Antibodies which target intracellular targets abnormally expressed by MHC class I molecules during cancer have been developed by different groups. However, these antibodies focus mostly on HLA*A02 which is the predominant allele in Caucasians, for instance among the 14 most common HLA*A types in Europe HLA*A02 represent ~30%. HLA-A distribution in Asia is more scattered, and HLA*A24 and HLA*A11 are common alleles too.

Summary

In one aspect, the present disclosure refers to an antibody or antigen binding fragment, optionally isolated, which is capable of binding to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule.

In another aspect, the present disclosure refers to an antibody or antigen binding fragment, optionally isolated, which is capable of binding to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule, comprising a light chain and a heavy chain variable region sequence, wherein: the light chain comprises a LC-CDR1, LC-CDR2, LC-CDR3, having at least 85% overall sequence identity to LC-CDR1: one of $X_1GSX_2SNIGX_3X_4YX_5X_6X_7$ (SEQ ID NO:46), TGTSSDVGGYNYVS (SEQ ID NO:29) or RASQSIGTDLA (SEQ ID NO:21); LC-CDR2: one of GNX_8NRPS (SEQ ID NO:47), DASNRAT (SEQ ID NO:22) or DVSSRPS (SEQ ID NO:30); LC-CDR3: one of $QSYDSX_9LSX_{10}X_{11}WV$ (SEQ ID NO:48), QQRSNWPPT (SEQ ID NO:23) or SSYTVFSTLV (SEQ ID NO:31); and the heavy chain comprises a HC-CDR1, HC-CDR2, HC-CDR3, having at least 85% overall sequence identity to HC-CDR1: one of $SGGYYWX_{12}$ (SEQ ID NO:49) or $X_{13}YYX_{14}H$ (SEQ ID NO:50); HC-CDR2: one of $YIYYSGX_{15}TYYNPSLKS$ (SEQ ID NO:51) or $WX_{16}X_{17}PX_{18}SX_{19}X_{20}TX_{2'}YAQKFQG$ (SEQ ID NO:52); HC-CDR2: one of $ENFGX_{22}X_{23}DX_{24}$ (SEQ ID NO:53), EGADGIYYFDY (SEQ ID NO:39) or DTYGHDY (SEQ ID NO:45); wherein X_1 = T or A, X_2 = S or Y, X_3 = A or D, X_4 = G or D, X_5 = D or E, X_6 = V or T, X_7 = H or N, X_8 = N or T, X_9 = N or S, X_{10} = Absent or D, X_{11} = A or T, X_{12} = S or A, X_{13} = G or D, X_{14} = M or I, X_{15} = S or T, X_{16} = I or M, X_{17} = N or S, X_{18} = N or D, X_{19} = A or G, X_{20} = G or A, X_{21} = N or Y, X_{22} = A or S, X_{23} = F or Y, and X_{24} = H or Y. In another aspect, the present disclosure refers to an antibody or antigen binding fragment, optionally isolated, which is capable of binding to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule, comprising a light chain and a heavy chain variable region sequence, wherein: the light chain sequence has at least 85% sequence identity to the light chain sequence of one of SEQ ID NOs:1 to 7, and; the heavy chain sequence has at least 85% sequence identity to the

heavy chain sequence of one of SEQ ID NOs:8 to 16. In yet another aspect, there is provided a chimeric antigen receptor (CAR) comprising an antigen binding fragment as disclosed herein. In yet another aspect, there is provided an *in vitro* complex, optionally isolated, comprising an antibody, antigen binding fragment or CAR as disclosed herein bound to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule. In a further aspect, the present disclosed refers to a composition comprising the antibody, antigen binding fragment or CAR according to the present disclosure and at least one pharmaceutically-acceptable carrier. In still another aspect, the present disclosure refers to an isolated nucleic acid encoding the antibody, antigen binding fragment or CAR as disclosed herein. In another aspect, there is also provided a vector comprising the nucleic acid as disclosed herein. In a another aspect, there is also provided a cell comprising the nucleic acid or the vector as disclosed herein. In yet anther aspect, the present invention refers to a method for making an antibody, antigen binding fragment or CAR according to the present disclosure, comprising culturing the cell as disclosed herein under conditions suitable for the expression of the antibody or antigen binding fragment or CAR. In a further aspect, there is also provided an antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to the present disclosure for use in therapy, or in a method of medical treatment. Another aspect of the present disclosure refers to the use of an antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to the present invention in the manufacture of a medicament for treating or preventing a cancer. In yet another aspect, there is provided a method comprising: modifying at least one cell isolated from a subject to express or comprise the antibody, antigen binding fragment, CAR, nucleic acid or vector according to the present disclosure, wherein the subject is in need of treatment of prevention of a cancer; and wherein the modified at least one cell is to be administered to a subject. In still another aspect, the present disclosure refers to a method comprising: introducing into at least one cell isolated from a subject the nucleic acid according to the present disclosure, wherein the subject is in need of treatment of prevention of a cancer, thereby modifying the at least one cell; and wherein the modified at least one cell is to be administered to a subject. In yet another aspect, there is also provided a kit of parts comprising a predetermined quantity of the antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell as disclosed herein. In yet another aspect, the present disclosure refers to a method of diagnosing a disease or a condition in a subject, the method comprising contacting a sample containing, or suspected to contain, peptide-MHC complex with an antibody or antigen binding fragment as disclosed herein and

