

What is claimed is:

1. An *in vitro* method for selecting a patient for an amyotrophic lateral sclerosis (ALS) therapy, the method comprising: determining a concentration of interleukin 17F (IL-17F) in a serum sample collected from a patient diagnosed with or suspected of having ALS, wherein if the IL-17F concentration in the serum sample is at least 2.0 pg/mL the patient is excluded from a treatment with the ALS therapy, otherwise the patient is selected for the treatment with the ALS therapy.

2. Use of a composition in the manufacture of a medicament for treating ALS, the medicament comprising an ALS therapy to be administered to a patient diagnosed with ALS, wherein it has been determined that a serum sample collected from the patient contains an interleukin 17F (IL-17F) concentration of less than 2.0 pg/mL.

3. An *in vitro* method for selecting a patient for an ALS therapy, the method comprising: determining whether a concentration of at least one serum immune-based biomarker in a serum sample collected from a patient diagnosed with or suspected of having ALS is less than, equal to, or greater than, a reference concentration,

wherein the at least one serum immune-based biomarker is IL-17F, oxidized low-density lipoprotein receptor 1 (OLR1), neurofilament light chain (NF-L), oxidized low-density lipoprotein (ox-LDL), or interleukin 17C (IL-17C); and

wherein if the concentration of the at least one serum immune-based biomarker is greater than the reference concentration, the patient is excluded from a treatment with the ALS therapy, otherwise the patient is selected for treatment with the ALS therapy.

4. The method of claim 3, wherein:

(i) the concentration of one serum immune-based biomarker is determined;

(ii) concentrations of at least two serum immune-based biomarkers are each determined to be less than, equal to, or greater than, a reference concentration, and if the concentrations of two serum immune-based biomarkers are each determined to be greater than its reference concentration, the patient is excluded from a treatment with the ALS therapy, otherwise the patient is selected for the treatment with the ALS therapy;

(iii) concentrations of at least three serum immune-based biomarkers are each determined to be less than, equal to, or greater than, a reference concentration, and if the concentrations of three serum immune-based biomarkers are each determined to be greater than its reference concentration, the patient is excluded from a treatment with the ALS therapy, otherwise the patient is selected for the treatment with the ALS therapy;

(iv) concentrations of at least four serum immune-based biomarkers are each determined to be less than, equal to, or greater than, a reference concentration, and if the concentrations of four serum immune-based biomarkers are each determined to be greater than its reference concentration, the patient is excluded from a treatment with the ALS therapy, otherwise the patient is selected for the treatment with the ALS therapy; or

(v) concentrations of at least five serum immune-based biomarkers are each determined to be less than, equal to, or greater than, a reference concentration, and if the concentrations of five serum immune-based biomarkers are each determined to be greater than its reference concentration, the patient is excluded from a treatment with the ALS therapy, otherwise the patient is selected for the treatment with the ALS therapy.

5. Use of a composition in the manufacture of a medicament for treating ALS, the medicament comprising an ALS therapy to be administered to a patient diagnosed with ALS, wherein it has been determined that a serum sample collected from the patient contains a concentration of at least one serum immune-based biomarker that is less than, or equal to, a reference concentration, wherein the at least one serum immune-based biomarker is IL-17F, OLR1, NF-L, ox-LDL, or IL-17C.

6. The use of claim 5, wherein a concentration of:

(i) one serum immune-based biomarker has been determined to be less than, or equal to, a reference concentration;

(ii) at least two serum immune-based biomarkers had been determined to be less than, or equal to, a reference concentration;

(iii) at least three serum immune-based biomarkers had been determined to be less than, or equal to, a reference concentration;

(iv) at least four serum immune-based biomarkers had been determined to be less than, or equal to, a reference concentration; or

(v) at least five serum immune-based biomarkers had been determined to be less than, or equal to, a reference concentration.

7. The method of claim 1 or 3 or the use of claim 2 or 5, wherein (i) the ALS therapy comprises a Treg infusion or, (ii) the ALS therapy comprises a plurality of Treg infusions.

8. The method of claim 1 or 3 or the use of claim 2 or 5, wherein the serum sample:

(i) had been collected from the patient prior to the ALS therapy;

(ii) had been collected from the patient prior to any Treg infusion; or

(iii) had been collected from the patient after a Treg infusion has been administered to the patient.

9. The method of claim 1 or 3 or the use of claim 2 or 5, wherein the serum sample had been collected from the patient on the day following the Treg infusion.

