WHAT IS CLAIMED IS:

1. A method comprising:

a) providing a blood sample from a subject;

b) isolating central nervous system ("CNS") derived exosomes from the blood sample;

c) removing proteins from the surface of the isolated exosomes to produce scrubbed exosomes;

d) isolating the internal contents of the scrubbed exosomes;

e) separating from the isolated internal contents, species of oligomeric α-synuclein into a plurality of fractions;

f) determining a quantitative measure of each of one or a plurality of the separated oligomeric α-synuclein species.

2. The method of claim **1**, wherein the blood sample is a plasma sample.

3. The method of claim **1 or 2**, wherein the blood sample comprises between 5 ml and 20 ml of blood.

4. The method of any one of claims **1 to 3**, wherein the subject is a human subject.

5. The method of any one of claims **1 to 5**, wherein the subject has a synucleinopathy.

6. The method of claim 5, wherein the synucleinopathy is selected from Parkinson's Disease, Lewy Body dementia and multiple system atrophy.

7. The method of any one of claims **1 to 6**, wherein isolating CNS-derived exosomes comprises: (i) isolating total exosomes from the blood sample and (ii) isolating CNS-derived exosomes from total exosomes.

8. The method of any one of claims **1 to 7**, wherein isolating CNS-derived exosomes comprises:

(i) ultra-centrifugation;

(ii) density gradient centrifugation; or

(iii) size exclusion chromatography.

9. The method of any one of claims **1 to 8**, wherein isolating CNS-derived exosomes comprises capturing the CNS-derived exosomes using a binding moiety that binds to CNS-specific protein.

10. The method of claim **9**, wherein the CNS-specific protein is L1CAM.

11. The method of any one of claims **1 to 10**, wherein the quantitative measures are total amounts of the protein forms.

12. The method of any one of claims **1 to 10**, further comprising determining, in the isolated internal contents of the scrubbed exosomes, a quantitative measure of monomeric α-synuclein.

13. The method of any one of claims **1 to 10**, further comprising determining, in the isolated internal contents of the scrubbed exosomes, a quantitative measure of one or a plurality of species selected from monomeric tau, oligomeric tau and phosphorylated tau.

14. The method of any one of claims **1 to 10** wherein determining a quantitative measure comprises determining a quantitative measure of oligomers comprising p129 alpha-synuclein.

15. The method of any one of claims **1 to 10**, further comprising determining, in the isolated internal contents of the scrubbed exosomes, a quantitative measure of one or a plurality of species selected from amyloid beta 1-40, amyloid beta 1-42, and oligomeric amyloid beta.

16. The method of any one of claims **1 to 16**, wherein separating species into a plurality of fractions comprises:

(i) separating by electrophoresis; or

(ii) separating by chromatography

17. The method of any one of claims **1 to 16**, comprising determining among the separated species, at least one oligomeric form of α-synuclein selected from forms having between 2 and 100 monomeric units, between 4 and 16 monomeric units and no more than 30 monomeric units.

18. The method of any one of claims **1 to 17**, comprising determining among the separated species:

(i) a quantitative measure of monomeric α-synuclein;

(ii) a quantitative measure of a plurality of different oligomeric α-synuclein species;

(iii) a quantitative measure of a co-polymer comprising α-synuclein and tau; or

(iv) a quantitative measure of a co-polymer comprising α-synuclein and amyloid beta.

19. The method of claim **18**, wherein determining a quantitative measure in the separated species comprises detecting one or a plurality of separated species by immunoassay.

20. The method of claim **19**, wherein the immunoassay comprises immunoblotting or Western blot.

21. The method of any one of claims **18 to 20**, wherein the immunoassay uses an antibody coupled to a direct label or an antibody coupled to an indirect label.

22. The method of any one of claims **1 to 21**, further comprising:

g) based on the quantitative measures of one or a plurality of the separated oligomeric α-synuclein species, determining a diagnosis of Parkinson's disease in the subject.

23. The method of any one of claims **1 to 21**, further comprising:

g) determining quantitative amounts of proteins in the subject before and after administration of a putative neuroprotective agent; and

h) determining changes in amounts of proteins or patterns of biomarker profiles, wherein changes toward normal amounts or profile indicate efficacy of the neuroprotective agent.

24. The method of any one of claims **1 to 21**, further comprising:

g) determining quantitative amounts of proteins in the subject at two different times; and

h) determining changes in amounts of proteins or patterns of biomarker profiles, wherein changes indicate a change in a neurodegenerative state.