detecting the formation of a complex of antibody, or antigen binding fragment, and the peptide-MHC complex.

In one example, the present disclosure provides an antibody or antigen binding fragment, optionally isolated, which is capable of binding to a complex of a peptide of an intracellular protein, and an MHC class I molecule. In some examples, the intracellular protein is p53.

In another example, the present disclosure provides an antibody or antigen binding fragment, optionally isolated, which is capable of binding to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule.

In some examples in accordance with various examples of the disclosure, the MHC class I molecule comprises an MHC class I α-chain encoded by an HLA-A*24 allele. In some examples, the peptide of p53 comprises, or consists of, the amino acid sequence of SEQ ID NO:75, or a variant having thereof having one or two or three amino acid substitutions in the amino acid sequence. In some examples, the antibody or antigen binding fragment comprises the amino acid sequences i) to vi):

i) LC-CDR1: $X_1GSX_2SNIGX_3X_4YX_5X_6X_7$ (SEQ ID NO:46);
TGTSSDVGGYNYVS (SEQ ID NO:29); or
RASQSIGTDLA (SEQ ID NO:21);

ii) LC-CDR2: GNX_8NRPS (SEQ ID NO:47);
DASNRAT (SEQ ID NO:22); or
DVSSRPS (SEQ ID NO:30)

iii) LC-CDR3: $QSYDSX_9LSX_{10}X_{11}WV$ (SEQ ID NO:48);
QQRSNWPPT (SEQ ID NO:23); or
SSYTVFSTLV (SEQ ID NO:31);

iv) HC-CDR1: $SGGYYWX_{12}$ (SEQ ID NO:49); or
$X_{13}YYX_{14}H$ (SEQ ID NO:50);

v) HC-CDR2: YIYYSGX$_{15}$TYYNPSLKS (SEQ ID NO:51); or

WX$_{16}$X$_{17}$PX$_{18}$SX$_{19}$X$_{20}$TX$_{2}$YAQKFQG (SEQ ID NO:52);

vi) HC-CDR3: ENFGX$_{22}$X$_{23}$DX$_{24}$ (SEQ ID NO:53);

EGADGIYYFDY (SEQ ID NO:39); or

DTYGHDY (SEQ ID NO:45);

or a variant thereof in which one or two or three amino acids in one or more of the sequences i) to vi) are replaced with another amino acid;

wherein X$_1$ = T or A, X$_2$ = S or Y, X$_3$ = A or D, X$_4$ = G or D, X$_5$ = D or E, X$_6$ = V or T, X$_7$ = H or N, X$_8$ = N or T, X$_9$ = N or S, X$_{10}$ = Absent or D, X$_{11}$ = A or T, X$_{12}$ = S or A, X$_{13}$ = G or D, X$_{14}$ = M or I, X$_{15}$ = S or T, X$_{16}$ = I or M, X$_{17}$ = N or S, X$_{18}$ = N or D, X$_{19}$ = A or G, X$_{20}$ = G or A, X$_{21}$ = N or Y, X$_{22}$ = A or S, X$_{23}$ = F or Y, and X$_{24}$ = H or Y.