10. An *in vitro* method of monitoring efficacy of Treg therapy to treat ALS, the method comprising:

determining whether a concentration of at least one serum immune-based biomarker in a serum sample collected from a patient diagnosed with ALS who has been administered a Treg therapy that comprises a first Treg infusion is less than, equal to, or greater than, a reference concentration, wherein the at least one serum immune-based biomarker comprises:

oxidized low density lipoprotein (ox-LDL),

oxidized low density lipoprotein receptor 1 (OLR1),

soluble CD14 (sCD14),

lipopolysaccharide binding protein (LBP),

C reactive protein (CRP),

IL-17F, or

IL-17C;

wherein the serum sample was collected from the patient after the first Treg infusion, and

wherein the ALS therapy has poor efficacy where the concentration of the at least one serum immune-based biomarker is greater than its reference concentration.

11. The method of claim 10, wherein the ALS therapy has poor efficacy where the concentration of one serum immune-based biomarker is greater than its reference concentration.

12. The method of claim 10, wherein the concentration of at least 2, at least 3, at least 4, or at least 5 serum immune-based biomarkers are each greater than its reference concentration.

13. An *in vitro* method for selecting a patient for receiving treatment for ALS comprising: comparing a concentration of at least one serum immune-based biomarker in a serum sample obtained from a patient diagnosed with ALS who has been administered a first Treg infusion to a reference concentration;

wherein the at least one immune-based biomarker comprises ox-LDL, OLR1, sCD14, LBP, CRP, IL-17F, or IL-17C;

wherein the serum sample was collected from the patient after the first Treg infusion, and

wherein the patient is selected for treatment for ALS comprising a second Treg infusion if the concentration of the at least one serum immune-based biomarker is equal to or below the reference concentration.

14. The method of claim 13, wherein the ALS therapy is administered to the patient if the concentration of one serum immune-based biomarker is equal to or below the reference concentration.

15. The method of claim 13, wherein the ALS therapy is administered to the patient if the concentration of at least 2, at least 3, at least 4 or at least 5 serum immune-based biomarkers are each equal to or below its reference concentration.

16. An *in vitro* method for selecting a patient for receiving treatment with a Treg therapy, wherein the patient is suffering from ALS, the method comprising:

comparing concentrations of at least one serum immune-based biomarker in serum samples to a reference concentration, wherein the patient has received a Treg therapy comprising Treg infusions administered on different days, wherein each of the serum samples is obtained from the patient after a Treg infusion, and

wherein the at least one serum immune-based biomarker comprises ox-LDL, OLR1, sCD14, LBP, CRP, IL-17F, or IL-17C; such that the patient is selected for being maintained on the Treg therapy if the concentration of the at least one serum immune-based biomarker is at, or less than, the reference concentration in at least one of serum samples.

17. The method of claim 16, wherein the patient is selected for being maintained on the Treg therapy if the concentration of the at least one serum immune-based biomarker is at, or less than, the reference concentration in all or at least 50% of the serum samples.

18. The method of claim 17, wherein the at least one serum immune-based biomarker consists of one serum immune-based biomarker.

19. The method of claim 17, wherein the at least one serum immune-based biomarker comprises at least 2, at least 3, at least 4 or at least 5 serum immune-based biomarkers.

20. An *in vitro* method for selecting a patient for ALS treatment in a serum sample obtained from a patient diagnosed therewith, the method comprising:

determining whether the concentration of at least one serum immune-based biomarker in a serum sample obtained from a patient diagnosed with ALS is (i) elevated, or (ii) at, or below, a reference concentration, wherein the serum sample is obtained from the patient after being administered with a Treg infusion,

wherein the at least one serum immune-based biomarker comprises ox-LDL, OLR1, sCD14, LBP, CRP, IL-17F, or IL-17C; and

the patient is selected for Treg therapy comprising a plurality of Treg infusions if the concentration of the at least one serum immune-based biomarker is determined to be (ii) at, or below, its reference concentration.

21. The method of claim 20, wherein the Treg therapy is administered to the patient if the concentration of one serum immune-based biomarker is determined to be (ii) at, or below, its reference concentration.

22. The method of claim 20, wherein the Treg therapy is administered to the patient if the concentration of at least 2, at least 3, at least 4 or at least 5 serum immune- based biomarkers are each determined to be (ii) at, or below, its reference concentration.

23. The use of claim 5 or the method of any one of claims 3, 9, 11, 13 or 16, wherein the reference concentration for the at least one serum immune-based biomarker is:

(i) obtained from healthy individuals; or

(ii) a concentration in a serum sample obtained from the patient prior to any Treg infusion being administered to the patient.

