

What is claimed is:

1. A method of treating or preventing multiple sclerosis (MS) in a subject, comprising administering to the subject autologous cytotoxic T cells (CTLs) expressing a T cell receptor that specifically binds to an EBV peptide presented on a class I MHC.
2. The method of claim 1, wherein at least 5% of the CTLs express CD107a.
3. The method of claim 1, wherein at least 10% of the CTLs express CD107a.
4. The method of claim 1, wherein at least 15% of the CTLs express CD107a.
5. The method of claim 1, wherein at least 20% of the CTLs express CD107a.
6. The method of any one of claims 1 to 5, wherein at least 5% of the CTLs express IFN γ .
7. The method of claim 6, wherein at least 10% of the CTLs express IFN γ .
8. The method of claim 7, wherein at least 15% of the CTLs express IFN γ .
9. The method of claim 8, wherein at least 20% of the CTLs express IFN γ .
10. The method of any one of claims 1 to 9, wherein at least 5% of the CTLs express TNF.
11. The method of claim 10, wherein at least 10% of the CTLs express TNF.
12. The method of claim 11, wherein at least 15% of the CTLs express TNF.
13. The method of claim 12, wherein at least 20% of the CTLs express TNF.
14. The method of any one of claims 1 to 13, wherein at least 1% of the CTLs express IL-2.
15. The method of claim 14, wherein at least 5% of the CTLs express IL-2.
16. The method of claim 15, wherein at least 10% of the CTLs express IL-2.
17. The method of claim 16, wherein at least 15% of the CTLs express IL-2.
18. The method of claim 1, wherein at least 30% of the CTLs express CD107a, IFN γ , TNFa, and IL-2.
19. The method of claim 1, wherein at least 40% of the CTLs express CD107a, IFN γ , TNFa, and IL-2.
20. The method of claim 1, wherein at least 50% of the CTLs express CD107a, IFN γ , TNFa, and IL-2.

21. The method of claim 1, wherein at least 70% of the CTLs express CD107a, IFN γ , TNF α , and IL-2.
22. The method of any preceding claim, wherein the CTLs have at least 5% EBV reactivity.
23. The method of claim 22, wherein the CTLs have at least 7% EBV reactivity.
24. The method of claim 23, wherein the CTLs have at least 10% EBV reactivity.
25. The method of claim 24, wherein the CTLs have at least 15% EBV reactivity.
26. The method of claim 25, wherein the CTLs have at least 20% EBV reactivity.
27. The method of claim 26, wherein the CTLs have at least 30% EBV reactivity.
28. A method of treating or preventing multiple sclerosis (MS) in a subject comprising:
 - a) isolating a sample comprising cytotoxic T cells (CTLs) expressing a T cell receptor that specifically binds to an EBV peptide presented on a class I MHC from the subject;
 - b) administering the CTLs to the subject.
29. A method of treating or preventing MS in a subject, comprising:
 - a) incubating a sample comprising autologous cytotoxic T cells (CTLs) with antigen-presenting cells (APCs) presenting an EBV peptide, thereby inducing proliferation of peptide-specific T cells in the sample;
 - b) administering the peptide-specific autologous CTLs to the subject.
30. A method of treating or preventing MS in a subject, comprising:
 - a) incubating antigen-presenting cells (APCs) with a nucleic acid construct encoding for an EBV peptide, thereby inducing the APCs to present an EBV peptide;
 - b) inducing peptide-specific CTL proliferation by incubating a sample comprising autologous CTLs with the antigen-presenting cells (APCs), thereby inducing the autologous CTLs to proliferate; and
 - c) administering the peptide-specific autologous CTLs to the subject.
31. The method of claim 30, wherein the nucleic acid construct is a viral vector.
32. The method of claim 31, wherein the viral vector is AdE1-LMPpoly.
33. The method of any one of claims 29 to 32, wherein the method further comprises analyzing the expression of CD107a by the proliferated peptide-specific autologous CTLs, and, if at least 5% of the proliferated peptide-specific autologous CTLs express CD107a, administering the peptide-specific autologous CTLs to the subject.