In some examples, LC-CDR1 is one of TGSSSNIGADYETH (SEQ ID NO:17), AGSYSNIGDDYETH (SEQ ID NO:20), TGSSSNIGAGYDVH (SEQ ID NO:24), TGSSSNIGAGYDVN (SEQ ID NO:27), TGTSSDVGGYNYVS (SEQ ID NO:29) or RASQSIGTDLA (SEQ ID NO:21). In some examples, LC-CDR2 is one of GNTNRPS (SEQ ID NO:18), GNNNRPS (SEQ ID NO:25), DASNRAT (SEQ ID NO:22) or DVSSRPS (SEQ ID NO:30). In some examples, LC-CDR3 is one of QSYDSNLSAWV (SEQ ID NO:19), QSYDSNLSDTWV (SEQ ID NO:26), QSYDSSLSAWV (SEQ ID NO:28), QQRSNWPPT (SEQ ID NO:23) or SSYTVFSTLV (SEQ ID NO:31). In some examples, HC-CDR1 is one of SGGYYWS (SEQ ID NO:32), SGGYYWA (SEQ ID NO:35), SGGYYWS (SEQ ID NO:40), GYYMH (SEQ ID NO:37), or DYYIH (SEQ ID NO:43). In some examples, HC-CDR2 is one of YIYYSGSTYYNPSLKS (SEQ ID NO:33), YIYYSGTTYYNPSLKS (SEQ ID NO:41), WINPNSAGTNYAQKFQG (SEQ ID NO:38) or WMSPDSGATYYAQKFQG (SEQ ID NO:44). In some examples, HC-CDR3 is one of ENFGAFDH (SEQ ID NO:34), ENFGSYDY (SEQ ID NO:36), EGADGIYYFDY (SEQ ID NO:39), or DTYGHDY (SEQ ID NO:45).

In some examples, the antibody or antigen binding fragment has at least one light chain variable region incorporating the following CDRs:

LC-CDR1: TGSSSNIGADYETH (SEQ ID NO:17)
LC-CDR2: GNTNRPS (SEQ ID NO:18)
LC-CDR3: QSYDSNLSAWV (SEQ ID NO:19);

or

LC-CDR1: AGSYSNIGDDYETH (SEQ ID NO:20)
LC-CDR2: GNTNRPS (SEQ ID NO:18)
LC-CDR3: QSYDSNLSAWV (SEQ ID NO:19);

or

LC-CDR1: RASQSIGTDLA (SEQ ID NO:21)
LC-CDR2: DASNRAT (SEQ ID NO:22)
LC-CDR3: QQRSNWPPT (SEQ ID NO:23);

or

LC-CDR1: TGSSSNIGAGYDVH (SEQ ID NO:24)
LC-CDR2: GNNNRPS (SEQ ID NO:25)
LC-CDR3: QSYDSNLSDTWV (SEQ ID NO:26);

or

LC-CDR1: TGSSSNIGAGYDVN (SEQ ID NO:27)
LC-CDR2: GNNNRPS (SEQ ID NO:25)
LC-CDR3: QSYDSSLSAWV (SEQ ID NO:28);

or

LC-CDR1: TGTSSDVGGYNYVS (SEQ ID NO:29)
LC-CDR2: DVSSRPS (SEQ ID NO:30)
LC-CDR3: SSYTVFSTLV (SEQ ID NO:31).

In some examples, the antibody or antigen binding fragment has at least one heavy chain variable region incorporating the following CDRs:

HC-CDR1: SGGYYWS (SEQ ID NO:32)
HC-CDR2: YIYYSGSTYYNPSLKS (SEQ ID NO:33)
HC-CDR3: ENFGAFDH (SEQ ID NO:34);

or

HC-CDR1: SGGYYWA (SEQ ID NO:35)
HC-CDR2: YIYYSGSTYYNPSLKS (SEQ ID NO:33)
HC-CDR3: ENFGAFDH (SEQ ID NO:34);

or

HC-CDR1: SGGYYWS (SEQ ID NO:32)
HC-CDR2: YIYYSGSTYYNPSLKS (SEQ ID NO:33)
HC-CDR3: ENFGSYDY (SEQ ID NO:36);

or

HC-CDR1: SGGYYWA (SEQ ID NO:35)
HC-CDR2: YIYYSGSTYYNPSLKS (SEQ ID NO:33)
HC-CDR3: ENFGSYDY (SEQ ID NO:36);

or

HC-CDR1: GYYMH (SEQ ID NO:37)
HC-CDR2: WINPNSAGTNYAQKFQG (SEQ ID NO:38)
HC-CDR3: EGADGIYYFDY (SEQ ID NO:39);

or

HC-CDR1: SGGYYWS (SEQ ID NO:40)
HC-CDR2: YIYYSGTTYYNPSLKS (SEQ ID NO:41)
HC-CDR3: ENFGAFDY (SEQ ID NO:42);

or

HC-CDR1: DYYIH (SEQ ID NO:43)
HC-CDR2: WMSPDSGATYYAQKFQG (SEQ ID NO:44)
HC-CDR3: DTYGHDY (SEQ ID NO:45).

