

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;
 - 5 (ii) a proteinic domain comprising at least one transmembrane and at least one intracellular domain; 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 said cell.
2. An EVIR according to claim 1 wherein the extracellular antibody domain is a scFv.
- 10 3. An EVIR according to claims 1 or 2, wherein 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 claims 1 or 2, wherein the extracellular antibody domain 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.
- 15 5. An EVIR according to any one of claims 1 to 3, wherein the extracellular antibody domain comprises a sequence selected from SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29 and SEQ ID NO: 30 or a variant thereof.
- 20 6. An EVIR according to claim 4 wherein the extracellular antibody domain comprises a sequence of an antibody, or a fragment thereof, specific for tyrosinase-related protein-1 (TYRP1) or gangliosides (GD2).
7. An EVIR according to claim 6, wherein the extracellular antibody domain comprises a sequence selected from SEQ ID NO: 113 and SEQ ID NO: 114.
- 25 8. An EVIR according to any one of claims 1 to 7 wherein the proteinic domain is selected from SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40 and SEQ ID NO: 41 or a variant thereof.

9. An EVIR according to any one of claims 1 to 8 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 derivative thereof.
- 5 11. An EVIR according to anyone of claims 1 to 3, 5, 8 or 9 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 variant thereof.
- 10 12. An EVIR according to anyone of claims 1 to 2, 4, 6 to 8 or 9 to 10 comprising an amino acid sequence selected from SEQ ID NO: 132 and SEQ ID NO: 133 or a variant thereof.
13. An isolated nucleic acid sequence encoding an EVIR according to any one of claims 1 to 12.
- 15 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 or a variant thereof.
15. An isolated nucleic acid according to claim 13 comprising a sequence selected from SEQ ID NO: 130 and SEQ ID NO: 131 or a variant thereof.
- 20 16. A vector comprising at least one nucleic acid sequence of any one of claims 13 to 15.
- 25 17. A vector according to claim 16 further comprising a least one nucleic acid encoding for 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.

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 said cell with a vector encoding at least one EVIR according to any of any one of claims 1 to 12; and
 - (ii) optionally inducing cell differentiation, maturation or activation.
19. A method according to claim 18 wherein the vector comprises a nucleic acid sequence according to claim 13 to 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 one of claims 1 to 12.
21. An *ex vivo* method of preparing EVIR-expressing, TAAs-presenting cells, comprising the steps of:
- (i) providing at least one cancer cell or at least one cancer cell-derived 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 said at least one cancer cell or EV provided under (i);
 - (iv) collecting cells obtained in step (iii);
- wherein cells obtained under (iv) have an enhanced ability to present TAAs from said cancer subject as compared to a cell not expressing an EVIR and treated as in (iii), once administered to said subject.
22. A pharmaceutical composition comprising at least one vector encoding at least one EVIR according to any of any one of claims 1 to 12 or cells according to claim 20 or cells obtainable from a method according to claims 18 or 21 and at least one pharmaceutically acceptable carrier, diluent or excipient thereof.
23. A pharmaceutical composition according to claim 22, wherein said composition is a vaccine composition.
24. A pharmaceutical composition according to claim 22 or 23 for use in the prevention and/or treatment of a cancer.

25. A kit comprising at least one EVIR according to any one 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.
26. A method of preventing and/or treating a cancer comprising administering an effective amount of EVIR-expressing cells according to claim 20 or at least one recombinant vector according to claim 16 or 17 in a subject in need thereof.
27. A method of inducing *in vivo* the expression of at least one EVIR according to any one of claims 1 to 12 in an APC or a stem/progenitor cell thereof in a subject in need thereof, said method comprising the steps of:
- (i) administering a vector encoding an EVIR according to claim 16 or 17 to said subject under suitable conditions for inducing transduction of the subject's APCs or stem/progenitor cell thereof *in vivo* with said vector; and
 - (ii) optionally inducing APC differentiation, maturation or activation *in vivo*.