

WHAT IS CLAIMED IS:

1. A process of enriching cell-type specific extracellular vesicles (EVs) in a biological fluid sample from a subject, comprising:
 - a. providing a biological fluid sample from the subject;
 - b. contacting the sample with antibodies specific for a cell surface marker for one or more cell types, optionally wherein the antibodies are attached to a matrix; and
 - c. isolating antibody-bound EVs from unbound EVs in the sample.
2. The process of claim 1, wherein the sample comprises a volume from 100 μ l to 7 mL, from 200 μ l to 6.5 mL, from 250 μ l to 6.5 mL, from 200 μ l to 6 mL, from 250 μ l to 6 mL, from 200 μ l to 5 mL, from 200 μ l to 4 mL, from 200 μ l to 3 mL, from 200 μ l to 2 mL, from 100 μ l to 1 mL, from 150 μ l to 1 mL, from 200 μ l to 1 mL, from 250 μ l to 1mL, from 200 μ l to 500 μ l, from 200 μ l to 500 μ l, from 200 μ l to 400 μ l, from 250 μ l to 500 μ l, or from 250 μ l to 400 μ l.
- ~~3. The process of claim 1 or 2, wherein the EVs comprise EVs from epithelial cells, lung tissue cells, breast tissue cells, liver tissue cells, prostate tissue cells, kidney tissue cells, urinary tract cells, neural cells, tumor cells, solid tumor cells, lung tumor cells, breast tumor cells, liver tumor cells, prostate tumor cells, kidney tumor cells, urinary tumor cells, glioblastoma cells, or amyloid beta expressing cells.~~
- ~~4.3.~~ The process of claim 1, ~~2, or 3~~, wherein the cell surface marker is an epithelial cell surface marker.
- ~~5.4.~~ The process of ~~any one of claims 1-4~~ claim 1, wherein the cell surface marker is:
 - a. an epithelial cell surface marker, optionally wherein the epithelial cell surface marker is such as EpCAM, EGFR, PSMA, GSP64, CD3, CD49b, CD87, CD95, E-Cadherin CA9, CA12, N-cadherin, OB-cadherin, cadherin-11, a cytokeratin or epithelial membrane antigen (EMA);
 - b. a lung tissue marker, optionally wherein the lung tissue marker is such as EpCAM, CA9, CA12, DSG3, FAT2, GPR87, KISS1R, LYPD3, SLC7A11, TMPRSS4, CD133, prominin-1, AC133, programmed death-1 receptor (PD1) or FAS;
 - c. a breast tissue marker, optionally wherein the breast tissue marker is such as E-cadherin, epithelial membrane antigen (EMA), human epidermal growth factor

receptor type 2 (Her2/neu), $\alpha\text{v}\beta 6$ integrin, EpCAM, carcinoembryonic antigen (CEA), folate receptor-alpha (FR- α), urokinase-type plasminogen activator receptor (uPAR) or placental-specific protein 1 (PLAC1);

- d. a liver cell marker, optionally wherein the liver cell marker is such as CD133, Prominin-1, CD44, EpCAM, delta-like 1 non-canonical Notch ligand 1 (DLK1), ALDH, CD13, CD90, CD24, OV6, ICAM-1, CD34, C-kit, $\alpha 2\delta 1$, K19, LGR5, GPC3, Annexin A2, CD15, ABC transporters, Nope, DCLK1, ASGPR, CK or CD47;
- e. a glioblastoma biomarker, optionally wherein the glioblastoma biomarker is such as fibronectin, CD63, HSP70, Annexin A2, CD9, CD81, CD44, GRP78, CD133, CD15, a sialoglycoprotein, SLC1A3, PTPRZ1, GPR56, CLU or ALD1A3;
- f. a urinary tract cell marker, optionally wherein the urinary tract cell marker is such as a tetraspanin, CD9, CD81, LAMP-1, CD10, CD24, CD44 or CD63; or
- g. an amyloid marker, optionally wherein the amyloid marker is such as beta-amyloid precursor protein (β -APP), presenilin protein PS-1, or proinsulin protein PS-2.

~~6. The process of any one of claims 1-5, wherein the matrix comprises particles such as beads, pellets, or chips, which are optionally magnetic.~~

~~7. The process of any one of claims 1-6, wherein the biological fluid sample comprises tears, saliva, lymph fluid, urine, serum, cerebral spinal fluid, pleural effusion, ascites, or plasma.~~

~~8.5.~~ The process of claim ~~7~~1, wherein the sample comprises serum or plasma.

~~9. The process of any one of claims 1-8, wherein the subject is a human.~~

~~10.6.~~ The process of ~~any one of claims 1-9~~claim 1, wherein the subject is a cancer subject, ~~or a~~ suspected cancer subject, an infectious disease subject, or a suspected infectious disease subject.

