HD striatum can occur (Ernst A *et al*., *Cell 156*:1072-1083 (2014)). Transcriptional dysregulation can be an early feature of HD; for example, expression of SEMA4D and its major CNS receptor, Plexin-B1, can be elevated in the HD striatum and cortex, but not cerebellum (Hodges *et al*., *Hum. Mol. Genet. 15*:965-977 (2006)).

[0009] Inhibition of SEMA4D signaling through anti-SEMA4D treatment represents a novel approach to therapy for HD. In particular aspects, work with the YAC128 transgenic mouse model of HD demonstrated that treatment with an anti-SEMA4D antibody ameliorated certain neuropathological effects, including striatal atrophy, cortical atrophy, and corpus callosum atrophy, and prevented testicular degeneration. Also, a subset of behavioral symptoms was improved in YAC128 mice treated with an anti-SEMA4D antibody, including reduced anxiety-like behavior and rescue of cognitive deficits. *See* Southwell AL, *et al*. *Neurobiol. Dis. 76*:46-56 (2015) and U.S. Patent No. 9,249,227, granted Feb. 2, 2016. Given the long time periods involved in the development of measurable HD symptoms and alleviation of those symptoms, there remains a need for a method of early, reproducible detection of whether a given therapy, in particular, anti-SEMA4D treatment will be effective in individuals genetically predisposed to develop HD.

SUMMARY

[0010] This disclosure provides a method for determining whether a semaphorin 4D (SEMA4D) antagonist antibody or antigen-binding fragment thereof could be effective in treating a neurodegenerative or neuroinflammatory disease, disorder, or injury.

[0010a] In one aspect, the disclosure refers to a method for determining whether a semaphorin 4D (SEMA4D) antagonist antibody or antigen-binding fragment thereof will be effective in treating a neurodegenerative or neuroinflammatory disease, disorder, or injury, comprising: (a) measuring the baseline level of glucose uptake in a sample obtained from the brain of a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury; (b) remeasuring the level of glucose uptake in a sample obtained from the subject's brain after that subject was administered the SEMA4D antagonist antibody or antigen-binding fragment thereof; and i. wherein administration of the SEMA4D antagonist antibody or fragment thereof is to be continued if an increase in glucose uptake over baseline is detected; or ii. wherein administration of the SEMA4D antagonist antibody or fragment thereof is to be discontinued if no change or a decrease in glucose uptake relative to baseline is detected.

[0010b] In another aspect, the present disclosure refers to a method for determining an effective dose of a semaphorin 4D (SEMA4D) antagonist antibody or antigen-binding fragment thereof for treating a neurodegenerative or neuroinflammatory disease, disorder, or injury, comprising: (a) measuring the level of glucose uptake in a sample obtained from the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of a starting dose of a SEMA4D antagonist antibody or antigen-binding fragment thereof; and i. adjusting the dose of the SEMA4D antagonist antibody or antigen-binding fragment thereof to be administered if an increase in glucose uptake over baseline is detected, the adjustment determined on the level of increase, or ii. discontinuing administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected.

[0010c] In another aspect, the present disclosure refers to the use of a SEMA4D antagonist antibody or antigen-binding fragment thereof in the manufacture of medicament for treating a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury, comprising: (a) measuring the level of glucose uptake in a sample obtained from the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof; and i. wherein administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof is to be continued if an increase in glucose uptake over baseline is detected; or ii. wherein administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof is to be discontinued if no change or a decrease in glucose uptake relative to baseline is detected.

[0010d] In another aspect, the present disclosure refers to a method for determining whether a semaphorin 4D (SEMA4D) antagonist antibody or antigen-binding fragment thereof will be effective in treating a neurodegenerative or neuroinflammatory disease, disorder, or injury, comprising: (a) ordering the measurement of the level of glucose uptake in a sample obtained from the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof; and i. wherein administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof is to be continued if an increase in glucose uptake over baseline is detected; or ii. wherein administration of the

SEMA4D antagonist antibody or antigen-binding fragment thereof is to be discontinued if no change or a decrease in glucose uptake relative to baseline is detected.

[0011] In one example the method includes administering an effective amount of a SEMA4D antagonist antibody or antigen-binding fragment thereof to a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury; measuring the level of glucose uptake in the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of the SEMA4D antagonist; and continuing administration of the SEMA4D antagonist antibody or fragment thereof if an increase in glucose uptake over baseline is detected; or discontinuing administration of the SEMA4D antagonist antibody or fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected.

