

CLAIMS

1. An antibody, or antigen binding fragment thereof, that specifically binds to human growth differentiation factor 15 (GDF15), comprising at least one of the following:
 - a) a light chain complementarity determining region 1 (LCDR-1) comprising the amino acid sequence of SEQ ID NO:95, a LCDR-2 comprising the amino acid sequence of SEQ ID NO:28, a LCDR-3 comprising the amino acid sequence of SEQ ID NO:9, a heavy chain complementarity determining region 1 (HCDR-1) comprising the amino acid sequence of SEQ ID NO:32, a HCDR-2 comprising the amino acid sequence of SEQ ID NO:165, and a HCDR-3 comprising the amino acid sequence of SEQ ID NO:52;
 - b) the HCDR-1, HCDR-2, and HCDR-3 amino acid sequences as set forth in the amino acid sequence of SEQ ID NO:166, and the LCDR-1, LCDR-2, and LCDR-3 amino acid sequences as set forth in the amino acid sequence of SEQ ID NO:163;
 - c) the amino acid sequence encoded by the insert of the plasmid deposited at the ATCC and having ATCC Accession No. PTA-125038, and the amino acid sequence encoded by the insert of the plasmid deposited at the ATCC and having ATCC Accession No. PTA-125039;
 - d) a VH comprising the amino acid sequence of SEQ ID NO:166 and a VL comprising the amino acid sequence of SEQ ID NO:163; and
 - e) a HC comprising the amino acid sequence of SEQ ID NO:164, and a LC comprising the amino acid sequence of SEQ ID NO:162.
2. The antibody, or antigen binding fragment thereof, of claim 1, comprising a human Fc domain selected from the group consisting of an Fc domain of IgA₁, IgA₂, IgD, IgE, IgM, IgG₁, IgG₂, IgG₃, or IgG₄.
3. The antibody, or antigen binding fragment thereof, of any one of claims 1, comprising:
a HC comprising the amino acid sequence of SEQ ID NO:164, and a LC comprising the amino acid sequence of SEQ ID NO:162.
4. The antibody, or antigen binding fragment thereof, of any one of claims 1, wherein the antibody, or antigen binding fragment thereof, binds human or cynomolgus monkey GDF15 with a K_D about or less than a value selected from the group consisting of about 10nM, 5nM, 2nM, 1nM, 900pM, 800pM, 700pM, 600pM, 500pM, 400pM, 300pM, 250pM, 200pM, 150pM, 100pM, 50pM, 40pM, 30pM, 25pM, 20pM, 15pM, and 10pM.

5. An isolated nucleic acid encoding the antibody, or antigen-binding portion thereof, of any one of claims 1 .
6. An isolated nucleic acid comprising:
 - a) the nucleic acid sequence of SEQ ID NO:167, the nucleic acid sequence of SEQ ID NO:168, or both,
 - b) the nucleic acid sequence of SEQ ID NO:169, the nucleic acid sequence of SEQ ID NO:170, or both, and
 - c) the nucleic acid sequence of the insert of the plasmid deposited with the ATCC and having the Accession Number PTA-125038, the nucleic acid sequence of the insert of the plasmid deposited with the ATCC and having the Accession Number PTA-125039, or both.
7. A vector comprising the nucleic acid of claim 5 .
8. A host cell comprising the vector of claim 7.
9. The host cell of claim 8, wherein said host cell is a mammalian cell selected from the group consisting of a CHO cell, a COS cell, a HEK-293 cell, an NS0 cell, a PER.C6 cell, or an Sp2.0 cell.
10. A method of making an antibody, or antigen binding fragment thereof, comprising culturing the host cell of claim 8 under a condition wherein said antibody, or antigen binding fragment thereof, is expressed by said host cell.
11. A pharmaceutical composition comprising an antibody, or antigen binding fragment thereof, of any one of claims 1 , and a pharmaceutically acceptable carrier or excipient.

12. A therapeutically effective amount of the antibody, or antigen binding fragment thereof, of any one of claims 1 - 4, or the pharmaceutical composition of claim 11, for use in the treatment of a medical condition, disease or disorder mediated by or associated with expression of GDF15, in a subject in need thereof.

13. A therapeutically effective amount of the antibody, or antigen binding fragment thereof, of any one of claims 1 - 4, or the pharmaceutical composition of claim 11, for use in the treatment of decreasing the level of free GDF15 in a subject in need thereof.

14. A therapeutically effective amount of the antibody, or antigen binding fragment thereof, of any one of claims 1 - 4, or the pharmaceutical composition of claim 11, for use in the treatment of reducing the activity of GDF15 in a subject in need thereof.

15. A therapeutically effective amount of the antibody, or antigen binding fragment thereof, of any one of claims 1 - 4, or the pharmaceutical composition of claim 11, for use in the treatment of cancer in a patient in need thereof, wherein the antibody, or antigen binding fragment thereof, or pharmaceutical composition, is to be administered in combination with:

- a) a synergistic therapeutically effective amount of an anti-CD40 antagonist antibody; or
- b) a synergistic therapeutically effective amount of a PD-1 axis binding antagonist, wherein the PD-1 axis binding antagonist is not avelumab.

16. An effective amount of the antibody, or antigen binding fragment thereof, of any one of claims 1 - 4, or the pharmaceutical composition of claim 11, for use in a method for enhancing the therapeutic effect of an immune modulator to be administered to a subject for the treatment of cancer.

17. An effective amount of the antibody, or antigen binding fragment thereof, of any one of claims 1 - 4, or the pharmaceutical composition of claim 11, for use in a method of decreasing or inhibiting toxicity in a subject experiencing cytokine release syndrome (CRS) or cytokine storm or vulnerable to CRS or cytokine storm.