Claims

1. A method for preparing a nucleic acid encoding the T cell receptor (TCR) alpha chain construct (TRA) and TCR beta chain construct (TRB) of a TCR construct specific for an epitope from a defined antigen presented on a MHC, comprising
   (a) stimulating T cells isolated from a donor with professional antigen presenting cells presenting epitopes of said defined antigen, to enrich antigen-specific T cells; and
   (b) contacting said T cells with a library of cells, wherein each cell expresses a single MHC allele, wherein the library comprises cells expressing all human MHC I or human MHC II alleles present in the donor, and wherein the cells of said library present epitopes of said defined antigen; and
   (c) selecting T cells activated by said contact; and
   (d) isolating the nucleic acids encoding the TCR alpha and TCR beta chains of the TCR of said T cells.

2. The method of claim 1, wherein the MHC is MHC I, wherein the library of cells preferably comprises MHC I-expressing K562 cells.

3. The method of any of claim 1 or claim 2, wherein the method further comprises optimizing the sequence and/or modifying the TCR alpha and beta chains.

4. A method for preparing a nucleic acid encoding the TRA and TRB of a TCR construct specific for an epitope from a defined antigen presented on a MHC, comprising preparing a nucleic acid obtainable from the method of any one of claims 1 to 3 with optimized sequence, wherein said optimization comprises:

   - optimizing codon usage of the TRA and TRB; and/or
   - combining human variable regions with murine constant regions or minimal murine constant regions; and/or
   - affinity maturation of the TCR sequences; and/or
   - generating soluble receptor molecules containing the variable regions of the TRA and TRB chain genes; and/or
   - fusing TRA and TRB via a genetic linker to provide a single transgene cassette encoding both chains of a functional TCR construct or preparing a single chain TCR construct.

5. The method of any one of claims 1 to 4, wherein the nucleic acid is a vector comprising the TRA and TRB operably linked to a promotor suitable for expression in T cells, wherein the vector is selected from the group comprising a γ-retroviral vector, a lentiviral vector and a transposon-based vector.

6. A method for preparing a host cell expressing a TCR construct specific for an epitope from a defined antigen presented on a MHC, comprising carrying out the method of any one of claims 1 to 5, and expressing said nucleic acids encoding the TRA and TRB in the host cell.

7. A method for identifying an epitope capable of being presented by a MHC in a defined antigen, comprising carrying out steps (a)-(d) of claim 1 and identifying the epitope capable of activating T cells transfected with nucleic acids encoding the isolated TRA and TRB constituting the TCR construct, wherein the epitope is optionally prepared in peptide or nucleic acid form.

8. A nucleic acid encoding a TRA and/or TRB of a TCR construct specific for an epitope in complex with a human MHC I, wherein the epitope is an epitope of human papillomavirus 16 oncoprotein E5, which comprises SEQ ID NO: 1.

9. The nucleic acid of claim 8, wherein the TRA comprises a CDR3 having at least 84% sequence identity to SEQ ID NO: 2, wherein the CDR3 preferably contains SEQ ID NO: 2, wherein the variable region of the TRA preferably has at least 80% sequence identity to SEQ ID NO: 3, and wherein the TRA preferably comprises SEQ ID NO: 4 and is encoded by SEQ ID NO: 5; and/or wherein the TRB comprises a CDR3 having at least 84% sequence identity to SEQ ID NO: 6, wherein the CDR3 preferably contains SEQ ID NO: 6, wherein the variable region of TRB preferably has at least 80% sequence identity to SEQ ID NO: 7, and wherein the TRA preferably comprises SEQ ID NO: 8 and is encoded by SEQ ID NO: 9.

10. A method for preparing a T cell expressing a TCR construct specific for an epitope of human papillomavirus 16 oncoprotein E5, comprising providing a T cell expressing the nucleic acid of claim 8 or claim 9 encoding the TRA and TRB of said TCR construct , and expressing said TCR, wherein the T cell preferably is a CD8+ T cell.

11. A protein encoded by the nucleic acid of claim 8 or claim 9, preferably, comprising TRA and TRB.

12. A T cell obtained according to the method of claim 10.

13. A nucleic acid obtained according to the method of any one of claims 1 to 5.

14. A pharmaceutical composition comprising the protein of claim 11, the T cell of claim 12, or the nucleic acid of any claim 8 or claim 9, wherein the TCR construct comprises TRA and TRB.

15. Use of the pharmaceutical composition of claim 14 in the preparation of a medicament for treating human papillomavirus 16 in a patient, wherein the TCR construct is specific for an epitope of human papillomavirus 16 oncoprotein E5 in complex with HLA-B*15:01 and wherein the patient is HLA-B*15:01-positive.

16. A nucleic acid encoding a fragment of human papillomavirus 16 oncoprotein E5 having a length of up to 40 amino acids comprising an epitope, or a peptide fragment of human papillomavirus 16 oncoprotein E5 having a length of up to 40 amino acids comprising an epitope, wherein the epitope is capable of being recognized by the TCR construct of the T cell of claim 12, wherein the E5 epitope is selected from the group consisting of SEQ ID NO: 1, 45, 47, 49, 51, and 52.

17. A pharmaceutical composition comprising the nucleic acid or peptide of claim 16.

18. Use of the pharmaceutical composition of claim 17 in the preparation of a medicament for treating a patient infected with human papillomavirus 16 or for preventing infection with human papillomavirus 16.