~~Claims~~

1. ~~A nucleic acid encoding a TCR alpha chain construct (TRA) and/or a TCR beta chain construct (TRB) of a TCR construct specific for an epitope in complex with a human MHC I, wherein the epitope is an epitope of an Epstein-Barr-virus (EBV) protein,~~

~~a) wherein the epitope has the sequence of SEQ ID NO: 1, the MHC I is HLA-A*02:01, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 13 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 18;~~

~~b) wherein the epitope has the sequence of SEQ ID NO: 2, the MHC I is HLA-B*57:01, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 23 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 28;~~

~~c) wherein the epitope has the sequence of SEQ ID NO: 3, the MHC I is HLA-C*15:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 33 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 38;~~

~~d) wherein the epitope has the sequence of SEQ ID NO: 4, the MHC I is HLA-C*06:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 43 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 48;~~

~~e) wherein the epitope has the sequence of SEQ ID NO: 5, the MHC I is HLA-B*44:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 53 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 58;~~

~~f) wherein the epitope has the sequence of SEQ ID NO: 5, the MHC I is HLA-B*44:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 63 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 68;~~

~~g) wherein the epitope has the sequence of SEQ ID NO: 6, the MHC I is HLA-B*07:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 73 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 78; and/or~~

~~h) wherein the epitope has the sequence of SEQ ID NO: 6, the MHC I is HLA-B*07:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 83 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 88.~~

2. ~~A nucleic acid of claim 1, wherein the epitope has the sequence of SEQ ID NO: 1, the MHC I is HLA-A*02:01, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 13 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 18;~~

~~wherein, optionally, the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 11, a CDR2 having at least 80% sequence identity to SEQ ID NO: 12 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 13, and the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 16, a CDR2~~

~~having at least 80% sequence identity to SEQ ID NO: 17 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 18;~~

~~wherein, most preferably, the TRA comprises a variable region having at least 90% sequence identity to SEQ ID NO: 15 and the TRB comprises a variable region having at least 90% sequence identity to SEQ ID NO: 20.~~

~~3. A nucleic acid of claim 1, wherein the epitope has the sequence of SEQ ID NO: 2, the MHC I is HLA-B*57:01, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 23 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 28;~~

~~wherein, optionally, the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 21, a CDR2 having at least 80% sequence identity to SEQ ID NO: 22 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 23, and the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 26, a CDR2 having at least 80% sequence identity to SEQ ID NO: 27 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 28;~~

~~wherein, most preferably, the TRA comprises a variable region having at least 90% sequence identity to SEQ ID NO: 25 and the TRB comprises a variable region having at least 90% sequence identity to SEQ ID NO: 30.~~

~~4. A nucleic acid of claim 1, wherein the epitope has the sequence of SEQ ID NO: 3, the MHC I is HLA-C*15:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 33 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 38;~~

~~wherein, optionally, the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 31, a CDR2 having at least 80% sequence identity to SEQ ID NO: 32 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 33, and the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 36, a CDR2 having at least 80% sequence identity to SEQ ID NO: 37 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 38;~~

~~wherein, most preferably, the TRA comprises a variable region having at least 90% sequence identity to SEQ ID NO: 35 and the TRB comprises a variable region having at least 90% sequence identity to SEQ ID NO: 40.~~

~~5. A nucleic acid of claim 1, wherein the epitope has the sequence of SEQ ID NO: 4, the MHC I is HLA-C*06:02, and the TRA comprises a CDR3 having at least 90% sequence identity to~~

~~SEQ ID NO: 43 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 48;~~

~~wherein, optionally, the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 41, a CDR2 having at least 80% sequence identity to SEQ ID NO: 42 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 43, and the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 46, a CDR2 having at least 80% sequence identity to SEQ ID NO: 47 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 48;~~

~~wherein, most preferably, the TRA comprises a variable region having at least 90% sequence identity to SEQ ID NO: 45 and the TRB comprises a variable region having at least 90% sequence identity to SEQ ID NO: 50.~~

~~6. A nucleic acid of claim 1, wherein the epitope has the sequence of SEQ ID NO: 5, the MHC I is HLA-B*44:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 53 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 58;~~