~~11. The process of claim 10, wherein the cancer is a solid tumor.~~

~~12. The process of claim 11, wherein the cancer is breast cancer, triple negative breast cancer, lung cancer, NSCLC, SCLC, liver cancer, urinary tract cancer, bladder cancer, brain cancer, or glioblastoma.~~

~~13. The process of any one of claims 1-9, wherein the subject is an infectious disease subject or suspected infectious disease subject.~~

~~14. The process of any one of claims 1-9, wherein the subject is an inflammatory disease subject or suspected inflammatory disease subject.~~

~~15. The process of any one of claims 1-14, wherein the cell surface marker is EpCAM.~~

~~16. The process of any one of claims 1-9, wherein the subject is an amyloid disease subject or suspected amyloid disease subject.~~

~~17.7.~~ The process of ~~any one of claims 1-16~~claim 1, further comprising isolating total extracellular vesicles (EVs) from the sample, ~~such as~~ by membrane capture or differential ultracentrifugation, determining total protein levels in the isolated total extracellular vesicles, and optionally comparing the total protein levels from the total EVs to levels of cell surface marker in the EVs.

~~18.8.~~ The process of ~~any one of claims 1-17~~claim 1, wherein isolation of antibody bound EVs from unbound EVs is through attachment to the matrix.

~~19. The process of claim 18, wherein isolation of the antibody bound EVs from unbound EVs comprises separating the matrix from supernatant in the sample, such as by allowing the matrix to precipitate by gravity or centrifugation.~~

~~20.9.~~ The process of ~~any one of claims 1-19~~claim 1, further comprising contacting the antibody bound EVs with a detection agent specific for a second biomarker.

~~21. The process of claim 20, wherein the antibody bound EVs are resuspended in lysis buffer prior to being contacted with the detection agent specific for the second biomarker.~~

~~22. The process of claim 20 or 21, wherein the detection agent is an antibody.~~

~~23. The process of any one of claims 20-22, wherein the second biomarker comprises a protein, a polynucleotide (e.g. an RNA molecule), a lipid, a drug, or a drug metabolite.~~

24.10. The process of ~~any one of claims 20-23~~claim 9,

a. wherein the subject has cancer or is suspected of having cancer, and

b. where the second biomarker is

i. a polypeptide expressed or overexpressed in tumor cells, ~~and/or wherein the second biomarker is a~~

ii. cytokine, cytokine receptor, or an immune checkpoint regulator, ~~and/or~~

iii. one or more of PD-L1, SCF, IL-3, GM-CSF, G-CSF, M-CSF, TNF-alpha, IL-2, IL-5, TMB, CTLA-4, ICOS, 4-1BB (CD137), PD-1, CTLA-4, LAG-3, Tim-3, CD39, IFN- β , IFN- γ , IL-2, IL-10, TGF- β , CCR10, CXCR4, CCR7, sMICA, IL-8, IDO1, GBP1, class II MHC molecules, CXCL9, CXCL10 (IP-10), CXCL11, IL-6, CCL4, CCL5, IFNGR1, IFNGR2, JAK2, IRF1, IFIT1, IFIT2, MTAP, miR3, SOCA1, PIAS4, GZMA, GZMB, PRF1, HLA-DQA1, HLA-DRB1, IFNG, STAT1, ICAM1-5, VCAM-1, JAK1, JAK2, CCR5, HLA-DRA, CXCR6, TIGIT, CD27, CD274, PDCD1LG2 (PD-L2), LAG3, NKG7, PSMB10, CMKLR1, CD8A, CD8B, HLA-DB1, HLA-E, CD276, CD3D, CD3E, CD3G, CD247, ZAP70, CD2, CD28, ICOS, IL12Rb1, GZMM, FLTSLG, IL-15, Eotazin, GRO-1, VEGF, HGF, AFP, BCR-ABL, BRCA1/BRCA2, B-Raf V600E, CA-125, CA19-9, CEA, EGFR, HER-2/neu, KIT, PSA, S100, KRAS, UGT1A1 or CD20.