In another example, the present disclosure provides an antibody or antigen binding fragment, optionally isolated, which is capable of binding to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule, comprising a light chain and a heavy chain variable region sequence, wherein:

the light chain comprises a LC-CDR1, LC-CDR2, LC-CDR3, having at least 85% overall sequence identity to LC-CDR1: one of $X_1GSX_2SNIGX_3X_4YX_5X_6X_7$ (SEQ ID NO:46), TGTSSDVGGYNYVS (SEQ ID NO:29) or RASQSIGTDLA (SEQ ID NO:21); LC-CDR2: one of GNX_8NRPS (SEQ ID NO:47), DASNRAT (SEQ ID NO:22) or DVSSRPS (SEQ ID NO:30); LC-CDR3: one of $QSYDSX_9LSX_{10}X_{11}WV$ (SEQ ID NO:48), QQRSNWPPT (SEQ ID NO:23) or SSYTVFSTLV (SEQ ID NO:31); and

the heavy chain comprises a HC-CDR1, HC-CDR2, HC-CDR3, having at least 85% overall sequence identity to HC-CDR1: one of $SGGYYWX_{12}$ (SEQ ID NO:49) or $X_{13}YYX_{14}H$ (SEQ ID NO:50); HC-CDR2: one of $YIYYSGX_{15}TYYNPSLKS$ (SEQ ID NO:51) or $WX_{16}X_{17}PX_{18}SX_{19}X_{20}TX_{21}YAQKFQG$ (SEQ ID NO:52); HC-CDR2: one of $ENFGX_{22}X_{23}DX_{24}$ (SEQ ID NO:53), EGADGIYYFDY (SEQ ID NO:39) or DTYGHDY (SEQ ID NO:45);

wherein X_1 = T or A, X_2 = S or Y, X_3 = A or D, X_4 = G or D, X_5 = D or E, X_6 = V or T, X_7 = H or N, X_8 = N or T, X_9 = N or S, X_{10} = Absent or D, X_{11} = A or T, X_{12} = S or A, X_{13} = G or D, X_{14} = M or I, X_{15} = S or T, X_{16} = I or M, X_{17} = N or S, X_{18} = N or D, X_{19} = A or G, X_{20} = G or A, X_{21} = N or Y, X_{22} = A or S, X_{23} = F or Y, and X_{24} = H or Y.

In another example, the present disclosure provides an antibody or antigen binding fragment, optionally isolated, which is capable of binding to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule, comprising a light chain and a heavy chain variable region sequence, wherein:

the light chain sequence has at least 85% sequence identity to the light chain sequence of one of SEQ ID NOs:1 to 7, and;

the heavy chain sequence has at least 85% sequence identity to the heavy chain sequence of one of SEQ ID NOs:8 to 16.

In some examples in accordance with various examples of the disclosure, the antibody or antigen binding fragment displays antibody-dependent cell-mediated cytotoxicity (ADCC) to cells comprising or expressing peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule. In some examples, the antibody or antigen binding fragment is internalised by cells comprising or expressing peptide-MHC complex

comprising a peptide of p53 and an MHC class I molecule. In some examples, the antibody or antigen binding fragment is a fully human antibody or a fully human antibody fragment. In some examples, the antibody or antigen binding fragment is conjugated to a drug moiety or a detectable moiety.

In some examples in accordance with various examples of the disclosure, the antibody or antigen binding fragment further comprises an antibody or antigen binding fragment specific for a target other than a peptide-MHC complex. In some embodiments, the antibody or antigen binding fragment specific for a target other than a peptide-MHC complex is an antibody or antigen binding fragment capable of binding to an immune cell surface molecule, i.e. the target other than a peptide-MHC complex is an immune cell surface molecule.

In another example, the present disclosure provides a chimeric antigen receptor (CAR) comprising an antigen binding fragment according to the present disclosure.

In another example, the present disclosure provides an *in vitro* complex, optionally isolated, comprising an antibody, antigen binding fragment or CAR according to the present disclosure bound to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule.

In another example, the present disclosure provides a composition comprising the antibody, antigen binding fragment or CAR according to the present disclosure and at least one pharmaceutically-acceptable carrier.