24. The use of claim 5 or the method of any one claims 3, 10, 13, 16 or 20 wherein the reference concentration for each of ox-LDL, OLR1, sCD14, LBP, CRP, IL-17F, and IL-17C is as follows:

Biomarker	Ref. Conc.
ox-LDL	56.8 ± 7.0 U/L
OLR1	299.6 ± 128.1 pg/mL
sCD14	2.56 ± 0.44 ug/mL
LBP	20.18 ± 7.48 ug/mL
CRP	1.08 ± 1.04 ug/mL
IL-17F	0.34 ± 0.54 pg/mL
IL-17C	8.47 ± 3.08 pg/mL.

25. The use of claim 5 or the method of any one of claims 3, 10, 13, 16 or 20, wherein the at least one serum immune-based biomarker comprises:

(i) ox-LDL, OLR1, sCD14, or LBP;

(ii) ox-LDL, OLR1, IL-17C, or IL-17F;

(iii) ox-LDL;

(iv) OLR1;

(v) sCD14;

(vi) IL-17C; or

(vii) IL-17F.

26. The use of claim 2 or 5 or the method according to any one of claims 1, 3, 10, 13, 16 or 20, wherein the concentration of the at least one serum immune-based biomarker is determined using an enzyme-linked immunosorbent assay (ELISA).

27. An *in vitro* method for selecting a patient for ALS treatment in a serum sample obtained from a patient diagnosed therewith, the method comprising:

- a) determining whether the concentration of at least one serum immune-based biomarker in a serum sample obtained from a patient diagnosed with ALS is at or below that of a reference concentration of the at least one serum immune-based biomarker, wherein the serum sample is obtained from the patient after being administered with a first ALS therapy,

wherein the at least one serum immune-based biomarker comprises ox-LDL, OLR1, sCD14, LBP, CRP, 4-HNE, IL-17F, or IL-17C; and

- b) the patient is selected for a second ALS therapy if the concentration of the at least one serum immune-based biomarker is determined to be at or below its reference concentration.

28. The method of claim 27, wherein:

- (i) the first ALS therapy is the same as the second ALS therapy;
- (ii) the first ALS therapy is different than the second ALS therapy;
- (iii) the first and/or second ALS therapy comprises administering one or more Treg infusions to the patient;
- (iv) the first and/or second ALS therapy comprises administering a CTLA-4 fusion protein and IL-2 to the patient;
- (v) the first and/or second ALS therapy comprises administering abatacept and IL-2 to the patient; or
- (vi) the first and/or second ALS therapy comprises administering one or more Treg extracellular vesicle (EV), e.g., exosome, infusions to the patient.

- 29.** The method of claim 27, wherein the at least one serum immune-based biomarker comprises ox-LDL or 4-HNE.
- 30.** An *in vitro* method for selecting a patient for treating ALS in a serum sample obtained from a patient diagnosed therewith, the method comprising:
- assessing the responsiveness of the ALS patient to the ALS therapy; and
 - selecting the patient for continued ALS therapy if the ALS patient is assessed to be responsive to the ALS therapy,
- wherein the responsiveness of the ALS patient to the ALS therapy comprises comparing the serum concentration of at least one immune-based biomarker to a reference concentration of the of least one immune-based biomarker, and wherein the ALS patient is assessed to be responsive to the ALS therapy if the serum concentration of the immune-based biomarker decreases or remains within the reference concentration in at least one successive serum sample taken from the ALS patient.
- 31.** The method of claim 30, wherein the responsiveness of the ALS patient to the ALS therapy comprises comparing the serum concentration of an immune-based biomarker to a reference concentration for a set of immune-based biomarkers, and the ALS patient is assessed to be responsive to the ALS therapy if the serum concentration of at least 50% of the immune-based biomarkers in the set decreases or remains within its reference concentration in at least one successive serum sample taken from the ALS patient,
- 32.** The method of claim 30, wherein the set comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 immune-based biomarkers.
- 33.** The method of claim 30, wherein the ALS patient is assessed to be responsive to the ALS therapy if the serum concentration of the immune-based biomarker:
- (i) decreases or remains within the reference concentration in at least 2, 3, 4, 5, 6, 7, 8, or 9 successive serum samples taken from the ALS patient; or
 - (ii) decreases or remains within the reference concentration in a majority of 3 or more successive serum samples taken from the ALS patient.
- 34.** The method of claim 30, wherein the immune-based biomarker comprises ox-LDL, OLR1, sCD14, LBP, CRP, 4-HNE, IL-17F, or IL-17C.

- 35.** The method of claim 30, wherein the ALS therapy comprises:
- (i) administering one or more Treg infusions to the patient;
 - (ii) administering a CTLA-4 fusion protein and IL-2 to the patient,
 - (iii) administering abatacept and IL-2 to the patient; or,
 - (iv) administering one or more Treg extracellular vesicle (EV), e.g., exosome, infusions to the patient.