

CLAIMS

1. A method for predicting the usefulness of a protein or a fragment thereof expressed by diseased cells for immunotherapy, the method comprising ascertaining the distribution or
5 localization of the protein or a nucleic acid coding therefor, or of a fragment of the protein.
2. The method of claim 1, which comprises ascertaining whether the protein or a nucleic acid coding therefor, or a fragment of the protein is located or abundant in the cytosol and/or within exosomes *in vivo*.
- 10 3. The method of claim 1 or 2, wherein localization or abundance of the protein or a nucleic acid coding therefor, or of a fragment of the protein in the cytosol and/or within exosomes indicates that the protein or a fragment thereof is useful for immunotherapy.
- 15 4. The method of claim 2 or 3, wherein the protein fragment is present within exosomes as MHC peptide complex, preferably on the surface of exosomes.
5. The method of claim 2 or 3, wherein localization or abundance of the protein or a nucleic acid coding therefor, or of a fragment of the protein in the cytosol indicates processing
20 and presentation of the protein in the MHC I pathway, preferably of diseased cells.
6. The method of claim 5, wherein processing and presentation of the protein in the MHC I pathway results in recognition of complexes formed by MHC I and fragments of the protein by CD8+ T cells.
- 25 7. The method of claim 2 or 3, wherein localization or abundance of the protein or a nucleic acid coding therefor, or of a fragment of the protein within exosomes indicates accumulation of the protein or a nucleic acid coding therefor, or of a fragment of the protein in antigen presenting cells, preferably professional antigen presenting cells.
- 30 8. The method of claim 7, wherein accumulation of the protein or a nucleic acid coding therefor, or of a fragment of the protein in antigen presenting cells indicates processing and presentation of the protein in the MHC I and/or MHC II pathway, preferably of the antigen presenting cells.

9. The method of claim 8, wherein processing and presentation of the protein in the MHC I pathway results in recognition of complexes formed by MHC I and fragments of the protein by CD8⁺ T cells.
- 5 10. The method of any one of claims 1 to 9, wherein the protein or a fragment thereof comprises a disease specific amino acid modification.
- 10 11. The method of claim 10, wherein the amino acid modification is due to a disease specific somatic mutation.
12. The method of any one of claims 1 to 11, wherein the disease is cancer and the immunotherapy is anti-cancer immunotherapy.
- 15 13. The method of any one of claims 1 to 12, wherein the protein fragment is a MHC binding peptide or a potential MHC binding peptide.
14. A method for selecting and/or ranking disease specific amino acid modifications for their usefulness in immunotherapy, the method comprising the steps of:
- 20 (i) identifying proteins expressed by diseased cells each protein comprising at least one disease specific amino acid modification, and
- (ii) ascertaining the distribution or localization of a protein identified under (i) or a nucleic acid coding therefor, or of a fragment of the protein, and
- (iii) repeating step (ii) for at least one further protein identified under (i).
- 25 15. The method of claim 14, wherein step (ii) comprises ascertaining whether the protein or a nucleic acid coding therefor, or a fragment of the protein is located or abundant in the cytosol and/or within exosomes *in vivo*.
- 30 16. The method of claim 14 or 15, wherein localization or abundance of the protein or a nucleic acid coding therefor, or of a fragment of the protein in the cytosol and/or within exosomes indicates that the disease specific amino acid modification is useful for immunotherapy.

17. The method of any one of claims 14 to 16, wherein the disease specific amino acid modification is comprised by a protein fragment which is a MHC binding peptide or a potential MHC binding peptide.

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18. The method of any one of claims 1 to 17, which is used in the manufacture of a vaccine.

19. The method of claim 18, wherein the vaccine is derived from one or more proteins or fragments thereof or one or more disease specific amino acid modifications which are predicted as being useful for immunotherapy.

20. A method for providing a vaccine comprising the step:
identifying one or more proteins or fragments thereof or one or more disease specific amino acid modifications which are predicted as being useful for immunotherapy by the method of any one of claims 1 to 19.

21. The method of claim 20 further comprising the step:
providing a vaccine comprising a peptide or polypeptide comprising one or more proteins or fragments thereof or one or more disease specific amino acid modifications which are predicted as being useful for immunotherapy, or a nucleic acid encoding the peptide or polypeptide.

22. A vaccine produced according to the method of any one of claims 18 to 21.

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