34. The method of claim 33, wherein the CTLs are administered if at least 10% of the proliferated peptide-specific autologous CTLs in the sample express CD107a.
35. The method of claim 33 or 34, wherein the CTLs are administered if at least 15% of the proliferated peptide-specific autologous CTLs in the sample express CD107a.
36. The method of any one of claims 33 to 35, wherein the CTLs are administered if at least 20% of the proliferated peptide-specific autologous CTLs in the sample express CD107A.
37. The method of any one of claims 29 to 36, wherein the method further comprises analyzing the expression of IFN γ by the proliferated peptide-specific autologous CTLs, and, if at least 5% of the proliferated peptide-specific autologous CTLs express IFN γ , administering the peptide-specific autologous CTLs to the subject.
38. The method of claim 37, wherein the CTLs are administered if at least 10% of the proliferated peptide-specific autologous CTLs in the sample express IFN γ .
39. The method of claim 37 or 38, wherein the CTLs are administered if at least 15% of the proliferated peptide-specific autologous CTLs in the sample express IFN γ .
40. The method of any one of claims 37 to 39, wherein the CTLs are administered if at least 20% of the proliferated peptide-specific autologous CTLs in the sample express IFN γ .
41. The method of any one of claims 29 to 40, wherein the method further comprises analyzing the expression of TNF by the proliferated peptide-specific autologous CTLs, and, if at least 5% of the proliferated peptide-specific autologous CTLs express TNF, administering the peptide-specific autologous CTLs to the subject.
42. The method of claim 41, wherein the CTLs are administered if at least 10% of the proliferated peptide-specific autologous CTLs in the sample express TNF.
43. The method of claim 41 or 42, wherein the CTLs are administered if at least 15% of the proliferated peptide-specific autologous CTLs in the sample express TNF.
44. The method of any one of claims 41 to 43, wherein the CTLs are administered if at least 20% of the proliferated peptide-specific autologous CTLs in the sample express TNF.
45. The method of any one of claims 29 to 44, wherein the method further comprises analyzing the expression of IL-2 by the proliferated peptide-specific autologous CTLs, and, if at least 1% of the proliferated peptide-specific autologous CTLs express IL-2, administering the peptide-specific autologous CTLs to the subject.

46. The method of claim 45, wherein the CTLs are administered if at least 5% of the peptide-specific autologous CTLs in the sample express IL-2.
47. The method of claim 45 or 46, wherein the CTLs are administered if at least 10% of the peptide-specific autologous CTLs in the sample express IL-2.
48. The method of any one of claims 45 to 47, wherein the CTLs are administered if at least 15% of the proliferated peptide-specific autologous CTLs in the sample express IL-2.
49. The method of any one of claims 29 to 32, wherein the method further comprises analyzing the expression of CD107a, TNF, IFN γ , and IL-2 by the proliferated peptide-specific autologous CTLs, and, if at least 20% of the proliferated peptide-specific autologous CTLs express CD107a, TNF, IFN γ , and IL-2, administering the peptide-specific autologous CTLs to the subject.
50. The method of claim 49, wherein the CTLs are administered if at least 30% of the proliferated peptide-specific autologous CTLs in the sample express CD107a, TNF, IFN γ , and IL-2.
51. The method of claim 49 or 50, wherein the CTLs are administered if at least 40% of the proliferated peptide-specific autologous CTLs in the sample express CD107a, TNF, IFN γ , and IL-2.
52. The method of any one of claims 49 to 51, wherein the CTLs are administered if at least 50% of the proliferated peptide-specific autologous CTLs in the sample express CD107a, TNF, IFN γ , and IL-2.
53. The method of any one of claims 29 to 52, wherein the method further comprises analyzing the EBV reactivity of the proliferated peptide-specific autologous CTLs, and, if the reactivity is above a predetermined threshold, administering the peptide-specific autologous CTLs to the subject.
54. The method of claim 53, wherein the threshold is 5%.
55. The method of claim 53, wherein the threshold is 7%.
56. The method of claim 53, wherein the threshold is 10%.
57. The method of claim 53, wherein the threshold is 20%.
58. The method of claim 53, wherein the threshold is 30%.
59. The method of claim 53, wherein the threshold is 50%.

60. The method of any one of claims 29 to 59, wherein the sample is incubated with one or more cytokines in step (a).
61. The method of any one of claims 29 to 60, wherein the APCs comprise B cells.
62. The method of any one of claims 29 to 61, wherein the APCs comprise antigen-presenting T-cells.
63. The method of any one of claims 29 to 62, wherein the APCs comprise dendritic cells.
64. The method of any one of claims 29 to 63, wherein the APCs comprise artificial antigen-presenting cells.
65. The method of claim 64, wherein the artificial antigen-presenting cells are aK562 cells.
66. The method of any one of claims 28 to 65, wherein the sample comprises peripheral blood mononuclear cells (PBMCs).
67. The method of any one of claims 1 to 66, further comprising obtaining the sample from the subject.
68. The method of any one of claims 1 to 67, wherein the EBV peptide comprises an amino acid sequence listed in Table 1.
69. The method of any one of claims 1 to 67, wherein the EBV peptide comprises a LMP1 peptide or fragment thereof.
70. The method of any one of claims 1 to 67, wherein the EBV peptide comprises a LMP2A peptide or fragment thereof.
71. The method of any one of claims 1 to 67, wherein the EBV peptide comprises an EBNA1 peptide or fragment thereof.
72. The method of any one of the preceding claims, comprising administering about 5×10^6 CTLs to the subject in a dose.
73. The method of any one of claims 1 to 71, comprising administering about 1×10^7 CTLs to the subject in a dose.
74. The method of any one of claims 1 to 71, comprising administering about 1.5×10^7 CTLs to the subject in a dose.
75. The method of any one of claims 1 to 71, comprising administering about 2×10^7 CTLs to the subject in a dose.