~~25. The process of claim 24, wherein the second biomarker is one or more of PD-L1, SCF, IL-3, GM-CSF, G-CSF, M-CSF, TNF-alpha, IL-2, IL-5, TMB, CTLA-4, ICOS, 4-1BB (CD137), PD-1, CTLA-4, LAG-3, Tim-3, CD39, IFN- β , IFN- γ , IL-2, IL-10, TGF- β , CCR10, CXCR4, CCR7, sMICA, IL-8, IDO1, GBP1, class II MHC molecules, CXCL9, CXCL10 (IP-10), CXCL11, IL-6, CCL4, CCL5, IFNGR1, IFNGR2, JAK2, IRF1, IFIT1, IFIT2, MTAP, miR3, SOCA1, PIAS4, GZMA, GZMB, PRF1, HLA-DQA1, HLA-DRB1, IFNG, STAT1, ICAM1-5, VCAM-1, JAK1, JAK2, CCR5, HLA-DRA, CXCR6, TIGIT, CD27, CD274, PDCD1LG2 (PD-L2), LAG3, NKG7, PSMB10, CMKLR1, CD8A, CD8B, HLA-DB1, HLA-E, CD276, CD3D, CD3E, CD3G, CD247, ZAP70, CD2, CD28, ICOS, IL12Rb1, GZMM, FLTSLG, IL-15, Eotazin, GRO-1, VEGF, HGF, AFP, BCR-ABL, BRCA1/BRCA2, B-Raf V600E, CA-125, CA19-9, CEA, EGFR, HER-2/neu, KIT, PSA, S100, KRAS, UGT1A1 or CD20.~~

26.11. The process of ~~any one of claims 1-25~~claim 1, wherein the process has one or more of the following characteristics:

- the sample is not subjected to chromatography either before or after contacting the sample

with the antibodies;

- the sample is not treated before contacting the sample with the antibodies other than optionally to remove particles above 1 μm , above 2 μm , above 5 μm , above 10 μm , or above 20 μm in diameter and/or to remove cellular bodies and debris larger than EVs;
- the EVs are not subjected to chromatography either before or after contacting the sample with the antibodies;
- the antibodies are attached to a matrix, and the matrix is not a filter, an ion-exchange medium, or a membrane; or
- the antibodies are attached to a matrix and the matrix is not charged.

~~27.12.~~ The process of ~~any one of claims 1-26~~claim 1, wherein isolating the cell-type specific EVs from the sample consists essentially of: contacting the sample with antibodies specific for the cell surface marker for the one or more cell types, optionally wherein the antibodies are attached to a matrix; and isolating the antibody-bound EVs from unbound EVs in the sample.

~~28.13.~~ A process of enriching cell-type specific extracellular vesicles (EVs) from a subject, comprising:

- a. providing a biological fluid sample from the subject;
- b. contacting the sample with antibodies specific for a cell surface marker, optionally wherein the antibodies are attached to a matrix;
- c. isolating antibody-bound EVs from unbound EVs in the sample;
- d. optionally resuspending the antibody-bound EVs in a lysis buffer; and
- e. contacting the EVs with a detection agent specific for a second biomarker; optionally wherein the cell surface marker is:
 - i. an epithelial cell surface marker, optionally wherein the epithelial cell surface marker is EpCAM, EGFR, PSMA, GSP64, CD3, CD49b, CD87, CD95, E-Cadherin CA9, CA12, N-cadherin, OB-cadherin, cadherin-11, a cytokeratin or epithelial membrane antigen (EMA);
 - ii. a lung tissue marker, optionally wherein the lung tissue marker is EpCAM, CA9, CA12, DSG3, FAT2, GPR87, KISS1R, LYPD3, SLC7A11, TMPRSS4, CD133, prominin-1, AC133, programmed death-1 receptor (PD1) or FAS;
 - iii. breast tissue marker, optionally wherein the breast tissue marker is E-cadherin, epithelial membrane antigen (EMA), human epidermal growth factor receptor type 2 (Her2/neu), $\alpha\text{v}\beta 6$ integrin, EpCAM, carcinoembryonic antigen (CEA), folate

receptor-alpha (FR- α), urokinase-type plasminogen activator receptor (uPAR) or placental-specific protein 1 (PLAC1);

iv. a liver cell marker, optionally wherein the liver cell marker is CD133, Prominin-1, CD44, EpCAM, delta-like 1 non-canonical Notch ligand 1 (DLK1), ALDH, CD13, CD90, CD24, OV6, ICAM-1, CD34, C-kit, α 2 δ 1, K19, LGR5, GPC3, Annexin A2, CD15, ABC transporters, Nope, DCLK1, ASGPR, CK or CD47;

v. a glioblastoma biomarker, optionally wherein the glioblastoma biomarker is fibronectin, CD63, HSP70, Annexin A2, CD9, CD81, CD44, GRP78, CD133, CD15, a sialoglycoprotein, SLC1A3, PTPRZ1, GPR56, CLU or ALD1A3;

vi. a urinary tract cell marker, optionally wherein the urinary tract cell marker is a tetraspanin, CD9, CD81, LAMP-1, CD10, CD24, CD44 or CD63; or

vii. an amyloid marker, optionally wherein the amyloid marker is beta-amyloid precursor protein (β -APP), presenilin protein PS-1, or proinsulin protein PS-2.