In another example, the present disclosure provides an isolated nucleic acid encoding the antibody, antigen binding fragment or CAR according to the present disclosure.

In another example, the present disclosure provides a vector comprising the nucleic acid according to the present disclosure.

In another example, the present disclosure provides a cell comprising the nucleic acid according to the present disclosure or the vector according to the present disclosure.

In another example, the present disclosure provides a method for making an antibody, antigen binding fragment or CAR according to the present disclosure, comprising culturing

the cell of the present disclosure under conditions suitable for the expression of the antibody or antigen binding fragment or CAR.

In another example, the present disclosure provides an antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to the present disclosure for use in therapy, or in a method of medical treatment.

In another example, the present disclosure provides an antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to the present disclosure for use in the treatment or prevention of a cancer.

In another example, the present disclosure provides the use of an antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to the present disclosure in the manufacture of a medicament for treating or preventing a cancer.

In another example, the present disclosure provides a method of treating or preventing a cancer, comprising administering to a subject a therapeutically or prophylactically effective amount of the antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to the present disclosure.

In another example, the present disclosure provides a method of treating or preventing a cancer in a subject, comprising:

(a) isolating at least one cell from a subject;

(b) modifying the at least one cell to express or comprise the antibody, antigen binding fragment, CAR, nucleic acid or vector according to the present disclosure and;

(c) administering the modified at least one cell to a subject.

In another example, the present disclosure provides a method of treating or preventing a cancer in a subject, comprising:

(a) isolating at least one cell from a subject;

(b) introducing into the at least one cell the nucleic acid according to the present disclosure or the vector according to the present disclosure, thereby modifying the at least one cell and;

(c) administering the modified at least one cell to a subject.

In another example, the present disclosure provides a kit of parts comprising a predetermined quantity of the antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to the present disclosure.

In another example, the present disclosure provides a method of diagnosing a disease or a condition in a subject, the method comprising contacting a sample containing, or suspected to contain, peptide-MHC complex with an antibody or antigen binding fragment according to any one of claims 1 to 21 and detecting the formation of a complex of antibody, or antigen binding fragment, and the peptide-MHC complex.

Description

The present invention relates to antibodies and antigen binding fragments which bind to peptide-MHC complexes, in particular antibodies capable of binding to peptide-MHC complex comprising a p53 peptide bound to (i.e. presented by) an MHC class I molecule.

Antibodies/fragments that mimic the TCR's specificity for a tumour associated peptide-MHC complex, e.g. p53/HLA*A24, are useful as tumour-specific targeting agents. Such species are effective as a therapeutics on their own, or as a targeting tool for specific delivery of payloads such as drugs and toxins, and also as a diagnostic tools.

Peptide-MHC complexes

T cell receptors (TCRs) recognise antigen peptides presented by MHC molecules. Antigens are processed by the molecular machinery of antigen presenting cells (APCs) to peptides, which then become associated with MHC molecules and presented as peptide-MHC complexes at the cell surface. Different TCRs display different ability to bind to, and therefore different reactivity to, different peptide-MHC complexes. Antigen processing, loading and presentation on MHC is described in detail in, for example, Immunobiology, 5th Edn. Janeway CA Jr, Travers P, Walport M, et al. New York: Garland Science (2001), Chapter 5, hereby incorporated by reference in entirety.

The present invention is particularly concerned with TCR-like antibodies, which are capable of specific binding to peptide-MHC complexes. In particular, the present invention is concerned with antibodies capable of binding to peptide-MHC complexes comprising a peptide of an intracellular protein presented by an MHC class I molecule.

Claims:

1. An antibody or antigen binding fragment, optionally isolated, which is capable of binding to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule.

2. The antibody or antigen binding fragment according to claim 1, wherein the MHC class I molecule comprises an MHC class I α-chain encoded by an HLA-A*24 allele.

3. The antibody or antigen binding fragment according to claim 1 or claim 2, wherein the peptide of p53 comprises, or consists of, the amino acid sequence of SEQ ID NO:75, or a variant having thereof having one or two or three amino acid substitutions in the amino acid sequence.

