

CLAIMS

We claim:

1. A polynucleotide encoding a polypeptide comprising:
 - 5 (a) at least one fragment of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 1,
 - 10 (b) at least one fragment of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 6,
 - 15 (c) at least one fragment of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 11, and
 - 20 (d) at least one fragment of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 13;wherein the polynucleotide is operatively linked to one or more sequences which direct expression of said polypeptide in a host cell.
2. The polynucleotide of claim 1, wherein the polypeptide further comprises at
25 least one fragment of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 21.
- 30 3. The polynucleotide of claims 1 or 2, wherein the polypeptide comprises:
 - (a) at least two fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,

at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 1,

(b) at least two fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,
5 at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 6,

(c) at least two fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
10 acids of SEQ ID NO: 11,

(d) at least two fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 13, or

(e) at least two fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 21.

20 4. The polynucleotide of any of the preceding claims, wherein the polypeptide comprises:

(a) at least three fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
25 acids of SEQ ID NO: 1,

(b) at least three fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 6,

(c) at least three fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least

40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 11,

(d) at least three fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 13, or

(e) at least three fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 21.

5. The polynucleotide of any of the preceding claims, wherein the polypeptide comprises:

(a) at least four fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 1,

(b) at least four fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 6,

(c) at least four fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 11,

(d) at least four fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 13, or

(e) at least four fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,

at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 21.

6. The polynucleotide of any of the preceding claims, wherein the polypeptide
5 comprises:

- (a) at least five fragments of at least 8, at least 9, at least 10, at least 11,
at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,
at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
acids of SEQ ID NO: 1,
- 10 (b) at least five fragments of at least 8, at least 9, at least 10, at least 11,
at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,
at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
acids of SEQ ID NO: 6,
- (c) at least five fragments of at least 8, at least 9, at least 10, at least 11,
15 at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,
at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
acids of SEQ ID NO: 11,
- (d) at least five fragments of at least 8, at least 9, at least 10, at least 11,
at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,
20 at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
acids of SEQ ID NO: 13, or
- (e) at least five fragments of at least 8, at least 9, at least 10, at least 11,
at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,
at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
25 acids of SEQ ID NO: 21.

7. The polynucleotide of any of the preceding claims, wherein the polypeptide
comprises:

- (a) at least six fragments of at least 8, at least 9, at least 10, at least 11,
30 at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,
at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
acids of SEQ ID NO: 1,

- (b) at least six fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 6,
- 5 (c) at least six fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 11,
- (d) at least six fragments of at least 8, at least 9, at least 10, at least 11, 10 at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 13, or
- (e) at least six fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, 15 at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 21.
8. The polynucleotide of any of the preceding claims, wherein the polypeptide comprises:
- 20 (a) at least seven fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 1,
- (b) at least seven fragments of at least 8, at least 9, at least 10, at least 25 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 6,
- (c) at least seven fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 30 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 11,

- (d) at least seven fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 13, or
- 5 (e) at least seven fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 21.
- 10 9. The polynucleotide of any of the preceding claims, wherein the polypeptide comprises:
- (a) at least eight fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
- 15 acids of SEQ ID NO: 1,
- (b) at least eight fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 6,
- 20 (c) at least eight fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 11,
- (d) at least eight fragments of at least 8, at least 9, at least 10, at least
- 25 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 13, or
- (e) at least eight fragments of at least 8, at least 9, at least 10, at least
- 30 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 21.

10. The polynucleotide of any of the preceding claims, wherein the polypeptide comprises:

- 5 (a) at least nine fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 1,
- 10 (b) at least nine fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 6,
- 15 (c) at least nine fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 11,
- 20 (d) at least nine fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 13, or
- (e) at least nine fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 21.