~~wherein, optionally, the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 51, a CDR2 having at least 80% sequence identity to SEQ ID NO: 52 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 53, and the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 56, a CDR2 having at least 80% sequence identity to SEQ ID NO: 57 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 58;~~

~~wherein, most preferably, the TRA comprises a variable region having at least 90% sequence identity to SEQ ID NO: 55 and the TRB comprises a variable region having at least 90% sequence identity to SEQ ID NO: 60.~~

~~7. A nucleic acid of claim 1, wherein the epitope has the sequence of SEQ ID NO: 5, the MHC I is HLA-B*44:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 63 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 68;~~

~~wherein, optionlly, the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 61, a CDR2 having at least 80% sequence identity to SEQ ID NO: 62 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 63, and the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 66, a CDR2 having at least 80% sequence identity to SEQ ID NO: 67 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 68;~~

~~wherein, most preferably, the TRA comprises a variable region having at least 90% sequence identity to SEQ ID NO: 65 and the TRB comprises a variable region having at least 90% sequence identity to SEQ ID NO: 70.~~

~~8. A nucleic acid of claim 1, wherein the epitope has the sequence of SEQ ID NO: 6, the MHC I is HLA-B*07:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 73 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 78;~~

~~wherein, optionally, the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 71, a CDR2 having at least 80% sequence identity to SEQ ID NO: 72 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 73, and the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 76, a CDR2 having at least 80% sequence identity to SEQ ID NO: 77 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 78;~~

~~wherein, most preferably, the TRA comprises a variable region having at least 90% sequence identity to SEQ ID NO: 75 and the TRB comprises a variable region having at least 90% sequence identity to SEQ ID NO: 80.~~

~~9. A nucleic acid of claim 1, wherein the epitope has the sequence of SEQ ID NO: 6, the MHC I is HLA-B*07:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 83 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 88;~~

~~wherein, optionally, the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 81, a CDR2 having at least 80% sequence identity to SEQ ID NO: 82 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 83, and the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 86, a CDR2 having at least 80% sequence identity to SEQ ID NO: 87 and a CDR3 having at least 90%, preferably, 100% sequence identity to SEQ ID NO: 88;~~

~~wherein, most preferably, the TRA comprises a variable region having at least 90% sequence identity to SEQ ID NO: 85 and the TRB comprises a variable region having at least 90% sequence identity to SEQ ID NO: 90.~~

~~10. The nucleic acid of any of the preceding claims, wherein the sequence identity to the recited CDR1 and CDR2 and CDR3 regions is 100%.~~

~~11. The nucleic acid of any of the preceding claims, encoding at least one TCR alpha and beta chain construct of the TCR construct,~~

~~wherein the nucleic acid is selected from the group comprising a viral vector, a transposon, a vector suitable for CRISPR/CAS based recombination or a plasmid suitable for *in vitro* RNA transcription~~

~~wherein, preferably, the TCR alpha chain construct and/or the TCR beta chain construct further comprise a constant region selected from the group comprising a human constant region, a murine constant region or a chimeric constant region.~~

~~12. A protein encoded by the nucleic acid of any of the preceding claims.~~

~~13. A host cell comprising a nucleic acid and/or a protein of any of the preceding claims, wherein the host cell preferably is a human CD8+ T cell.~~

~~14. A pharmaceutical composition comprising~~

~~a) a nucleic acid of any of claims 1-11 encoding a TCR construct capable of specifically binding to said epitope in the context of said MHC I; or~~

~~b) a protein of claim 12 comprising a TCR construct capable of specifically binding to said epitope in the context of said MHC I; or~~

~~c) a host cell of claim 13 expressing a TCR construct capable of specifically binding to said epitope in the context of said MHC I,~~

~~wherein the TCR construct preferably is the TCR construct of claim 2.~~

~~15. A pharmaceutical composition or a kit comprising at least two pharmaceutical compositions comprising~~

~~a) at least two nucleic acids, each encoding a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I; or~~
~~b) at least two proteins, each comprising a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I; or~~
~~c) at least two host cells, each expressing a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I,~~

~~wherein the epitopes are peptides from different antigens expressed by the same cancer or infectious agent, wherein, optionally, the cancer is associated with EBV and the different EBV antigens are selected from the group comprising LMP2A, LMP1, EBNA1 and EBNA3C,~~

wherein, preferably, the kit of the pharmaceutical composition is for use in treatment of said cancer or infectious agent.