~~29. The process of claim 28, wherein the sample comprises a volume from 100 μ l to 7 mL, from 200 μ l to 6.5 mL, from 250 μ l to 6.5 mL, from 200 μ l to 6 mL, from 250 μ l to 6 mL, from 200 μ l to 5 mL, from 200 μ l to 4 mL, from 200 μ l to 3 mL, from 200 μ l to 2 mL, from 100 μ l to 1 mL, from 150 μ l to 1 mL, from 200 μ l to 1 mL, from 250 μ l to 1 mL, from 200 μ l to 500 μ l, from 200 μ l to 500 μ l, from 200 μ l to 400 μ l, from 250 μ l to 500 μ l, or from 250 μ l to 400 μ l.~~

~~30. The process of claim 28 or 29, wherein the EVs comprise EVs from epithelial cells, lung tissue cells, breast tissue cells, liver tissue cells, prostate tissue cells, kidney tissue cells, urinary tract cells, neural cells, tumor cells, solid tumor cells, lung tumor cells, breast tumor cells, liver tumor cells, prostate tumor cells, kidney tumor cells, urinary tumor cells, glioblastoma cells, or amyloid beta-expressing cells.~~

~~31. The process of any one of claims 28-30, wherein the cell surface marker is an epithelial cell surface marker.~~

~~32. The process of any one of claims 28-30, wherein the cell surface marker is:~~

~~a. an epithelial cell surface marker, such as EpCAM, EGFR, PSMA, GSP64, CD3, CD49b, CD87, CD95, E-Cadherin CA9, CA12, N-cadherin, OB-cadherin, cadherin-11, a cytokeratin or epithelial membrane antigen (EMA);~~

- b. ~~a lung tissue marker, such as EpCAM, CA9, CA12, DSG3, FAT2, GPR87, KISS1R, LYPD3, SLC7A11, TMPRSS4, CD133, prominin 1, AC133, programmed death 1 receptor (PD1) or FAS;~~
- c. ~~a breast tissue marker, such as E-cadherin, epithelial membrane antigen (EMA), human epidermal growth factor receptor type 2 (Her2/neu), α v β 6 integrin, EpCAM, carcinoembryonic antigen (CEA), folate receptor-alpha (FR- α), urokinase-type plasminogen activator receptor (uPAR) or placental specific protein 1 (PLAC1);~~
- d. ~~a liver cell marker, such as CD133, Prominin 1, CD44, EpCAM, delta-like 1 non-canonical Notch ligand 1 (DLK1), ALDH, CD13, CD90, CD24, OV6, ICAM-1, CD34, C-kit, α 2 δ 1, K19, LGR5, GPC3, Annexin A2, CD15, ABC transporters, Nope, DCLK1, ASGPR, CK or CD47;~~
- e. ~~a glioblastoma biomarker, such as fibronectin, CD63, HSP70, Annexin A2, CD9, CD81, CD44, GRP78, CD133, CD15, a sialoglycoprotein, SLC1A3, PTPRZ1, GPR56, CLU or ALD1A3;~~
- f. ~~a urinary tract cell marker, such as a tetraspanin, CD9, CD81, LAMP 1, CD10, CD24, CD44 or CD63; or~~
- g. ~~an amyloid marker such as beta-amyloid precursor protein (β -APP), presenilin protein PS 1, or proinsulin protein PS 2.~~

33. ~~The process of any one of claims 28-32, wherein the matrix comprises particles such as beads, pellets, or chips, which are optionally magnetic.~~

34. ~~The process of any one of claims 28-33, wherein the biological fluid sample comprises tears, saliva, lymph fluid, urine, serum, cerebral spinal fluid, pleural effusion, ascites, or plasma.~~

35. ~~The process of claim 34, wherein the sample comprises serum or plasma.~~

36. ~~The process of any one of claims 28-35, wherein the subject is a human.~~

37. ~~The process of any one of claims 28-36, wherein the subject is a cancer subject or suspected cancer subject.~~