11. The polynucleotide of any of the preceding claims, wherein the polypeptide comprises:

- 25 (a) at least ten fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 1,
- 30 (b) at least ten fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,

at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 6,

(c) at least ten fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40,
5 at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 11,

(d) at least ten fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino
10 acids of SEQ ID NO: 13, or

(e) at least ten fragments of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80 at least 90 or at least 100 amino acids of SEQ ID NO: 21.
15

12. The polynucleotide of any one of claims 3-11, wherein the fragments of SEQ ID NO: 1 are not adjacent to each other.

13. The polynucleotide of any one of claims 3-12, wherein the fragments of SEQ
20 ID NO: 6 are not adjacent to each other.

14. The polynucleotide of any one of claims 3-13, wherein the fragments of SEQ ID NO: 11 are not adjacent to each other.

25 15. The polynucleotide of any one of claims 3-14, wherein the fragments of SEQ ID NO: 13 are not adjacent to each other.

16. The polynucleotide of any one of claims 3-15, wherein the fragments of SEQ
30 ID NO: 21 are not adjacent to each other.

17. The polynucleotide of any one of claims 1-16, wherein the polypeptide comprises:

- (a) a first and a second fragment of LMP1, wherein said first and second fragments of LMP1 are selected from the group consisting SEQ ID NOs: 2-5 and wherein said first and second fragments of LMP1 are not adjacent to each other in the polypeptide,
- 5 (b) a first and a second fragment of LMP2, wherein said first and second fragments of LMP1 are selected from the group consisting SEQ ID NOs: 7-10 and wherein said first and second fragments of LMP2 are not adjacent to each other in the polypeptide,
- (c) a fragment of EBNA1 consisting of SEQ ID NO: 12, and
- 10 (d) a first and a second fragment of EBNA3A, wherein said first and second fragments of EBNA3A are selected from the group consisting SEQ ID NOs: 14-20 and wherein said first and second fragments of EBNA3A are not adjacent to each other in the polypeptide.
- 15 18. The polynucleotide of any one of claims 1-17, wherein the polypeptide comprises:
- (a) a first fragment of LMP1 consisting of SEQ ID NO: 2,
- (b) a second fragment of LMP1 consisting of SEQ ID NO: 3,
- (c) a third fragment of LMP1 consisting of SEQ ID NO: 4,
- 20 (d) a fourth fragment of LMP1 consisting of SEQ ID NO: 5,
- (e) a first fragment of LMP2 consisting of SEQ ID NO: 7,
- (f) a second fragment of LMP2 consisting of SEQ ID NO: 8,
- (g) a third fragment of LMP2 consisting of SEQ ID NO: 9,
- (h) a fourth fragment of LMP2 consisting of SEQ ID NO: 10,
- 25 (i) a first fragment of EBNA1 consisting of SEQ ID NO: 12,
- (j) a first fragment of EBNA3A consisting of SEQ ID NO: 14,
- (k) a second fragment of EBNA3A consisting of SEQ ID NO: 15,
- (l) a third fragment of EBNA3A consisting of SEQ ID NO: 16,
- (m) a fourth fragment of EBNA3A consisting of SEQ ID NO: 17,
- 30 (n) a fifth fragment of EBNA3A consisting of SEQ ID NO: 18,
- (o) a sixth fragment of EBNA3A consisting of SEQ ID NO: 19, and
- (p) a seventh fragment of EBNA3A consisting of SEQ ID NO: 20;

wherein the first, second, third and fourth LMP1 fragments are not adjacent to each other; the first, second, third and fourth LMP2 fragments are not adjacent to each other; and the first, second, third, fourth, fifth, sixth, and seventh EBNA3A fragments are not adjacent to each other.

5

19. The polynucleotide of claims 17 or 18, wherein the polypeptide further comprises:

- (a) a first fragment of ZEBRA consisting of SEQ ID NO: 22, and
- (b) a second fragment of ZEBRA consisting of SEQ ID NO: 23;

10 wherein the first and second ZEBRA fragments are not adjacent to each other.

20. The polynucleotide of any of the preceding claims, wherein the polypeptide is at least 80%, at least 85%, at least 90%, at least 95% or at least 99% identical to SEQ ID NO: 24 or SEQ ID NO: 26.