16. A pharmaceutical composition of any of claims 14-15 or a kit comprising the pharmaceutical composition or the kit of any of claims 14-15, comprising

a) at least two nucleic acids of any of claims 1-11, each encoding a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I; or

b) at least two proteins of claim 12, each comprising a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I; or

c) at least two host cells of claim 13, each expressing a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I,

wherein one of said TCR constructs preferably is the TCR construct of claim 2.

17. The pharmaceutical composition of any of claims 14-16 or the kit comprising the pharmaceutical composition or the kit of any of claims 14-16 for use in the treatment of a patient expressing said MHC I and having an EBV-associated disease selected from the group comprising Hodgkin's and non-Hodgkin lymphoma, Burkitt lymphoma, hemophagocytic lymphohistiocytosis, nasopharyngeal carcinoma, head and neck cancer, lung cancer, gastric cancer hairy leukoplakia, post transplant lymphoproliferative disorder and central nervous system lymphoma.

wherein the treatment preferably is an immunotherapy selected from the group of adoptive T cell therapy and TCR gene therapy.

18. A pharmaceutical composition comprising a peptide comprising an epitope capable of being presented by a human MHC I, wherein the epitope is selected from the group comprising epitopes

a) having at least 88% sequence identity to SEQ ID NO: 3, wherein the epitope is capable of being presented on HLA-C*15:02, and wherein the peptide comprises at most 11 consecutive amino acids identical to the sequence of amino acids ocurring in LMP1 of SEQ ID NO: 120;

b) having at at least 88% sequence identity to SEQ ID NO: 4, wherein the epitope is capable of being presented on HLA-C*06:02, and wherein the peptide comprises at most 11 consecutive amino acids identical to the sequence of amino acids ocurring in EBNA3C of SEQ ID NO: 121; and

c) having at at least 90% sequence identity to SEQ ID NO: 5, wherein the epitope is capable of being presented on HLA-B*44:02, and wherein the peptide comprises at most

~~11 consecutive amino acids identical to the sequence of amino acids ocurring in EBNA3C of SEQ ID NO: 121,~~

~~or comprising a nucleic acid encoding said peptide,~~

~~wherein said pharmaceuticla composition preferably is for use in vaccination against an EBV-associated disease selected from the group comprising Hodgkin's and non-Hodgkin lymphoma, Burkitt lymphoma, hemophagocytic lympohistiocytosis, nasopharyngeal carcinoma, head and neck cancer, lung cancer, gastric cancer hairy leukoplakia, post transplant lymphoproliferative disorder and central nervous system lymphoma.~~

Claims

1. A nucleic acid encoding a TCR alpha chain construct (TRA) and/or a TCR beta chain construct (TRB) of a TCR construct specific for an epitope in complex with a human MHC I, wherein the epitope is an epitope of an Epstein-Barr-virus (EBV) protein,
wherein the epitope has the sequence of SEQ ID NO: 1, the MHC I is HLA-A*02:01, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 13 and/or the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 18.

2. A nucleic acid of claim 1, wherein the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 11, a CDR2 having at least 80% sequence identity to SEQ ID NO: 12 and a CDR3 having at least 90% sequence identity to SEQ ID NO: 13, and/or the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 16, a CDR2 having at least 80% sequence identity to SEQ ID NO: 17 and a CDR3 having at least 90% sequence identity to SEQ ID NO: 18.

3. A nucleic acid of claim 2, wherein the TRA comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 11, a CDR2 having at least 80% sequence identity to SEQ ID NO: 12 and a CDR3 having 100% sequence identity to SEQ ID NO: 13, and the TRB comprises a CDR1 having at least 80% sequence identity to SEQ ID NO: 16, a CDR2 having at least 80% sequence identity to SEQ ID NO: 17 and a CDR3 having 100% sequence identity to SEQ ID NO: 18.

4. A nucleic acid of any of claims 2 or 3, wherein the TRA comprises a variable region having at least 90% sequence identity to SEQ ID NO: 15 and/or the TRB comprises a variable region having at least 90% sequence identity to SEQ ID NO: 20.

5. The nucleic acid of any of the preceding claims, wherein the sequence identity to the recited CDR1 and CDR2 and CDR3 regions is 100%.

