

WHAT IS CLAIMED IS:

1. A method comprising
 - a. obtaining a biological sample from a subject;
 - b. contacting the sample with highly purified VP1 particles (HPVLPs)
 - 5 under conditions suitable for binding of a JC Virus (JCV) antibody in the sample to an HPVLP;
 - c. detecting the level of JCV antibody binding in the sample to HPVLPs;
 - and
 - d. correlating the detected level with a reference set, wherein the
 - 10 reference set is selected to indicate a false negative rate not greater than 3%.
2. The method of claim 1, wherein the false negative rate is not greater than 1%.
3. The method of claim 1, wherein at least 20% of the HPVLPs comprise more
- 15 than five VP1 polypeptides in an HPVLP.
4. The method of claim 1, wherein at least 70% of the HPVLPs comprise more than five VP1 polypeptides in an HPVLP.
- 20 5. The method of claim 1, wherein the HPVLPs are immobilized on a solid substrate.
6. The method of claim 1, wherein an HPVLP consists essentially of VP1 polypeptides.
- 25 7. The method of claim 1, wherein an HPVLP further comprises at least one of a VP2, or a VP3.
8. The method of claim 1, wherein the VP1 in the HPVLP is a recombinant VP1.
- 30

9. The method of claim 1, wherein at least one VP1 in the HPVLP is a mutant VP1.

5 10. The method of claim 1, wherein the biological sample is serum.

11. The method of claim 1, wherein the sample is from a subject prescribed an immunomodulator, a subject considering taking an immunomodulator, or a subject suspected of having Progressive Multifocal Leukoencephalopathy (PML).

10 12. The method of claim 1, wherein detection of JCV antibody binding to the HPVLPs indicates that the subject is at an increased risk of PML.

13. The method of claim 1, wherein detection of JCV antibody binding to the HPVLPs indicates that the subject is not a candidate to receive treatment with an immunomodulator.

14. The method of claim 1, wherein failure to detect JCV antibody binding to HPVLPs indicates that the subject is a candidate to receive treatment with an immunomodulator.

15. The method of claim 1, wherein detection of JCV antibody binding to the HPVLPs indicates that the subject is a candidate to receive treatment with an immunomodulator and enhanced monitoring for adverse symptoms upon treatment with the immunomodulator.

16. The method of claim 15, wherein the adverse symptoms indicate the development of PML.

17. The method of claim 14, wherein the subject identified to receive treatment with the immunomodulator is further administered the immunomodulator.

18. The method of claim 1, wherein a subject having a biological sample determined not to have JCV antibodies in an initial testing is re-tested at least annually for the presence of JCV antibodies after the initial testing.

5 19. The method of claim 1, wherein a subject having a biological sample determined to have JCV antibodies, is subsequently determined at a later date not to have JCV antibodies.

10 20. The method of claim 19, wherein the subject is determined to be a candidate to receive treatment with an immunomodulator.

21. The method of claim 20, wherein the subject receives enhanced monitoring for adverse symptoms upon treatment with the immunomodulator.

15 22. The method of claim 11, or 13 to 15, wherein the immunomodulator is natalizumab.

20 23. The method of claim 11, wherein the subject prescribed an immunomodulator, or considering taking an immunomodulator, has not previously been administered the immunomodulator.

24. The method of claim 11, wherein the subject has previously received one or more doses of the immunomodulator.

25 25. The method of claim 1, further comprising
e. contacting a portion of the biological sample from the subject with HPVLP in a solution prior to step (b) and wherein the HPVLP of step (b) is attached to a solid substrate, thereby providing a secondary sample;

30 f. contacting the secondary sample with HPVLP under the same conditions as (b);

g. detecting the level of JCV antibody binding to HPVLP in the secondary sample; and

h. comparing the detected level of JCV antibody in the secondary sample to the level of binding in the biological sample when incubated with the solution without HPVLP, wherein a decrease in the detected level in the sample pre-incubated with HPVLP compared to the solution-incubated sample indicates that the sample is positive for a JCV antibody and no change in the detected level indicates that there is no JCV antibody present in the sample.

26. The method of claim 25, validated for use in MS and CD patients.

27. A kit comprising HPVLPs and at least one reagent for performing an assay to identify JCV antibody levels.

28. A solution comprising VP1 particles, consisting essentially of VP1-containing particles that are greater in size than a VP1 pentamer.

29. A method of preparing a solution of VP1 particles, the method comprising removing VP1 particles from the solution that are the size of a VP1 pentamer or less.

30. A method of identifying a subject at risk of developing PML, the method comprising

a. obtaining a biological sample from the subject;

b. contacting the biological sample with highly purified VP1 particles (HPVLPs) under conditions suitable for binding of a JC Virus (JCV) antibody in the sample to an HPVLP;

c. detecting the level of JCV antibody binding in the sample to HPVLPs;

and

d. correlating the detected level with a reference set, wherein the subject is at increased risk of PML if JCV antibody binding is detected.

31. The method of claim 29, wherein the reference set is selected to indicate a false negative rate not greater than 3%.

32. A method of identifying PML risk in a subject, the method comprising
5 a. determining the level of anti-JCV antibodies in a sample from the subject; and
 b. assigning a risk level to the subject according to the level of anti-JCV antibodies in the sample.

10 33. The method of claim 32, wherein the subject is receiving an anti-VLA4 treatment or is a candidate for receiving an anti-VLA4 treatment.

34. The method of claim 33, wherein the anti-VLA4 treatment is natalizumab.

15 35. The method of claim 32, wherein the subject has been diagnosed with multiple sclerosis or Crohn's disease.

36. The method of claim 32, wherein the level of anti-JCV antibodies is determined using a one-step assay or a two-step assay.

20 37. The method of claim 36, wherein the one-step assay or the two-step assay comprises an ELISA assay.

38. The method of claim 32, further comprising
25 c. determining the level of anti-JCV antibodies in the subject in a sample from a date subsequent to the initial sample of step (a);
 d. comparing the level of anti-JCV antibodies in the sample from the subsequent date to the level in the sample from the initial sample of step (a); and
 e. determining whether the subject is at increased risk of PML at the
30 subsequent date compared to the time of initial sample of step (a).

39. A method of monitoring PML risk in a subject, the method comprising
- a. determining the level of anti-JCV antibodies in a subject using a sample from a first date;
 - b. assigning a risk of PML based on the level of anti-JCV antibodies in the subject on the first date;
 - c. determining the level of anti-JCV antibodies in the subject using a sample from a second date; and
 - d. assigning a risk of PML based on the level of anti-JCV antibodies in the subject on the second date.
40. A method of making a preparation comprising HPVLPs comprising:
- a. providing a cell comprising a VP1 nucleic acid;
 - b. culturing the cell under conditions to express VP1;
 - c. lysing the cells;
 - d. treating the cell lysate with a nuclease;
 - e. precipitating cell debris from the lysate;
 - f. removing contaminating proteins by salt precipitation;
 - g. concentrating the VP1-containing supernatant;
 - h. diafiltering the concentrated VP1-containing supernatant; and
 - i. purifying the VP1-containing solution through ion-exchange purification, thereby making a preparation comprising HPVLPs.

WHAT IS CLAIMED IS:

1. An invention not claimed in any divisional application.