[0012] In another example the method includes measuring the baseline level of glucose uptake in the brain of a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury; administering an effective amount of a SEMA4D antagonist antibody or antigen-binding fragment thereof to the subject; remeasuring the level of glucose uptake in the subject's brain following administration of the SEMA4D antagonist antibody or fragment thereof; and continuing administration of the SEMA4D antagonist antibody or fragment thereof if an increase in glucose uptake over baseline is detected; or discontinuing administration of the SEMA4D antagonist antibody or fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected.

[0013] In another example the method includes administering a starting dose of a SEMA4D antagonist antibody or antigen-binding fragment thereof to a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury; measuring the level of glucose uptake in the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of the SEMA4D antagonist; and adjusting the dose of the SEMA4D antagonist antibody or fragment thereof if an increase in glucose uptake over baseline is detected, the adjustment determined on the level of increase, or discontinuing administration of the SEMA4D antagonist antibody or fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected. According to this example the method can further include increasing the dose of SEMA4D antagonist antibody relative to that tested in step (b) and remeasuring the change in level of glucose uptake relative to a

new baseline in a different previously untreated patient or in the same patient following withdrawal of treatment in the same patient for a period of time determined to allow accumulation of a historical deficit in that neurodegenerative or neuroinflammatory disease, disorder, or injury, and further adjusting the dose of the SEMA4D antagonist antibody if a further increase is detected.

[0014] In another example the method includes measuring the baseline level of glucose uptake in the brain of a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury; administering a starting dose of a SEMA4D antagonist antibody or antigen-binding fragment thereof to the subject; remeasuring the level of glucose uptake in the subject's brain following administration of the SEMA4D antagonist antibody or fragment thereof; and adjusting the dose of the SEMA4D antagonist antibody or fragment thereof if an increase in glucose uptake over baseline is detected, the adjustment determined on the level of increase, or discontinuing administration of the SEMA4D antagonist antibody or fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected. According to this example the method can further include increasing the dose of SEMA4D antagonist antibody relative to that tested in step (c) and remeasuring the change in level of glucose uptake relative to a new baseline in a different previously untreated patient or in the same patient following withdrawal of treatment in the same patient for a period of time determined to allow accumulation of a historical deficit in that neurodegenerative or neuroinflammatory disease, disorder, or injury, and further adjusting the dose of the SEMA4D antagonist antibody if a further increase is detected.

[0015] In another example the method includes administering a SEMA4D antagonist antibody or antigen-binding fragment thereof to a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury; measuring the level of glucose uptake in the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of SEMA4D antagonist; and continuing administration of the SEMA4D antagonist antibody or fragment thereof if an increase in glucose uptake over baseline is detected; or discontinuing administration of the SEMA4D antagonist antibody or fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected.

[0016] In another example the method includes measuring the baseline level of glucose uptake in the brain of a subject having, determined to have, or suspected of having a

neurodegenerative or neuroinflammatory disease, disorder, or injury; administering a SEMA4D antagonist antibody or antigen-binding fragment thereof to the subject; remeasuring the level of glucose uptake in the subject's brain following administration of the SEMA4D antagonist antibody or fragment thereof; and continuing administration of the SEMA4D antagonist antibody or fragment thereof if an increase in glucose uptake over baseline is detected; or discontinuing administration of the SEMA4D antagonist antibody or fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected.

[0017] In another example the method includes administering a SEMA4D antagonist antibody or antigen-binding fragment thereof to a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury; ordering the measurement of the level of glucose uptake in the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of the SEMA4D antagonist; and continuing administration of the SEMA4D antagonist antibody or fragment thereof if an increase in glucose uptake over baseline is detected; or discontinuing administration of the SEMA4D antagonist antibody or fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected.

[0018] In another example the method includes ordering the measurement of a baseline level of glucose uptake in the brain of a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury; administering a SEMA4D antagonist antibody or antigen-binding fragment thereof to the subject; ordering remeasurement of the level of glucose uptake in the subject's brain following administration of the SEMA4D antagonist antibody or fragment thereof; and continuing administration of the SEMA4D antagonist antibody or fragment thereof if an increase in glucose uptake over baseline is detected; or discontinuing administration of the SEMA4D antagonist antibody or fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected.

[0019] In another example the method includes measuring the baseline level of glucose uptake in the brain of a subject presented as having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury; and remeasuring the level of glucose uptake in the subject's brain following administration or a SEMA4D antagonist antibody or antigen-binding fragment thereof to the subject by a healthcare provider; and instructing the healthcare provider to continue administration of

the SEMA4D antagonist antibody or fragment thereof if an increase in glucose uptake over baseline is detected; or instructing the healthcare provider to discontinue administration of the SEMA4D antagonist antibody or fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected.