4. The antibody or antigen binding fragment according to any one of claims 1 to 3, comprising the amino acid sequences i) to vi):

i) LC-CDR1: $X_1GSX_2SNIGX_3X_4YX_5X_6X_7$ (SEQ ID NO:46);
TGTSSDVGGYNYVS (SEQ ID NO:29); or
RASQSIGTDLA (SEQ ID NO:21);

ii) LC-CDR2: GNX_8NRPS (SEQ ID NO:47);
DASNRAT (SEQ ID NO:22); or
DVSSRPS (SEQ ID NO:30)

iii) LC-CDR3: $QSYDSX_9LSX_{10}X_{11}WV$ (SEQ ID NO:48);
QQRSNWPPT (SEQ ID NO:23); or
SSYTVFSTLV (SEQ ID NO:31);

iv) HC-CDR1: $SGGYYWX_{12}$ (SEQ ID NO:49); or
$X_{13}YYX_{14}H$ (SEQ ID NO:50);

v) HC-CDR2: $YIYYSGX_{15}TYYNPSLKS$ (SEQ ID NO:51); or
$WX_{16}X_{17}PX_{18}SX_{19}X_{20}TX_{21}$·YAQKFQG (SEQ ID NO:52);

vi) HC-CDR3: $ENFGX_{22}X_{23}DX_{24}$ (SEQ ID NO:53);
EGADGIYYFDY (SEQ ID NO:39); or
DTYGHDY (SEQ ID NO:45);

or a variant thereof in which one or two or three amino acids in one or more of the sequences i) to vi) are replaced with another amino acid;

wherein X_1 = T or A, X_2 = S or Y, X_3 = A or D, X_4 = G or D, X_5 = D or E, X_6 = V or T, X_7 = H or N, X_8 = N or T, X_9 = N or S, X_{10} = Absent or D, X_{11} = A or T, X_{12} = S or A, X_{13} = G or

D, X_{14} = M or I, X_{15} = S or T, X_{16} = I or M, X_{17} = N or S, X_{18} = N or D, X_{19} = A or G, X_{20} = G or A, X_{21} = N or Y, X_{22} = A or S, X_{23} = F or Y, and X_{24} = H or Y.

5. The antibody or antigen binding fragment according to claim 4, wherein LC-CDR1 is one of TGSSSNIGADYETH (SEQ ID NO:17), AGSYSNIGDDYETH (SEQ ID NO:20), TGSSSNIGAGYDVH (SEQ ID NO:24), TGSSSNIGAGYDVN (SEQ ID NO:27), TGTSSDVGGYNYVS (SEQ ID NO:29) or RASQSIGTDLA (SEQ ID NO:21).

6. The antibody or antigen binding fragment according to claim 4 or claim 5, wherein LC-CDR2 is one of GNTNRPS (SEQ ID NO:18), GNNNRPS (SEQ ID NO:25), DASNRAT (SEQ ID NO:22) or DVSSRPS (SEQ ID NO:30).

7. The antibody or antigen binding fragment according to any one of claims 4 to 6, wherein LC-CDR3 is one of QSYDSNLSAWV (SEQ ID NO:19), QSYDSNLSDTWV (SEQ ID NO:26), QSYDSSLSAWV (SEQ ID NO:28), QQRSNWPPT (SEQ ID NO:23) or SSYTVFSTLV (SEQ ID NO:31).

8. The antibody or antigen binding fragment according to any one of claims 4 to 7, wherein HC-CDR1 is one of SGGYYWS (SEQ ID NO:32), SGGYYWA (SEQ ID NO:35), SGGYYWS (SEQ ID NO:40), GYYMH (SEQ ID NO:37), or DYYIH (SEQ ID NO:43).

9. The antibody or antigen binding fragment according to any one of claims 4 to 8, wherein HC-CDR2 is one of YIYYSGSTYYNPSLKS (SEQ ID NO:33), YIYYSGTTYYNPSLKS (SEQ ID NO:41), WINPNSAGTNYAQKFQG (SEQ ID NO:38) or WMSPDSGATYYAQKFQG (SEQ ID NO:44).

10. The antibody or antigen binding fragment according to any one of claims 4 to 9, wherein HC-CDR3 is one of ENFGAFDH (SEQ ID NO:34), ENFGSYDY (SEQ ID NO:36), EGADGIYYFDY (SEQ ID NO:39), or DTYGHDY (SEQ ID NO:45).