38. ~~The process of claim 37, wherein the cancer is a solid tumor.~~

- ~~39. The process of claim 38, wherein the cancer is breast cancer, triple negative breast cancer, lung cancer, NSCLC, SCLC, liver cancer, urinary tract cancer, bladder cancer, brain cancer, or glioblastoma.~~
- ~~40. The process of any one of claims 28-39, wherein the subject is an infectious disease subject or suspected infectious disease subject.~~
- ~~41. The process of claim 40, wherein (a) the cell surface marker comprises EpCAM, EGFR, PSMA, GSP64, CD3, CD49b, CD87, CD95, E-Cadherin CA9, CA12, N-cadherin, OB-cadherin, cadherin-11, cytokeratins and epithelial membrane antigen (EMA) and/or (b) the second biomarker comprises one or more of IL-4, IL-5, IL-8, IL-10, IL-35, IFN- α , IFN- γ , CXCL10 (IP-10), C-reactive protein, hemagglutinin, virus RNA, virus DNA, viral proteins (such as hepatitis B surface antigen, and HIV p24 antigen), bacterial RNA, bacterial DNA, a bacterial protein, a surface immunoglobulin or a receptor for C3 complement component.~~
- ~~42. The process of any one of claims 28-39, wherein the subject is an inflammatory disease subject or suspected inflammatory disease subject.~~
- ~~43. The process of claim 42, wherein the second biomarker comprises one or more of TNF- α , IL-16, IL-17, IL-21, IL-22, IL-33, CD86, CD80, CRP, IL-1, IL-1 α , IL-1 β , IL-2, IL-6, IL-8, IL-12, IFN- γ , serum amyloid (SAA), COX2, NK- κ B, CCL2, CXCL10, CCL2, CXCL5, CXCL9, CXCL6, MMP-7, MMP-2, MMP-9 or CSF1R; and optionally, wherein the cell surface marker is an epithelial cell surface marker, such as EpCAM, EGFR, PSMA, GSP64, CD3, CD49b, CD87, CD95, E-Cadherin CA9, CA12, N-cadherin, OB-cadherin, cadherin-11, a cytokeratin or epithelial membrane antigen (EMA).~~
- ~~44. The process of any one of claims 28-43, wherein the cell surface marker is EpCAM.~~
- ~~45. The process of any one of claims 28-39, wherein the subject is an amyloid disease subject or suspected amyloid disease subject.~~
- ~~46. The process of claim 45, wherein the cell surface marker is β -APP, PS-1, or PS-2, and/or wherein the second biomarker is one or more of CD3, CD4, CD8, CD40L, CD45RO, CD45RA, sCD40L, Fas/CD95, CD14, APP, CD19, CD69, IL-2, IFN- α , sCD40, CD11b,~~

~~CD14, Iba1, CD11b, CD11c, RCA-1, MHCII (including HLA-DR), ferritin, IL-1 α , CD68, CD163, Ricinus communis agglutinin-1 (RCA-1), translocator protein (TSPO), triggering receptor expressed on myeloid cells-2 (TREM2), CR3 or CD33~~

~~47.14.~~ The process of ~~any one of claims 28-46~~claim 13, further comprising isolating total extracellular vesicles (EVs) from the sample, ~~such as~~ by membrane capture or differential ultracentrifugation, determining total protein levels in the isolated total extracellular vesicles, and optionally comparing the total protein levels from the total EVs to levels of cell surface marker in the EVs.

~~48.15.~~ The process of ~~any one of claims 28-47~~claim 13, wherein isolation of antibody bound EVs from unbound EVs is through attachment to the matrix.

~~49. The process of claim 48, wherein isolation of the antibody bound EVs from unbound EVs comprises separating the matrix from supernatant in the sample, such as by allowing the matrix to precipitate by gravity or centrifugation.~~

~~50.16.~~ The process of ~~any one of claims 28-49~~claim 13, wherein the process has one or more of the following characteristics:

- the sample is not subjected to chromatography either before or after contacting the sample with the antibodies;
- the sample is not treated before contacting the sample with the antibodies other than optionally to remove particles above 1 μ m, above 2 μ m, above 5 μ m, above 10 μ m, or above 20 μ m in diameter from the sample and/or to remove cellular bodies and debris larger than EVs;
- the EVs are not subjected to chromatography either before or after contacting the sample with the antibodies;
- the antibodies are attached to a matrix, and the matrix is not a filter, an ion-exchange medium, or a membrane; or
- the antibodies are attached to a matrix and the matrix is not charged.

~~51.17.~~ The process of ~~any one of claims 28-50~~claim 13, wherein isolating the cell-type specific EVs from the sample consists essentially of: contacting the sample with antibodies specific for the cell surface marker for the one or more cell types, optionally wherein the antibodies are attached to a matrix; isolating the antibody-bound EVs from unbound EVs in the sample,

resuspending the antibody-bound EVs in a lysis buffer, and contacting the EVs with a detection agent specific for a second biomarker.

~~52. The process of any one of claims 28-51, wherein the detection agent is an antibody.~~

~~53. The process of any one of claims 28-52, wherein the second biomarker comprises a protein, a polynucleotide (e.g. an RNA molecule), a lipid, a drug, or a drug metabolite.~~

