The inventors have developed a binary classifier that is able to separate subjects having cancer from a background population. Using this classifier, the inventors were able to demonstrate a clear association between HLA genotype and cancer risk. These findings confirm the central role of tumor specific T cell responses in the control of tumor growth and mean that HLA genotype analysis may be used to improve diagnostic tests for the early identification of subjects at a high risk of developing cancer.

Accordingly, in a first aspect, the disclosure provides a method for determining the risk that a human subject will develop a cancer, the method comprising quantifying the HLA triplets (HLAT) of the subject that are capable of binding to T cell epitopes in the amino acid sequence of tumor associated antigens (TAAs), wherein each HLA of a HLAT is capable of binding to the same T cell epitope, and determining the risk that the subject will develop a cancer, wherein, with respect to a TAA, a lower number of HLATs capable of binding to T cell epitopes of the TAA corresponds to a higher risk that the subject will develop cancer, and wherein an HLAT is any combination of three class I HLA alleles expressed by the subject.

Accordingly, in a further aspect, the disclosure provides a use of one or more peptides or one of more polynucleic acids or vectors in the manufacture of a medicament for treating cancer in a subject, wherein the subject has been determined to have an elevated risk of developing cancer using a method according to claim 1 or claim 2, and wherein the use comprises that the one or more peptides or one of more polynucleic acids or vectors that encode one or more peptides, that comprise an amino acid sequence that (i) is a fragment of a TAA; and (ii) comprises a T cell epitope capable of binding to an HLAT of the subject; optionally wherein the TAA fragment is flanked at the N and/or C terminus by additional amino acids that are not part of the sequence of the TAA, are to be administered to the subject.

Accordingly, in a further aspect, the disclosure provides a system for determining the risk that a human subject will develop a cancer, the system comprising: (a) a storage module configured to store data comprising the HLA class I genotype of a subject and the amino acid sequences of TAAs; (b) a computation module configured to quantify the HLAT of the subject that are capable of binding to T cell epitopes in the amino acid sequence of the TAAs, wherein each HLA of a HLAT is capable of binding to the same T cell epitope, and wherein an HLAT is any combination of three class I HLA alleles expressed by the subject; and (c) an output module configured to display an indication of the risk that the subject will develop a cancer and/or a recommended treatment for the subject; wherein the system is configured to

display a higher risk that the subject will develop cancer when a lower number of HLATs are capable of binding to T cell epitopes of the TAAs.

Accordingly, in a first example the disclosure provides a method for determining the risk that a human subject will develop a cancer, the method comprising quantifying the HLA triplets (HLAT) of the subject that are capable of binding to T cell epitopes in the amino acid sequence of tumor associated antigens (TAAs), wherein each HLA of a HLAT is capable of binding to the same T cell epitope, and determining the risk that the subject will develop a cancer, wherein, with respect to a TAA, a lower number of HLATs capable of binding to T cell epitopes of the TAA corresponds to a higher risk that the subject will develop cancer.

The findings described herein also suggest that the risk of cancer can be reduced by using vaccines that are personalised to effectively activate a subject's immune system to kill tumor cells.

Accordingly, in a further example the disclosure provides a method of treating cancer in a subject, wherein the subject has been determined to have an elevated risk of developing cancer using the method above, and wherein the method of treatment comprises administering to the subject one or more peptides or one of more polynucleic acids or vectors that encode one or more peptides, that comprise an amino acid sequence that (i) is a fragment of a TAA; and (ii) comprises a T cell epitope capable of binding to HLAT of the subject.

In further examples, the disclosure provides

- a peptide, or polynucleic acids or vectors that encode a peptide, for use in a method of treating cancer in a specific human subject, wherein the peptides comprises an amino acid sequence that (i) is a fragment of a TAA; and (ii) comprises a T cell epitope capable of binding to an HLAT of the subject ; and
- a peptide, or polynucleic acids or vectors that encode a peptide for use in the manufacture of a medicament for treating cancer in a specific human subject, wherein the peptides comprises an amino acid sequence that (i) is a fragment of a TAA; and (ii) comprises a T cell epitope capable of binding to an HLAT of the subject.

CLAIMS

1. A method for determining the risk that a human subject will develop a cancer, the method comprising quantifying the HLA triplets (HLAT) of the subject that are capable of binding to T cell epitopes in the amino acid sequence of tumor associated antigens (TAAs), wherein each HLA of a HLAT is capable of binding to the same T cell epitope, and determining the risk that the subject will develop a cancer, wherein, with respect to a TAA, a lower number of HLATs capable of binding to T cell epitopes of the TAA corresponds to a higher risk that the subject will develop cancer, and wherein an HLAT is any combination of three class I HLA alleles expressed by the subject.

2. The method according to claim 1, wherein the cancer is selected from melanoma, lung cancer, renal cell cancer, colorectal cancer, bladder cancer, glioma, and head and neck cancer.

3. The method of claim 1 or claim 2, wherein the TAAs in any combination are together expressed in at least 50% of patients having the cancer.

4. The method of claim 3, wherein the TAAs are together expressed in at least 90% of patients having the cancer.

5. The method of any one of claims 1 to 4, wherein each TAA is expressed or over-expressed in at least 10% of patients having the cancer.

6. The method of claim 5, wherein each TAA is expressed or over-expressed in at least 20% of patients having the cancer.

7. Use of one or more peptides or one of more polynucleic acids or vectors in the manufacture of a medicament for treating cancer in a subject, wherein the subject has been determined to have an elevated risk of developing cancer using a method according to any one of claims 1 to 6, and wherein the use comprises that the one or more peptides or one of more polynucleic acids or vectors that encode one or more peptides, that comprise an amino acid sequence that

(i) is a fragment of a TAA; and

(ii) comprises a T cell epitope capable of binding to an HLAT of the subject;

optionally wherein the TAA fragment is flanked at the N and/or C terminus by additional amino acids that are not part of the sequence of the TAA, are to be administered to the subject.

8. A system for determining the risk that a human subject will develop a cancer, the system comprising:
   (a) a storage module configured to store data comprising the HLA class I genotype of a subject and the amino acid sequences of TAAs;
   (b) a computation module configured to quantify the HLAT of the subject that are capable of binding to T cell epitopes in the amino acid sequence of the TAAs, wherein each HLA of a HLAT is capable of binding to the same T cell epitope, and wherein an HLAT is any combination of three class I HLA alleles expressed by the subject; and
   (c) an output module configured to display an indication of the risk that the subject will develop a cancer and/or a recommended treatment for the subject;
   wherein the system is configured to display a higher risk that the subject will develop cancer when a lower number of HLATs are capable of binding to T cell epitopes of the TAAs.