11. The antibody or antigen binding fragment according to any one of claims 1 to 10, having at least one light chain variable region incorporating the following CDRs:

LC-CDR1: TGSSSNIGADYETH (SEQ ID NO:17)
LC-CDR2: GNTNRPS (SEQ ID NO:18)
LC-CDR3: QSYDSNLSAWV (SEQ ID NO:19);

or

LC-CDR1: AGSYSNIGDDYETH (SEQ ID NO:20)

LC-CDR2: GNTNRPS (SEQ ID NO:18)
LC-CDR3: QSYDSNLSAWV (SEQ ID NO:19);
or
LC-CDR1: RASQSIGTDLA (SEQ ID NO:21)
LC-CDR2: DASNRAT (SEQ ID NO:22)
LC-CDR3: QQRSNWPPT (SEQ ID NO:23);
or
LC-CDR1: TGSSSNIGAGYDVH (SEQ ID NO:24)
LC-CDR2: GNNNRPS (SEQ ID NO:25)
LC-CDR3: QSYDSNLSDTWV (SEQ ID NO:26);
or
LC-CDR1: TGSSSNIGAGYDVN (SEQ ID NO:27)
LC-CDR2: GNNNRPS (SEQ ID NO:25)
LC-CDR3: QSYDSSLSAWV (SEQ ID NO:28);
or
LC-CDR1: TGTSSDVGGYNYVS (SEQ ID NO:29)
LC-CDR2: DVSSRPS (SEQ ID NO:30)
LC-CDR3: SSYTVFSTLV (SEQ ID NO:31).

12. The antibody or antigen binding fragment according to any one of claims 1 to 11, having at least one heavy chain variable region incorporating the following CDRs:

HC-CDR1: SGGYYWS (SEQ ID NO:32)
HC-CDR2: YIYYSGSTYYNPSLKS (SEQ ID NO:33)
HC-CDR3: ENFGAFDH (SEQ ID NO:34);
or
HC-CDR1: SGGYYWA (SEQ ID NO:35)
HC-CDR2: YIYYSGSTYYNPSLKS (SEQ ID NO:33)
HC-CDR3: ENFGAFDH (SEQ ID NO:34);
or
HC-CDR1: SGGYYWS (SEQ ID NO:32)
HC-CDR2: YIYYSGSTYYNPSLKS (SEQ ID NO:33)
HC-CDR3: ENFGSYDY (SEQ ID NO:36);
or
HC-CDR1: SGGYYWA (SEQ ID NO:35)
HC-CDR2: YIYYSGSTYYNPSLKS (SEQ ID NO:33)
HC-CDR3: ENFGSYDY (SEQ ID NO:36);
or
HC-CDR1: GYYMH (SEQ ID NO:37)
HC-CDR2: WINPNSAGTNYAQKFQG (SEQ ID NO:38)
HC-CDR3: EGADGIYYFDY (SEQ ID NO:39);
or
HC-CDR1: SGGYYWS (SEQ ID NO:40)
HC-CDR2: YIYYSGTTYYNPSLKS (SEQ ID NO:41)
HC-CDR3: ENFGAFDY (SEQ ID NO:42);
or
HC-CDR1: DYYIH (SEQ ID NO:43)

HC-CDR2: WMSPDSGATYYAQKFQG (SEQ ID NO:44)
HC-CDR3: DTYGHDY (SEQ ID NO:45).

13. An antibody or antigen binding fragment, optionally isolated, which is capable of binding to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule, comprising a light chain and a heavy chain variable region sequence, wherein:

the light chain comprises a LC-CDR1, LC-CDR2, LC-CDR3, having at least 85% overall sequence identity to LC-CDR1: one of $X_1GSX_2SNIGX_3X_4YX_5X_6X_7$ (SEQ ID NO:46), TGTSSDVGGYNYVS (SEQ ID NO:29) or RASQSIGTDLA (SEQ ID NO:21); LC-CDR2: one of GNX_8NRPS (SEQ ID NO:47), DASNRAT (SEQ ID NO:22) or DVSSRPS (SEQ ID NO:30); LC-CDR3: one of $QSYDSX_9LSX_{10}X_{11}WV$ (SEQ ID NO:48), QQRSNWPPT (SEQ ID NO:23) or SSYTVFSTLV (SEQ ID NO:31); and

the heavy chain comprises a HC-CDR1, HC-CDR2, HC-CDR3, having at least 85% overall sequence identity to HC-CDR1: one of $SGGYYWX_{12}$ (SEQ ID NO:49) or $X_{13}YYX_{14}H$ (SEQ ID NO:50); HC-CDR2: one of $YIYYSGX_{15}TYYNPSLKS$ (SEQ ID NO:51) or $WX_{16}X_{17}PX_{18}SX_{19}X_{20}TX_{2}$·YAQKFQG (SEQ ID NO:52); HC-CDR2: one of $ENFGX_{22}X_{23}DX_{24}$ (SEQ ID NO:53), EGADGIYYFDY (SEQ ID NO:39) or DTYGHDY (SEQ ID NO:45);