~~54.18. The process of ~~any one of claims 28-39, 44, or 47-53~~claim 13, wherein the subject has cancer or is suspected of having cancer, and wherein the second biomarker is a polypeptide expressed or overexpressed in tumor cells, and/or wherein the second biomarker is a cytokine, cytokine receptor, or an immune checkpoint regulator chosen from one or more of PD-L1, SCF, IL-3, GM-CSF, G-CSF, M-CSF, TNF-alpha, IL-2, IL-5, TMB, CTLA-4, ICOS, 4-1BB (CD137), PD-1, CTLA-4, LAG-3, Tim-3, CD39, IFN-β, IFN-γ, IL-2, IL-10, TGF-β, CCR10, CXCR4, CCR7, sMICA, IL-8, IDO1, GBP1, class II MHC molecules, CXCL9, CXCL10 (IP-10), CXCL11, IL-6, CCL4, CCL5, IFNGR1, IFNGR2, JAK2, IRF1, IFIT1, IFIT2, MTAP, miR3, SOCA1, PIAS4, GZMA, GZMB, PRF1, HLA-DQA1, HLA-DRB1, IFNG, STAT1, ICAM1-5, VCAM-1, JAK1, JAK2, CCR5, HLA-DRA, CXCR6, TIGIT, CD27, CD274, PDCD1LG2 (PD-L2), LAG3, NKG7, PSMB10, CMKLR1, CD8A, CD8B, HLA-DB1, HLA-E, CD276, CD3D, CD3E, CD3G, CD247, ZAP70, CD2, CD28, ICOS, IL12Rb1, GZMM, FLTSLG, IL-15, Eotazin, GRO-1, VEGF, HGF, AFP, BCR-ABL, BRCA1/BRCA2, B-Raf V600E, CA-125, CA19-9, CEA, EGFR, HER-2/neu, KIT, PSA, S100, KRAS, UGT1A1 or CD20.~~

~~55. The process of claim 54, wherein the second biomarker is one or more of PD-L1, SCF, IL-3, GM-CSF, G-CSF, M-CSF, TNF-alpha, IL-2, IL-5, TMB, CTLA-4, ICOS, 4-1BB (CD137), PD-1, CTLA-4, LAG-3, Tim-3, CD39, IFN-β, IFN-γ, IL-2, IL-10, TGF-β, CCR10, CXCR4, CCR7, sMICA, IL-8, IDO1, GBP1, class II MHC molecules, CXCL9, CXCL10 (IP-10), CXCL11, IL-6, CCL4, CCL5, IFNGR1, IFNGR2, JAK2, IRF1, IFIT1, IFIT2, MTAP, miR3, SOCA1, PIAS4, GZMA, GZMB, PRF1, HLA-DQA1, HLA-DRB1, IFNG, STAT1, ICAM1-5, VCAM-1, JAK1, JAK2, CCR5, HLA-DRA, CXCR6, TIGIT, CD27, CD274, PDCD1LG2 (PD-L2), LAG3, NKG7, PSMB10, CMKLR1, CD8A, CD8B, HLA-DB1, HLA-E, CD276, CD3D, CD3E, CD3G, CD247, ZAP70, CD2, CD28, ICOS, IL12Rb1, GZMM, FLTSLG, IL-~~

~~15, Eotazin, GRO-1, VEGF, HGF, AFP, BCR-ABL, BRCA1/BRCA2, B-Raf V600E, CA-125, CA19-9, CEA, EGFR, HER-2/neu, KIT, PSA, S100, KRAS, UGT1A1 or CD20.~~

~~56. The process of claim 55, wherein the second biomarker comprises PD-L1.~~

~~57. The process of claim 56, wherein the tumor cell surface marker is EpCAM and the second biomarker comprises PD-L1.~~

~~58-19.~~ A process of identifying tumor-derived extracellular vesicles (EVs) in a subject, comprising:

- a. providing a plasma sample from the subject, optionally wherein the sample is from 100 μ l to 1 mL, 200 μ l to 1 mL, from 250 μ l to 1mL, from 100 μ l to 500 μ l, from 200 μ l to 500 μ l, from 200 μ l to 400 μ l, from 250 μ l to 500 μ l, or from 250 μ l to 400 μ l;
- b. contacting the plasma sample with antibodies specific for EpCAM, optionally wherein the antibodies are attached to a matrix;
- c. isolating EpCAM antibody-bound EVs from unbound EVs in the sample;
- d. optionally resuspending the EpCAM antibody-bound EVs in a lysis buffer; and
- e. contacting the EpCAM antibody-bound EVs with an antibody specific for PD-L1 and optionally determining the level of PD-L1 in the EpCAM antibody-bound EVs; optionally wherein the subject is a human having or suspected of having breast cancer, triple negative breast cancer, lung cancer, NSCLC, SCLC, liver cancer, urinary tract cancer, bladder cancer, brain cancer, or glioblastoma.