[0020] In certain examples, the SEMA4D antagonist antibody or fragment thereof for use in the provided method inhibits SEMA4D interaction with its receptor, e.g., Plexin-B1, Plexin-B2, or CD72. In certain examples the SEMA4D antagonist antibody or fragment thereof inhibits SEMA4D-mediated Plexin-B1 signal transduction.

[0021] In certain example the SEMA4D antagonist antibody or fragment thereof for use in the provided method competitively inhibits a reference antibody that includes a variable heavy chain region (VH) including the amino acid sequence SEQ ID NO: 1 and a variable light chain region (VL) including the amino acid sequence SEQ ID NO: 5 from binding to SEMA4D. In certain examples the SEMA4D antagonist antibody or fragment thereof for use in the provided method binds to the same SEMA4D epitope as a reference antibody that includes a VH including the amino acid sequence SEQ ID NO: 1 and a VL including the amino acid sequence SEQ ID NO: 5.

[0022] In certain examples the SEMA4D antagonist antibody for use in the provided method has a VH and a VL, where the VH includes three complementarity determining regions (CDRs) HCDR1, HCDR2, and HCDR3, where the VL has three CDRs LCDR1, LCDR2, and LCDR3, and where the CDRs include the amino acid sequences SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8, respectively except for at least one or two single conservative amino acid substitutions in one or more of the CDRs. In certain examples the SEMA4D antagonist antibody for use in the provided method has a VH and a VL, where the VH includes three complementarity determining regions (CDRs) HCDR1, HCDR2, and HCDR3, where the VL includes three CDRs LCDR1, LCDR2, and LCDR3, and where the CDRs include the amino acid sequences SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8, respectively. In certain examples the VH has an amino acid sequence at least 90% identical to SEQ ID NO: 1 and the VL has an amino acid sequence at least 90% identical to SEQ ID NO: 5. In certain examples the VH includes the amino acid sequence SEQ ID NO: 1 and the VL includes the amino acid sequence SEQ ID NO: 5.

[0023] In certain examples of the provided method, a first dose of the SEMA4D antagonist antibody is administered, and then the SEMA4D antagonist antibody is

administered at least once every week, at least once every two weeks, at least once every three weeks, at least once a month, or at least once every two months thereafter.

[0024] In certain examples of the provided method, the baseline measurement of glucose uptake is measured just prior to the first dose of the SEMA4D antagonist antibody. In certain examples of the provided method, the change in glucose uptake relative to baseline is measured at least one week after the first dose, at least two weeks after the first dose, at least one month after the first dose, at least two months after the first dose, at least three months after the first dose, at least four months after the first dose, at least five months after the first dose, at least six months after the first dose, or any combination thereof.

[0025] In certain examples of the provided method, glucose uptake in the subject's brain is measured by ^{18}F- Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) imaging.

[0026] In certain examples of the provided method, the subject is a human. In certain examples of the provided method, the neurodegenerative or neuroinflammatory disease, disorder or injury is Alzheimer's disease, Parkinson's disease, Huntington's disease, Down syndrome, ataxia, amyotrophic lateral sclerosis (ALS), multiple sclerosis, (MS), epilepsy, meningitis, brain edema, spinal cord injury, traumatic brain injury, frontotemporal dementia (FTD), HIV-related cognitive impairment, CNS Lupus, mild cognitive impairment, or a combination thereof.

[0027] In certain examples of the provided method, the neurodegenerative or neuroinflammatory disease, disorder or injury is Huntington's disease (HD). In certain examples the subject is at risk of developing HD due to familial history of HD or genetic testing, for example, where genetic testing reveals 36 or more CAG repeats in the subject's HTT gene. In certain examples the subject is suspected of having HD due to mild motor dysfunction, mild cognitive impairment, or mild neuropsychiatric features. In certain examples the subject is diagnosed as having HD due to brain atrophy, an elevated Uniform Huntington's Disease Rating Scale score (UHDRS), an increased Huntington's Disease Cognitive Assessment Battery (HD-CAB) score, an increased Huntington's Disease Quantitative Motor Assessment score or a combination thereof. In certain examples the subject is in the presymptomatic, early prodromal, late prodromal, early manifest, moderate manifest, or advanced manifest stage of HD.

BRIEF DESCRIPTION OF THE DRAWINGS/FIGURES

[0028] **FIGURE 1** is a schematic of the treatment plan for Cohort A of the SIGNAL clinical study.