25. A method comprising:

a) enriching each blood sample in a collection of blood samples for brain-derived exosomes, wherein:

(i) the collection of blood samples is from subjects in a cohort of subjects, wherein the cohort comprises subjects including:

(1) a plurality of subjects diagnosed with a synucleopathic condition at each of a plurality of different disease stages, wherein each of the diagnosed subjects has received a putative neuroprotective agent, and

(2) a plurality of healthy control subjects,

wherein the blood samples were collected before and again at one or more times during administration of the putative neuroprotective agent;

b) isolating protein contents from an internal compartment of the exosomes from which external proteins have been removed to produce a biomarker sample;

c) measuring, in the biomarker sample, amounts of each of one or a plurality of neurodegenerative protein forms to create a dataset, wherein the neurodegenerative protein forms include one or more oligomeric forms of α -synuclein; and

d) performing statistical analysis on the dataset to compare differences in the amounts of each of the neurodegenerative protein forms:

(i) in individual subjects over time to determine a diagnostic algorithm that predicts rates of disease progression or degree of response to the putative neuroprotective agent; or

(ii) between different subjects to determine a diagnostic algorithm that (1) makes a pathogenic diagnosis, (2) separates clinically similar but etiologically different neurodegenerative disorder subgroups, or (3) predicts whether or the degree to which a subject is likely to respond to the putative neuroprotective agent.

26. The method according to claim **25** wherein the neurodegenerative protein forms include one or more monomeric forms of α -synuclein.

27. A method comprising:

a) providing a dataset comprising, for each of a plurality of subjects, values indicating (1) state of a synucleopathic condition, and (2) quantitative measures of amounts of each of one or a plurality of neurodegenerative protein forms in a blood sample enriched for internal contents of CNS-derived exosomes from which external proteins have been removed, wherein the neurodegenerative protein forms include one or more oligomeric forms of α-synuclein; and

b) performing a statistical analysis on the dataset to develop a model that infers the state of the synucleopathic condition in an individual.

28. The method according to claim **27**, wherein the neurodegenerative protein forms include one or more monomeric forms of α-synuclein.

29. A method for qualifying subjects for a clinical trial of a therapeutic intervention for the treatment or prevention of a synucleopathic condition comprising:

a) determining that a subject is abnormal with respect to the synucleopathic condition characterized by a neurodegenerative protein by:

i) determining, from a blood sample from a subject that is enriched for internal contents of CNS-derived exosomes from which external proteins have been removed, a neurodegenerative protein profile comprising quantitative measures of each of one or a plurality of neurodegenerative protein forms to create a dataset, wherein the neurodegenerative protein forms include one or more oligomeric forms of α-synuclein; and

ii) executing a model, e.g., a model of claim **27,** on the profile to infer that the subject is abnormal with respect with the synucleopathic condition; and

c) enrolling the subject in the clinical trial of a potentially therapeutic intervention for said synucleopathic condition.

30. The method according to claim **29**, wherein the neurodegenerative protein forms include one or more monomeric forms of α-synuclein.

31. A method of inferring a risk of developing, a diagnosis of, a stage of, a prognosis of or

a progression of a synucleopathic condition characterized by a neurodegenerative protein, wherein the method comprises:

a) determining, from a blood sample from a subject that is enriched for CNS-derived exosomes from which external proteins have been removed, a neurodegenerative protein profile comprising quantitative measures of each of one or a plurality of neurodegenerative protein forms to create a dataset, wherein the neurodegenerative protein forms include one or more oligomeric forms of α-synuclein; and

b) correlating the neurodegenerative protein profile with a risk of developing, a diagnosis of, a stage of, a prognosis of or a progression of the synucleopathic condition.

32. The method according to claim **31**, wherein the neurodegenerative protein forms include one or more monomeric forms of α-synuclein.

33. A method of making a diagnosis of a synucleopathic condition in a human subject, comprising:

a) providing a blood sample from the human subject;

b) enriching the blood sample for central nervous system ("CNS") derived exosomes;

c) removing proteins from the surface of the isolated exosomes to produce scrubbed exosomes;

d) isolating the internal contents of the scrubbed exosomes;

e) measuring an amount of oligomeric α-synuclein in the isolated internal contents;

f) making a diagnosis of a synucleopathic condition, wherein an amount of oligomeric α-synuclein greater than an amount of oligomeric α-synuclein in a normal subject indicates the presence of the synucleopathic condition.

34. The method of claim **3**, wherein the synucleopathic condition is Parkinson's Disease, Lewy Body Dementia or multiple system atrophy.

35. The method of claim **33** or **34**, wherein the blood sample is a plasma sample.

36. The method of claim **35**, further comprising storing the blood sample at -80 degrees C.

37. The method of claim **33**, wherein the oligomeric α-synuclein species measured is selected from a form having between 2 and 100 monomeric units, between 4 and 16 monomeric units, and no more than 30 monomeric units.

38. The method of claim **33**, wherein the oligomeric α-synuclein species measured is selected from a 10-mer, 11-mer, 12-mer, 13-mer, 14-mer, 15-mer, 16-mer, and 18-mer.

39. The method of claim **33**, wherein the amount of oligomeric α-synuclein is a normalized amount.

40. The method of claim **39**, wherein the amount is normalized against an amount of monomeric α-synuclein.

41. The method of claim **33**, wherein measuring comprises separating forms of oligomeric α-synuclein into a plurality of fractions.

42. The method of claim **41**, wherein separating comprises electrophoresis.

43. The method of claim **33**, wherein measuring comprises immunoassay or Western blot.

44. The method according to any one of claims **1 to 30** or claims **31 to 43** wherein the blood sample is stored at -80˚C.