~~59-20.~~ A process of determining treatment for a subject with cancer, comprising:

- a. providing a plasma sample from the subject, optionally wherein the sample is 100 μ l to 1 mL, from 200 μ l to 1 mL, from 250 μ l to 1mL, from 100 μ l to 500 μ l, from 200 μ l to 500 μ l, from 200 μ l to 400 μ l, from 250 μ l to 500 μ l, or from 250 μ l to 400 μ l;
- b. contacting the plasma sample with antibodies specific for EpCAM, optionally wherein the antibodies are attached to a matrix;
- c. isolating antibody-bound extracellular vesicles (EVs) from unbound EVs in the sample;
- d. optionally resuspending the EpCAM antibody-bound EVs in a lysis buffer;
- e. contacting the EVs with an antibody specific for PD-L1;

- f. determining the level of PD-L1 in the EpCAM antibody-bound EVs; ~~and~~
- g. determining whether the subject should receive treatment with an immune checkpoint inhibitor (e.g. a PD-1 or PD-L1 inhibitor) based on the determined level of PD-L1 in the EpCAM antibody-bound EVs, wherein increases in PD-L1 levels correlate with need for treatment with the inhibitor; optionally wherein the treatment is chosen from:
 - i. a PD-L1 inhibitor, optionally wherein the PD-L1 inhibitor is atezolimumab, durvalumab, avelumab, envafolimab, BMS-936559, CK-301, CS-1001, SHR-1316, CBT-502, or BGB-A333;
 - ii. a PD-1 inhibitor, optionally wherein the PD-1 inhibitor is nivolumab, pembrolizumab, cemiplimab, spartalizumab, camrelizumab, sintilimab, tislelizumab, toripalimab, AMP-224, or AMP-514; or
 - iii. a CTLA-4 inhibitor, optionally wherein the CTLA-4 inhibitor is ipilimumab.

~~60. The process of claim 59, wherein the process comprises determining whether the subject should receive a PD-L1 inhibitor such as atezolimumab, durvalumab, avelumab, envafolimab, BMS-936559, CK-301, CS-1001, SHR-1316, CBT-502, or BGB-A333.~~

~~61. The process of claim 59, wherein the process comprises determining whether the subject should receive a PD-1 inhibitor such as nivolumab, pembrolizumab, cemiplimab, spartalizumab, camrelizumab, sintilimab, tislelizumab, toripalimab, AMP-224, or AMP-514, or a CTLA-4 inhibitor such as ipilimumab.~~

~~62. The process of any one of claims 58-61, wherein the subject is a human having or suspected of having breast cancer, triple negative breast cancer, lung cancer, NSCLC, SCLC, liver cancer, urinary tract cancer, bladder cancer, brain cancer, or glioblastoma.~~

~~63. The process of any one of claims 59-62, wherein the process further comprises administering an immune checkpoint inhibitor such as a PD-1 or PD-L1 inhibitor to the subject.~~

~~64. The process of any one of the preceding claims, wherein prior to contacting the sample with the antibodies specific to the cell surface marker, the sample has been treated to remove particles above 1 μm , above 2 μm , above 5 μm , above 10 μm , or above 20 μm in diameter and/or to remove cellular bodies and debris larger than EVs.~~

~~65. The process of any one of the preceding claims, wherein the EVs have a particle size of less than 1 micron, such as 40 nm to less than 1 micron, 40-500 nm, 40-300 nm, 100-400 nm, or 100-300 nm, or have a mean particle size of 150-200 nm.~~

~~66-21.~~ A kit for enriching or identifying cell-type specific extracellular vesicles (EVs) in a biological fluid sample from a subject, the kit comprising antibodies specific for a cell surface marker attached to a matrix, and optionally further comprising: (a) one or more detection reagents for detection of a second biomarker, (b) one or more buffers for resuspending antibody-bound EVs and/or for detection of a second biomarker, and (c) instructions for use in enriching EVs from a biological fluid sample of a subject; optionally wherein the cell surface marker is:

i. an epithelial cell surface marker, optionally wherein the epithelial cell surface marker is EpCAM, EGFR, PSMA, GSP64, CD3, CD49b, CD87, CD95, E-Cadherin CA9, CA12, N-cadherin, OB-cadherin, cadherin-11, a cytokeratin or epithelial membrane antigen (EMA);

ii. a lung tissue marker, optionally wherein the lung tissue marker is EpCAM, CA9, CA12, DSG3, FAT2, GPR87, KISS1R, LYPD3, SLC7A11, TMPRSS4, CD133, prominin-1, AC133, programmed death-1 receptor (PD1) or FAS;

iii. a breast tissue marker, optionally wherein the breast tissue marker is E-cadherin, epithelial membrane antigen (EMA), human epidermal growth factor receptor type 2 (Her2/neu), $\alpha\beta6$ integrin, EpCAM, carcinoembryonic antigen (CEA), folate receptor-alpha (FR- α), urokinase-type plasminogen activator receptor (uPAR) or placental-specific protein 1 (PLAC1);

