

CLAIMS

1. A recombinant extra-cellular vesicle internalizing receptor (EVIR) comprising:
 - (i) an extracellular antibody domain specific for a membrane molecule of a cancer cell, in which the membrane molecule is a tumor-associated antigen;
 - 5 (ii) a proteinic domain comprising at least one transmembrane and at least one intracellular domain, in which the proteinic domain is selected from sequences of the nerve growth factor receptor (NGFR), C-C chemokine receptor type 2 (CCR2), C-C chemokine receptor type 5 (CCR5), and P-selectin glycoprotein-1 ligand receptor (SELPLG), or a homologous variant thereof, in which the variant has an amino acid
 - 10 sequence which is at least 90% identical to the original amino acid sequence and has the ability to anchor the EVIR to the membrane of an antigen-presenting cell when expressed in the cell; and
 - (iii) optionally, a cell membrane export domain increasing the export of the EVIR to the cellular membrane of an antigen-presenting cell when expressed in the cell.
- 15 2. An EVIR according to Claim 1, in which the extracellular antibody domain is a scFv.
3. An EVIR according to Claim 1 or 2, in which the extracellular antibody domain comprises a sequence of an antibody, or a fragment thereof, specific for human epidermal growth factor receptor 2 (HER2).
4. An EVIR according to Claim 1 or 2, in which the extracellular antibody domain
 - 20 comprises a sequence of an antibody, or a fragment thereof, specific for tyrosinase-related protein-1 (TYRP1), carcinoembryonic antigen (CEA), mesothelin, PMEL (gp100), gangliosides (GD2, GD3), or mucins.
5. An EVIR according to Claim 1, 2 or 3, in which the extracellular antibody domain comprises a sequence selected from SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29 and
 - 25 SEQ ID NO: 30 or a homologous variant thereof, in which the variant has an amino acid sequence which is at least 90% identical to the original amino acid sequence and which binds to and has specificity for the tumor-associated antigen.

6. An EVIR according to Claim 4, in which the extracellular antibody domain comprises a sequence of an antibody, or a fragment thereof, specific for tyrosinase-related protein-1 (TYRP1) or ganglioside GD2.
7. An EVIR according to Claim 6, in which the extracellular antibody domain comprises a sequence selected from SEQ ID NO: 113 and SEQ ID NO: 114.
8. An EVIR according to any preceding claim, in which the proteinic domain is selected from SEQ ID NO: 31, SEQ ID NO: 35, SEQ ID NO: 39 and SEQ ID NO: 41.
9. An EVIR according to any preceding claim, comprising a cell membrane export domain comprising an IgK domain.
10. An EVIR according to Claim 9, comprising a cell membrane export domain comprising an IgK domain of SEQ ID NO 42 or a homologous derivative thereof, in which the derivative has an amino acid sequence which is at least 90% identical to the original amino acid sequence and has the ability to increase the exporting of the EVIR to the membrane of an antigen-presenting cell when expressed in the cell.
11. An EVIR according to any of Claims 1 to 3, 5 and 8 to 10 comprising an amino acid sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63 and SEQ ID NO: 64 or a homologous variant thereof, in which the variant has an amino acid sequence which is at least 90% identical to the original amino acid sequence and in which the EVIR binds to and/or internalizes extra-cellular vesicles comprising the tumor-associated antigen when expressed in an antigen-presenting cell.
12. An EVIR according to any of Claims 1, 2, 4 and 6 to 10 comprising an amino acid sequence selected from SEQ ID NO: 132 and SEQ ID NO: 133 or a homologous variant thereof, in which the variant has an amino acid sequence which is at least 90% identical to the original amino acid sequence and in which the EVIR binds to and/or internalizes extra-cellular vesicles comprising the tumor-associated antigen when expressed in an antigen-presenting cell.
13. An isolated nucleic acid sequence encoding an EVIR according to any preceding claim.

14. An isolated nucleic acid according to Claim 13 comprising a sequence selected from SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74 and SEQ ID NO: 75.
- 5 15. An isolated nucleic acid according to Claim 13 comprising a sequence selected from SEQ ID NO: 130 and SEQ ID NO: 131.
16. A vector comprising at least one nucleic acid sequence of according to Claim 13, 14 or 15.
17. A vector according to Claim 16 further comprising a least one nucleic acid encoding for
10 a functional protein that promotes survival, differentiation, proliferation, activation, maturation, phagocytosis, endocytosis, antigen-processing and presentation, T-cell recruitment in monocyte, macrophage and/or dendritic cells or a protein capable of inducing antigen presenting cell (APC) differentiation, survival, activation and/or cross-presentation or attracting and/or activating T cells.
- 15 18. An *ex vivo* method of inducing expression of at least one EVIR according to any of Claims 1 to 12, in an antigen-presenting cell (APC) or a stem/progenitor cell thereof, comprising the steps of:
 - (i) *ex vivo* transducing the cell with a vector encoding at least one EVIR according to any of Claims 1 to 12; and
 - 20 (ii) optionally inducing cell differentiation, maturation or activation.
19. A method according to Claim 18, in which the vector comprises a nucleic acid sequence according to Claim 13, 14 or 15 or is a vector according to Claim 16 or 17.
20. An isolated antigen presenting cell (APC) or a stem or progenitor cell thereof expressing at least one EVIR according to any of Claims 1 to 12.
- 25 21. An *ex vivo* method of preparing EVIR-expressing, tumor-associated antigens (TAAs)-presenting cells, comprising the steps of:
 - (i) providing at least one cancer cell or at least one cancer cell-derived extracellular vesicle (EV) obtained from a cancer subject;

- (ii) providing an EVIR-expressing cell according to Claim 20;
- (iii) contacting, *ex vivo*, an EVIR-expressing cell provided under (ii) with the at least one cancer cell or EV provided under (i);
- (iv) collecting cells obtained in step (iii);

5 in which cells obtained under (iv) have an enhanced ability to present TAAs from the cancer subject as compared to a cell not expressing an EVIR and treated as in (iii), once administered to the subject.

22. A pharmaceutical composition comprising at least one vector encoding at least one EVIR according to any of Claims 1 to 12 or cells according to Claim 20 or cells obtainable
10 from a method according to Claim 18 or 21 and at least one pharmaceutically acceptable carrier, diluent or excipient thereof.

23. A pharmaceutical composition according to Claim 22, in which the composition is a vaccine composition.

24. A pharmaceutical composition according to Claim 22 or 23 for use in the prevention
15 and/or treatment of a cancer.

25. A kit comprising at least one EVIR according to any of Claims 1 to 12 , or at least one recombinant expression vector according to Claim 16 or 17, or at least one EVIR-expressing cell according to Claim 20.