wherein X_1 = T or A, X_2 = S or Y, X_3 = A or D, X_4 = G or D, X_5 = D or E, X_6 = V or T, X_7 = H or N, X_8 = N or T, X_9 = N or S, X_{10} = Absent or D, X_{11} = A or T, X_{12} = S or A, X_{13} = G or D, X_{14} = M or I, X_{15} = S or T, X_{16} = I or M, X_{17} = N or S, X_{18} = N or D, X_{19} = A or G, X_{20} = G or A, X_{21} = N or Y, X_{22} = A or S, X_{23} = F or Y, and X_{24} = H or Y.

14. An antibody or antigen binding fragment, optionally isolated, which is capable of binding to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule, comprising a light chain and a heavy chain variable region sequence, wherein:

the light chain sequence has at least 85% sequence identity to the light chain sequence of one of SEQ ID NOs:1 to 7, and;

the heavy chain sequence has at least 85% sequence identity to the heavy chain sequence of one of SEQ ID NOs:8 to 16.

15. The antibody or antigen binding fragment according to any one of claims 1 to 14, which displays antibody-dependent cell-mediated cytotoxicity (ADCC) to cells comprising or expressing peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule.

16. The antibody or antigen binding fragment according to any one of claims 1 to 15, which is internalised by cells comprising or expressing peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule.

17. The antibody or antigen binding fragment according to any one of claims 1 to 16, which is a fully human antibody or a fully human antibody fragment.

18. The antibody or antigen binding fragment according to any one of claims 1 to 17, conjugated to a drug moiety or a detectable moiety.

19. The antibody or antigen binding fragment according to any one of claims 1 to 18, further comprising an antibody or antigen binding fragment specific for a target other than a peptide-MHC complex.

20. The antibody or antigen binding fragment according to claim 19, wherein the target other than a peptide-MHC complex is an immune cell surface molecule.

21. A chimeric antigen receptor (CAR) comprising an antigen binding fragment according to any one of claims 1 to 20.

22. An *in vitro* complex, optionally isolated, comprising an antibody, antigen binding fragment or CAR according to any one of claims 1 to 21 bound to a peptide-MHC complex comprising a peptide of p53 and an MHC class I molecule.

23. A composition comprising the antibody, antigen binding fragment or CAR according to any one of claims 1 to 21 and at least one pharmaceutically-acceptable carrier.

24. An isolated nucleic acid encoding the antibody, antigen binding fragment or CAR according to any one of claims 1 to 21.

25. A vector comprising the nucleic acid of claim 24.

26. A cell comprising the nucleic acid according to claim 24 or the vector according to claim 25.

27. A method for making an antibody, antigen binding fragment or CAR according to any one of claims 1 to 21, comprising culturing the cell of claim 26 under conditions suitable for the expression of the antibody or antigen binding fragment or CAR.

28. An antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to any one of claims 1 to 21, or 23 to 26 for use in therapy, or in a method of medical treatment.

29. Use of an antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to any one of claims 1 to 21, or 23 to 26 in the manufacture of a medicament for treating or preventing a cancer.

30. A method comprising: modifying at least one cell isolated from a subject to express or comprise the antibody, antigen binding fragment, CAR, nucleic acid or vector according to any one of claims 1 to 21, or 24 to 26, wherein the subject is in need of treatment of prevention of a cancer; and wherein the modified at least one cell is to be administered to a subject.

31. A method comprising: introducing into at least one cell isolated from a subject the nucleic acid according to claim 24 or the vector according to claim 25, wherein the subject is in need of treatment of prevention of a cancer, thereby modifying the at least one cell; and wherein the modified at least one cell is to be administered to a subject.

32. A kit of parts comprising a predetermined quantity of the antibody, antigen binding fragment, CAR, composition, nucleic acid, vector or cell according to any one of claims 1 to 21, or 23 to 26.

33. A method of diagnosing a disease or a condition in a subject, the method comprising contacting a sample containing, or suspected to contain, peptide-MHC complex with an antibody or antigen binding fragment according to any one of claims 1 to 21 and detecting the formation of a complex of antibody, or antigen binding fragment, and the peptide-MHC complex.