76. The method of any one of the preceding claims, wherein multiple doses of CTLs are administered to the subject, e.g., in escalating doses.
77. The method of claim 76, wherein the doses are administered weekly.
78. The method of claim 76, wherein the doses are administered biweekly.
79. The method of claim 78, comprising administering four doses of successively higher numbers of CTLs.
80. The method of claim 79, comprising administering a first dose of 5×10^6 CTLs, a second dose of 1×10^7 CTLs, a third dose of 1.5×10^7 CTLs, and a fourth dose of 2×10^7 CTLs.
81. The method of any preceding claim, wherein the subject does not experience significant adverse effects as a result of CTL administration.
82. The method of any preceding claim, wherein the method further comprises assessing the efficacy of adoptive immunotherapy in a subject with multiple sclerosis, the method comprising:
- (a) obtaining a first sample of cerebral spinal fluid (CSF) from the subject,
 - (b) determining the amount of anti-EBV IgG in the CSF in the first sample before CTL administration,
 - (c) after a period of time, obtaining a second sample of CSF from the subject after CTL administration,
 - (d) determining the amount of anti-EBV IgG in the CSF in the second sample, and
if the amount of anti-EBV IgG in the second sample is less than the first sample, the disease has stabilized and/or not progressed.
83. The method of any one of the previous claims, wherein the MS is relapsing-remitting MS, secondary progressive MS, primary progressive MS, or progressively relapsing MS.
84. The method of claim 83, wherein the MS is primary progressive MS.
85. The method of any preceding claim, where the subject's motor skills/balance/manual dexterity, sleep, visual acuity or color vision, fatigue, and/or urinary urgency has improved after CTLs administration.
86. The method of any preceding claim, wherein the subject's EDSS score remains the same after CTL administration.

87. The method of any one of claims 1 to 85, wherein the subject's EDSS score decreases by at least 0.5 after CTL administration.
88. The method of any one of claims 1 to 85, wherein the subject's EDSS score decreases by at least 1.0 after CTL administration.
89. A method of reducing anti-EBV IgG levels in the CSF in a subject with MS comprising administering to the subject autologous cytotoxic T cells (CTLs) expressing a T cell receptor that specifically binds to an EBV peptide presented on a class I MHC.
90. A method of improving visual acuity, improving color vision, or stabilizing vision loss in a subject with MS, comprising administering to the subject autologous cytotoxic T cells (CTLs) expressing a T cell receptor that specifically binds to an EBV peptide presented on a class I MHC.
91. A method of improving motor skills, balance, or manual dexterity in a subject with MS, comprising administering to the subject autologous cytotoxic T cells (CTLs) expressing a T cell receptor that specifically binds to an EBV peptide presented on a class I MHC.
92. A method of improving sleep in a subject with MS, comprising administering to the subject autologous cytotoxic T cells (CTLs) expressing a T cell receptor that specifically binds to an EBV peptide presented on a class I MHC.
93. A method of treating or preventing fatigue in a subject with MS, comprising administering to the subject autologous cytotoxic T cells (CTLs) expressing a T cell receptor that specifically binds to an EBV peptide presented on a class I MHC.
94. A method of treating or preventing urinary urgency in a subject with MS, comprising administering to the subject autologous cytotoxic T cells (CTLs) expressing a T cell receptor that specifically binds to an EBV peptide presented on a class I MHC.
95. The method of any one of the preceding claims, wherein the MS is relapsing-remitting MS.
96. The method of any one of claims 1 to 94, where the MS is secondary progressive MS.
97. The method of any one of claims 1 to 94, where the MS is primary progressive MS.
98. The method of any one of claims 1 to 94, where the MS is primary progressive progressively relapsing MS.
99. A method of selecting a subject for adoptive immunotherapy, comprising:

(a) obtaining a sample comprising T cells from the subject,
(b) isolating the autologous T cells in the sample,
(c) determining the EBV reactivity of the autologous T cells in the sample, and if at least a threshold percentage of the autologous T cells are EBV reactive, selecting the subject for adoptive immunotherapy.