[0029] **FIGURE 2** is a schematic and timeline showing the various "groups" of patients to be compared in Cohort A of the SIGNAL clinical study: VV(7-0) is the group treated with VX15 during the first six-month blinded portion of the study; PV(7-0) is the group treated with placebo during the first six-month blinded portion of the study; VV(12-7) is the group treated with VX15 from the beginning of the study, evaluated for the period starting with month 7 through month 11; PV(12-7) is the group that received placebo for the first 6 months of the study and then crossed over at the beginning of month 7 to receive VX15, evaluated for the period starting with month 7 through month 11; VV(12-0) is the group treated with VX15 for the entire study, evaluated from day 0 through month 11; and PV(12-0) is the group that received placebo for the first 6 months of the study and then crossed over at the beginning of month 7 to receive VX15, evaluated for the period starting with day 0 through month 11.

WHAT IS CLAIMED IS:

1. A method for determining whether a semaphorin 4D (SEMA4D) antagonist antibody or antigen-binding fragment thereof will be effective in treating a neurodegenerative or neuroinflammatory disease, disorder, or injury, comprising:

(a) measuring the baseline level of glucose uptake in a sample obtained from the brain of a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury;

(b) remeasuring the level of glucose uptake in a sample obtained from the subject's brain after that subject was administered the SEMA4D antagonist antibody or antigen-binding fragment thereof; and

i. wherein administration of the SEMA4D antagonist antibody or fragment thereof is to be continued if an increase in glucose uptake over baseline is detected; or

ii. wherein administration of the SEMA4D antagonist antibody or fragment thereof is to be discontinued if no change or a decrease in glucose uptake relative to baseline is detected.

2. A method for determining an effective dose of a semaphorin 4D (SEMA4D) antagonist antibody or antigen-binding fragment thereof for treating a neurodegenerative or neuroinflammatory disease, disorder, or injury, comprising:

(a) measuring the level of glucose uptake in a sample obtained from the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of a starting dose of a SEMA4D antagonist antibody or antigen-binding fragment thereof; and

i. adjusting the dose of the SEMA4D antagonist antibody or antigen-binding fragment thereof to be administered if an increase in glucose uptake over baseline is detected, the adjustment determined on the level of increase, or

ii. discontinuing administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof if no change or a decrease in glucose uptake relative to baseline is detected.

3. The method of claim 2, further comprising that the dose of SEMA4D antagonist antibody is to be increased relative to that tested in step (b) and remeasuring the change in level of glucose uptake relative to a new baseline in a different previously untreated patient or in the same patient following withdrawal of treatment in the same patient for a period of time determined to allow accumulation of a historical deficit in that neurodegenerative or neuroinflammatory disease, disorder, or injury, and further adjusting the dose of the SEMA4D antagonist antibody to be administered if a further increase is detected.

4. Use of a SEMA4D antagonist antibody or antigen-binding fragment thereof in the manufacture of medicament for treating a subject having, suspected of having, or at risk of developing a neurodegenerative or neuroinflammatory disease, disorder, or injury, comprising:

(a) measuring the level of glucose uptake in a sample obtained from the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof; and

i. wherein administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof is to be continued if an increase in glucose uptake over baseline is detected; or

ii. wherein administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof is to be discontinued if no change or a decrease in glucose uptake relative to baseline is detected.

5. A method for determining whether a semaphorin 4D (SEMA4D) antagonist antibody or antigen-binding fragment thereof will be effective in treating a neurodegenerative or neuroinflammatory disease, disorder, or injury, comprising:

(a) ordering the measurement of the level of glucose uptake in a sample obtained from the subject's brain relative to a baseline level of glucose uptake in the subject's brain measured prior to administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof; and

i. wherein administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof is to be continued if an increase in glucose uptake over baseline is detected; or

ii. wherein administration of the SEMA4D antagonist antibody or antigen-binding fragment thereof is to be discontinued if no change or a decrease in glucose uptake relative to baseline is detected.

6. The method of any one of claims 1 to 3 and 5 or the use of claim 4, wherein the SEMA4D antagonist antibody or antigen-binding fragment thereof inhibits SEMA4D interaction with its receptor.

7. The method or the use of claim 6, wherein the receptor is Plexin-B1, Plexin-B2, or CD72.

8. The method of any one of claims 1-3, and 5 to 7, or the use of any one of claims 4 and 6 to 7, wherein the SEMA4D antagonist antibody or antigen-binding fragment thereof inhibits SEMA4D-mediated Plexin-B1 signal transduction.

