims 78 to 86, wherein:~~

6) DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 50 is shown as SEQ ID NO: 51.

~~88. The nucleotide composition of any one of claims 78 to 87, wherein:~~

7) DNA encoding a light chain as represented by an amino acid sequence of SEQ ID NO: 54 is shown as SEQ ID NO: 55.

~~89. The nucleotide composition of any one of claims 78 to 88, wherein:~~

8) DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 25 is shown as SEQ ID NO: 26.

~~90. The nucleotide composition of any one of claims 78 to 89, wherein:~~

9) DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 29 is shown as SEQ ID NO: 30.

~~91. The nucleotide composition of any one of claims 78 to 90, wherein:~~

10) DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 33 is shown as SEQ ID NO: 34.

~~92. The nucleotide composition of any one of claims 78 to 91, wherein:~~

11) DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 35 is shown as SEQ ID NO: 36.

~~93. The nucleotide composition of any one of claims 78 to 92, wherein:~~

12) DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 52 is shown as SEQ ID NO: 53.

~~94. The nucleotide composition of any one of claims 78 to 93, wherein: and/or~~

13) DNA encoding a heavy chain as represented by an amino acid sequence of SEQ ID NO: 56 is shown as SEQ ID NO: 57.

~~95~~17. A vector, comprising the nucleotide composition of any one of claims ~~60-12~~ to ~~94~~16.

~~96~~18. The vector of claim ~~95~~17, being a eukaryotic expression vector, a prokaryotic expression vector or a viral vector.

~~97~~19. A host cell comprising the vector of claim ~~95-17~~ or ~~96~~18.

~~98~~20. The host cell of claim ~~97~~19, wherein the host cell comprising the vector is obtained by vector transformation.

~~99~~21. The host cell of claims ~~97~~19 or ~~98~~20, being bacteria, yeast or mammalian cell.

~~100~~22. The host cell of any one of claims ~~97~~19 to ~~99~~21, being escherichia coli, pichia yeast, Chinese hamster ovary cells or human embryonic kidney 293 cells.

~~101~~23. A method of preparing the isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~59~~11, comprising expressing the antibody or antigen-binding fragment thereof in the host cell of any one of claims ~~97~~19 to ~~100~~21 and isolating the antibody or antigen-binding fragment thereof.

~~102~~24. A pharmaceutical composition comprising a therapeutically effective amount of the isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~59~~11, and a pharmaceutical acceptable excipient.

~~103~~25. A reagent for detecting LIF in biological samples comprising the isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~59~~11.

~~104~~26. The reagent of claim ~~103~~25, wherein the biological samples are blood, serum, urine, biopsy materials, tumor, or any tissues suspected of having abnormal LIF levels.

~~105. A method for inhibiting the expression of LIF and/or blocking the activity of LIF, comprising administering to the patient in need thereof a therapeutically effective amount of the isolated antibody or antigen binding fragment thereof of any one of claims 1 to 59, and/or the pharmaceutical composition of claim 102.~~

~~106~~27. Use of the isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~59~~11, and/or the pharmaceutical composition of claim ~~102~~24 in manufacture of a medicament ~~used~~ for inhibiting the expression of LIF and/or blocking the activity of LIF.

~~107. The isolated antibody or antigen binding fragment thereof of any one of claims 1 to 59 and/or the pharmaceutical composition of claim 102 for use in inhibiting the expression of LIF and/or blocking the activity of LIF.~~

~~10828~~. A *ex vivo* method for detecting the LIF in biological samples comprising (i) obtaining a subject's tissue or liquid sample, (ii) exposing the tissue or liquid sample to the isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~59-11~~ or the reagent of claim ~~103-25~~ or ~~10426~~; and (iii) comparing the LIF binding to the tissue or liquid sample of (ii) with the LIF binding to a control sample, wherein the increase in the amount of the bound LIF compared with the control sample shows the abnormal level of LIF production, expression or activation .

~~10929~~. The method of claim ~~10828~~, wherein the tissue or liquid sample comprises blood, serum, urine, biopsy materials, tumor, or any tissues suspected of having abnormal LIF levels.

~~110. A method for treating a disease or condition related to LIF comprising administering to a patient in need a therapeutically effective amount of the isolated antibody or antigen binding fragment of any one of claims 1 to 59, and/or the pharmaceutical composition of claim 102.~~

~~111. The method of claim 110, wherein the disease or condition related to LIF is tumor.~~

~~112. The method of claim 111, wherein the tumor is solid tumor.~~

~~113. The method of claim 112, wherein the solid tumor comprises glioblastoma, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer or prostate cancer.~~

~~11430~~. Use of the isolated antibody or antigen-binding fragment thereof of any one of claims 1 to ~~5911~~, and/or the pharmaceutical composition of claim ~~102-24~~ in manufacture of a medicament for treating a disease or condition related to LIF.

~~11531~~. The use of claim ~~11430~~, wherein the disease or condition related to LIF is tumor.

~~11632~~. The use of claim ~~11531~~, wherein the tumor is solid tumor.

~~11733~~. The use of claim ~~11632~~, wherein the solid tumor comprises glioblastoma, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer or prostate cancer.

~~118. The isolated antibody or antigen-binding fragment thereof of any one of claims 1 to 59, and/or the pharmaceutical composition of claim 102 for use in treating a disease or condition related to LIF.~~

~~119. The isolated antibody or antigen-binding fragment thereof and/or the pharmaceutical composition of claim 118, wherein the disease or condition related to LIF is tumor.~~

~~120. The isolated antibody or antigen-binding fragment thereof and/or the pharmaceutical composition of claim 119, wherein the tumor is solid tumor.~~

~~121. The isolated antibody or antigen-binding fragment thereof and/or the pharmaceutical composition of claim 120, wherein the solid tumor comprises glioblastoma, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer or prostate cancer.~~