100. The method of claim 99, wherein the threshold is 1%.

101. The method of claim 99, wherein the threshold is 2%.

102. The method of claim 99, wherein the threshold is 3%.

103. The method of claim 99, wherein the threshold is 5%.

104. The method of claim 99, wherein the threshold is 10%.

105. The method of claim 99, wherein the threshold is 20%.

106. A method of selecting a subject for adoptive immunotherapy, comprising:

(a) obtaining a sample comprising T cells from the subject,
(b) isolating the autologous T cells in the sample,
(c) determining percent of autologous T cells in the sample that express CD107A,
and if at least a certain percentage of the autologous T cells express CD107A, selecting the subject for adoptive immunotherapy.

107. The method of claim 106, wherein if at least 1% of the autologous T cells express CD107A, selecting the subject for adoptive immunotherapy.

108. The method of claim 106, wherein if at least 3% of the autologous T cells express CD107A, selecting the subject for adoptive immunotherapy.

109. The method of claim 106, wherein if at least 5% of the autologous T cells express CD107A, selecting the subject for adoptive immunotherapy.

110. The method of claim 106, wherein if at least 10% of the autologous T cells express CD107A, selecting the subject for adoptive immunotherapy.

111. A method of selecting a subject for adoptive immunotherapy, comprising:

(a) obtaining a sample comprising T cells from the subject,
(b) isolating the autologous T cells in the sample,
(c) determining percent of autologous T cells in the sample that express TNF, and if at least a certain percentage of the autologous T cells express TNF, selecting the subject for adoptive immunotherapy.

112. The method of claim 111, wherein if at least 1% of the autologous T cells express TNF, selecting the subject for adoptive immunotherapy.
113. The method of claim 111, wherein if at least 3% of the autologous T cells express TNF, selecting the subject for adoptive immunotherapy.
114. The method of claim 111, wherein if at least 5% of the autologous T cells express TNF, selecting the subject for adoptive immunotherapy.
115. The method of claim 111, wherein if at least 10% of the autologous T cells express TNF, selecting the subject for adoptive immunotherapy.
116. A method of selecting a subject for adoptive immunotherapy, comprising:
- (a) obtaining a sample comprising T cells from the subject,
 - (b) isolating the autologous T cells in the sample,
 - (c) determining percent of autologous T cells in the sample that express IFN γ , and if at least a certain percentage of the autologous T cells express IFN γ , selecting the subject for adoptive immunotherapy.
117. The method of claim 116, wherein if at least 1% of the autologous T cells express IFN γ , selecting the subject for adoptive immunotherapy.
118. The method of claim 116, wherein if at least 3% of the autologous T cells express IFN γ , selecting the subject for adoptive immunotherapy.
119. The method of claim 116, wherein if at least 5% of the autologous T cells express IFN γ , selecting the subject for adoptive immunotherapy.
120. The method of claim 116, wherein if at least 10% of the autologous T cells express IFN γ , selecting the subject for adoptive immunotherapy.
121. A method of selecting a subject for adoptive immunotherapy, comprising:
- (a) obtaining a sample comprising T cells from the subject,
 - (b) isolating the autologous T cells in the sample,
 - (c) determining percent of autologous T cells in the sample that express IL-2, and if at least a certain percentage of the autologous T cells express IL-2, selecting the subject for adoptive immunotherapy.
122. The method of claim 116, wherein if at least 1% of the autologous T cells express IL-2, selecting the subject for adoptive immunotherapy.

123. The method of claim 116, wherein if at least 3% of the autologous T cells express IL-2, selecting the subject for adoptive immunotherapy.
124. The method of claim 116, wherein if at least 5% of the autologous T cells express IL-2, selecting the subject for adoptive immunotherapy.
125. The method of claim 116, wherein if at least 10% of the autologous T cells express IL-2, selecting the subject for adoptive immunotherapy.
126. A method of selecting a subject for adoptive immunotherapy, comprising:
- (a) obtaining a PMBC sample from the subject,
 - (b) isolating the autologous T cells in the sample,
 - (c) determining percent of autologous T cells in the sample that express CD107a, IFN γ , TNF α , and IL-2, and if at least a certain percentage of the autologous T cells express CD107a, IFN γ , TNF α , and IL-2, selecting the subject for adoptive immunotherapy.
127. The method of claim 126, wherein if at least 1% of the autologous T cells express CD107a, IFN γ , TNF α , and IL-2, selecting the subject for adoptive immunotherapy.
128. The method of claim 126, wherein if at least 3% of the autologous T cells express CD107a, IFN γ , TNF α , and IL-2, selecting the subject for adoptive immunotherapy.
129. The method of claim 126, wherein if at least 5% of the autologous T cells express CD107a, IFN γ , TNF α , and IL-2, selecting the subject for adoptive immunotherapy.
130. The method of claim 126, wherein if at least 10% of the autologous T cells express CD107a, IFN γ , TNF α , and IL-2, selecting the subject for adoptive immunotherapy.