6. The nucleic acid of any of the preceding claims, encoding at least one TCR alpha and beta chain construct of the TCR construct.

7. The nucleic acid of claim 6, wherein the nucleic acid is selected from the group consisting of a viral vector, a transposon, a vector suitable for CRISPR/CAS based recombination or a plasmid suitable for *in vitro* RNA transcription.

8. The nucleic acid of any of claims 6 or 7,wherein the TCR alpha chain construct and the TCR beta chain construct further comprise a constant region selected from the group comprising a human constant region, a murine constant region or a chimeric constant region.

9. A protein encoded by the nucleic acid of any of the preceding claims.

10. A host cell comprising a nucleic acid and/or a protein of any of the preceding claims, wherein the host cell preferably is a human CD8+ T cell.

11. A pharmaceutical composition comprising

a) a nucleic acid of any of claims 1-8 encoding a TCR construct capable of specifically binding to said epitope in the context of said MHC I; or

b) a protein of claim 9 comprising a TCR construct capable of specifically binding to said epitope in the context of said MHC I; or

c) a host cell of claim 10 expressing a TCR construct capable of specifically binding to said epitope in the context of said MHC I.

12. A pharmaceutical composition or a kit comprising at least two pharmaceutical compositions comprising

a) at least two nucleic acids, each encoding a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I; or
b) at least two proteins, each comprising a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I; or
c) at least two host cells, each expressing a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I,

wherein the epitopes are peptides from different antigens expressed by the same cancer or infectious agent, wherein, optionally, the cancer is associated with EBV and the different EBV antigens are selected from the group comprising LMP2A, LMP1, EBNA1 and EBNA3C, wherein the composition or kit comprises a pharmaceutical composition of claim 11,

wherein, preferably, the kit of the pharmaceutical composition is for use in treatment of said cancer or infectious agent.

13. The pharmaceutical composition of any of claims 11-12 or a kit comprising the pharmaceutical composition or the kit of any of claims 11-12, comprising

a) a nucleic acid encoding a TCR alpha chain construct (TRA) and a TCR beta chain construct (TRB) of a TCR construct specific for an epitope in complex with a human MHC I, wherein the epitope is an epitope of an Epstein-Barr-virus (EBV) protein

(i) wherein the epitope has the sequence of SEQ ID NO: 2, the MHC I is HLA-B*57:01, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID

NO: 23 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 28;

(ii) wherein the epitope has the sequence of SEQ ID NO: 3, the MHC I is HLA-C*15:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 33 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 38;

(iii) wherein the epitope has the sequence of SEQ ID NO: 4, the MHC I is HLA-C*06:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 43 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 48;

(iv) wherein the epitope has the sequence of SEQ ID NO: 5, the MHC I is HLA-B*44:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 53 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 58;

(v) wherein the epitope has the sequence of SEQ ID NO: 5, the MHC I is HLA-B*44:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 63 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 68;

(vi) wherein the epitope has the sequence of SEQ ID NO: 6, the MHC I is HLA-B*07:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 73 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 78; and/or

(vii) wherein the epitope has the sequence of SEQ ID NO: 6, the MHC I is HLA-B*07:02, and the TRA comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 83 and the TRB comprises a CDR3 having at least 90% sequence identity to SEQ ID NO: 88.

each encoding a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I; or

b) a protein encoded by the nucleic acid of a) each comprising a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I; or

c) a host cell comprising a nucleic acid of a) and/or a protein of b), each expressing a TCR construct capable of specifically binding to its respective epitope in the context of the respective MHC I.

14. The pharmaceutical composition of any of claims 11-13 or the kit comprising the pharmaceutical composition or the kit of any of claims 11-13 for use in the treatment of a patient expressing HLA-A*02:01 and having an EBV-associated disease selected from the group comprising Hodgkin’s and non-Hodgkin lymphoma, Burkitt lymphoma.

hemophagocytic lympohistiocytosis, nasopharyngeal carcinoma, head and neck cancer, lung cancer, gastric cancer hairy leukoplakia, post transplant lymphoproliferative disorder and central nervous system lymphoma.

wherein the treatment preferably is an immunotherapy selected from the group of adoptive T cell therapy and TCR gene therapy.