15

21. The polynucleotide of any of the preceding claims, wherein the fragments are immunogenic fragments.

22. A vector comprising the polynucleotide of any of the preceding claims.

20

23. The vector of claim 22, wherein the vector is an adenovirus vector or a vaccinia virus vector.

24. The vector of claims 22 or 23, wherein the vector is a non-human simian adenovirus vector.

25

25. The vector of claim 24, wherein the non-human simian adenovirus vector is a chimpanzee adenovirus vector.

30 26. The vector of claim 22 or 23, wherein the vector is a modified vaccinia Ankara vector.

27. The vector of claims 22-25 which is a ChAd155-EBV-L expression vector comprising a nucleic acid sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to SEQ ID NO: 50.
- 5 28. The vector of claims 22-25 which is a ChAd155-EBV-LLy expression vector comprising a nucleic acid sequence at least 90%, at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identical to SEQ ID NO: 51.
29. A polypeptide encoded by the polynucleotide of any of claims 1-21 or the
10 vector of any of claims 22-28.
30. The polypeptide of claim 29 which is at least 80%, at least 85%, at least 90%, at least 95% or at least 99% identical to SEQ ID NO: 24 or SEQ ID NO: 26.
- 15 31. An immunogenic composition comprising the polynucleotide of any one of claims 1-21, the vector of any one of claims 22-28, or the polypeptide of any one of claims 29-30; and a pharmaceutically acceptable excipient.
32. The immunogenic composition of claim 31, further comprising an adjuvant.
20
33. Use of the polynucleotide of any one of claims 1-21, the vector of any one of claims 22-28, the polypeptide of any one of claims 29-30, or the immunogenic composition of any one of claims 31-32 in the manufacture of a medicament for the treatment or prophylaxis of a disease caused by Epstein-Barr Virus infection.
25
34. The polynucleotide of any one of claims 1-21, the vector of any one of claims 22-28, the polypeptide of any one of claims 29-30, or the immunogenic composition of any one of claims 31-32 for use in the treatment or prophylaxis of a disease caused by Epstein-Barr Virus infection.
30

35. A method of producing a recombinant viral particle capable of expressing an EBV antigen, comprising expressing the vector of any one of claims 22-28 in a host cell.
- 5 36. A method of inducing an immune response in a subject comprising administering the polynucleotide of any one of claims 1-21, the vector of any one of claims 22-28, the polypeptide of any one of claims 29-30, or the immunogenic composition of any one of claims 31-32 to the subject.
- 10 37. The method of claim 36, wherein the subject is Epstein-Barr virus seronegative.
38. The method of claim 36, wherein the subject is Epstein-Barr virus seropositive.
- 15 39. A method of treating or preventing an EBV-associated disease in a subject, comprising administering the polynucleotide of any one of claims 1-21, the vector of any one of claims 22-28, the polypeptide of any one of claims 29-30, or the immunogenic composition of any one of claims 31-32 to the subject.
- 20 40. The method of claim 39, wherein the EBV-associated disease is an EBV-associated autoimmune disease or an EBV-associated malignancy.
41. The method of claim 39, wherein the EBV-associated disease is selected from the group consisting of multiple sclerosis, rheumatoid arthritis and systemic lupus erythematosus.
- 25 42. A method of inducing an immune response in a subject comprising:
- 30 (a) administering an adenovirus vector comprising the polynucleotide of any one of claims 1-21, and
- (b) administering a vaccinia virus vector comprising the polynucleotide of any one of claims 1-21;

wherein steps (a) and (b) are conducted in either order.

43. A method of treating or preventing an EBV-associated disease in a subject, comprising:

- 5 (a) administering an adenovirus vector comprising the polynucleotide of any one of claims 1-21, and
- (b) administering a vaccinia virus vector comprising the polynucleotide of any one of claims 1-21;
- wherein steps (a) and (b) are conducted in either order.

10

44. The method of claim 42 or 43, wherein step (b) is carried out one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve or more weeks after step (a).