9. The method of any one of claims 1-3 and 5 to 8, or the use of any one of claims 4 and 6 to 8, wherein the SEMA4D antagonist antibody or antigen-binding fragment thereof competitively inhibits a reference antibody comprising a variable heavy chain region (VH) comprising the amino acid sequence SEQ ID NO: 1 and a variable light chain region (VL) comprising the amino acid sequence SEQ ID NO: 5 from binding to SEMA4D.

10. The method of any one of claims 1 to 3 and 5 to 9, or the use of any one of claims 4 and 6 to 9, wherein the SEMA4D antagonist antibody or antigen-binding fragment thereof binds to the same SEMA4D epitope as a reference antibody comprising a VH comprising the amino acid sequence SEQ ID NO: 1 and a VL comprising the amino acid sequence SEQ ID NO: 5.

11. The method or use of claim 9 or claim 10, wherein the SEMA4D antagonist antibody comprises a VH and a VL, wherein the VH comprises three complementarity determining regions (CDRs) HCDR1, HCDR2, and HCDR3, wherein the VL comprises

three CDRs LCDR1, LCDR2, and LCDR3, and wherein the CDRs comprise the amino acid sequences SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8, respectively except for at least one or two single conservative amino acid substitutions in one or more of the CDRs.

12. The method or use of claim 9 or claim 10, wherein the SEMA4D antagonist antibody comprises a VH and a VL, wherein the VH comprises three complementarity determining regions (CDRs) HCDR1, HCDR2, and HCDR3, wherein the VL comprises three CDRs LCDR1, LCDR2, and LCDR3, and wherein the CDRs comprise the amino acid sequences SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8, respectively.

13. The method or use of any one of claims 9 to 12, wherein the VH comprises an amino acid sequence at least 90% identical to SEQ ID NO: 1 and the VL comprises an amino acid sequence at least 90% identical to SEQ ID NO: 5.

14. The method or use of claim 13, wherein the VH comprises the amino acid sequence SEQ ID NO: 1 and the VL comprises the amino acid sequence SEQ ID NO: 5.

15. The method of any one of claims 1 to 3 and 5 to 14, or the use of any one of claims 4 and 6 to 14, wherein a first dose of the SEMA4D antagonist antibody is to be administered, and then the SEMA4D antagonist antibody is to be administered at least once every week, at least once every two weeks, at least once every three weeks, at least once a month, or at least once every two months thereafter.

16. The method or use of claim 15 wherein the change in glucose uptake relative to baseline is measured at least one week after the first dose, at least two weeks after the first dose, at least one month after the first dose, at least two months after the first dose, at least three months after the first dose, at least four months after the first dose, at least five months after the first dose, at least six months after the first dose, or any combination thereof.

17. The method of any one of claims 1 to 3 and 5 to 16, or the use of any one of claims 4 and 6 to 16, wherein glucose uptake in the subject's brain is measured by 18F-Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) imaging.

18. The method of any one of claims 1 to 3 and 5 to 17, or the use of any one of claims 4 and 6 to 17, wherein the subject is a human.

19. The method of any one of claims 1 to 3 and 5 to 18, or the use of any one of claims 4 and 6 to 18, wherein the neurodegenerative or neuroinflammatory disease, disorder or injury is Alzheimer's disease, Parkinson's disease, Huntington's disease, Down syndrome, ataxia, amyotrophic lateral sclerosis (ALS), multiple sclerosis, (MS), epilepsy, meningitis, brain edema, spinal cord injury, traumatic brain injury, frontotemporal dementia (FTD), HIV-related cognitive impairment, CNS Lupus, mild cognitive impairment, or a combination thereof.

20. The method or use of claim 19 wherein the neurodegenerative or neuroinflammatory disease, disorder or injury is Huntington's disease (HD).

21. The method or use of claim 20, wherein the subject is at risk of developing HD due to familial history of HD or genetic testing.

22. The method of or use claim 21, wherein genetic testing reveals 36 or more CAG repeats in the subject's HTT gene.

23. The method or use of any one of claims 20 to 22, wherein the subject is suspected of having HD due to mild motor dysfunction, mild cognitive impairment, or mild neuropsychiatric features.

24. The method or use of any one of claims 20 to 23, wherein the subject is diagnosed as having HD due to brain atrophy, an elevated Uniform Huntington's Disease Rating Scale score (UHDRS), an increased Huntington's Disease Cognitive Assessment Battery (HD-CAB) score, an increased Huntington's Disease Quantitative Motor Assessment score or a combination thereof.

25. The method or use of claim 24, wherein the subject is in the presymptomatic, early prodromal, late prodromal, early manifest, moderate manifest, or advanced manifest stage of HD.