iv. a liver cell marker, optionally wherein the liver cell marker is CD133, Prominin-1, CD44, EpCAM, delta-like 1 non-canonical Notch ligand 1 (DLK1), ALDH, CD13, CD90, CD24, OV6, ICAM-1, CD34, C-kit, $\alpha2\delta1$, K19, LGR5, GPC3, Annexin A2, CD15, ABC transporters, Nope, DCLK1, ASGPR, CK or CD47;

v. a glioblastoma biomarker, optionally wherein the glioblastoma biomarker is fibronectin, CD63, HSP70, Annexin A2, CD9, CD81, CD44, GRP78, CD133, CD15, a sialoglycoprotein, SLC1A3, PTPRZ1, GPR56, CLU or ALD1A3;

vi. a urinary tract cell marker, optionally wherein the urinary tract cell marker is a tetraspanin, CD9, CD81, LAMP-1, CD10, CD24, CD44 or CD63; or

vii. an amyloid marker, optionally wherein the amyloid marker is beta-amyloid precursor protein (β -APP), presenilin protein PS-1, or proinsulin protein PS-2.

~~67. The kit of claim 66, wherein the matrix comprises particles such as beads, pellets, or chips, which are optionally magnetic.~~

~~68. The kit of claim 66 or 67, wherein the kit enriches or identifies EVs from epithelial cells, lung tissue cells, breast tissue cells, liver tissue cells, prostate tissue cells, kidney tissue cells, urinary tract cells, neural cells, tumor cells, solid tumor cells, lung tumor cells, breast tumor cells, liver tumor cells, prostate tumor cells, kidney tumor cells, urinary tumor cells, glioblastoma cells, or amyloid beta-expressing cells.~~

~~69. The kit of any one of claims 66-68, wherein the cell surface marker is:~~

- ~~a. an epithelial cell surface marker, such as EpCAM, EGFR, PSMA, GSP64, CD3, CD49b, CD87, CD95, E-Cadherin CA9, CA12, N-cadherin, OB-cadherin, cadherin-11, a cytokeratin or epithelial membrane antigen (EMA);~~
- ~~b. a lung tissue marker, such as EpCAM, CA9, CA12, DSG3, FAT2, GPR87, KISS1R, LYPD3, SLC7A11, TMPRSS4, CD133, prominin-1, AC133, programmed death-1 receptor (PD1) or FAS;~~
- ~~c. a breast tissue marker, such as E-cadherin, epithelial membrane antigen (EMA), human epidermal growth factor receptor type 2 (Her2/neu), α v β 6 integrin, EpCAM, carcinoembryonic antigen (CEA), folate receptor alpha (FR- α), urokinase-type plasminogen activator receptor (uPAR) or placental specific protein-1 (PLAC1);~~
- ~~d. a liver cell marker, such as CD133, Prominin-1, CD44, EpCAM, delta-like 1 non-canonical Notch ligand 1 (DLK1), ALDH, CD13, CD90, CD24, OV6, ICAM-1, CD34, C-kit, α 2 δ 1, K19, LGR5, GPC3, Annexin A2, CD15, ABC transporters, Nope, DCLK1, ASGPR, CK or CD47;~~
- ~~e. a glioblastoma biomarker, such as fibronectin, CD63, HSP70, Annexin A2, CD9, CD81, CD44, GRP78, CD133, CD15, a sialoglycoprotein, SLC1A3, PTPRZ1, GPR56, CLU or ALD1A3;~~
- ~~f. a urinary tract cell marker, such as a tetraspanin, CD9, CD81, LAMP-1, CD10, CD24, CD44 or CD63; or~~
- ~~g. an amyloid marker such as beta-amyloid precursor protein (β -APP), presenilin protein PS-1, or proinsulin protein PS-2.~~

~~70. The kit of any one of claims 66-69, wherein the second biomarker comprises a protein, a polynucleotide (e.g. an RNA molecule), a lipid, a drug, or a drug metabolite.~~

~~71. The kit of any one of claims 66-70, wherein the second biomarker is one or more of PD-L1, SCF, IL-3, GM-CSF, G-CSF, M-CSF, TNF-alpha, IL-2, IL-5, TMB, CTLA-4, ICOS, 4-1BB (CD137), PD-1, CTLA-4, LAG-3, Tim-3, CD39, IFN-beta, IFN-gamma, IL-2, IL-10, TGF-beta, CCR10, CXCR4, CCR7, sMICA, IL-8, IDO1, GBP1, class II MHC molecules, CXCL9, CXCL10 (IP-10), CXCL11, IL-6, CCL4, CCL5, IFNGR1, IFNGR2, JAK2, IRF1, IFIT1, IFIT2, MTAP, miR3, SOCA1, PIAS4, GZMA, GZMB, PRF1, HLA-DQA1, HLA-DRB1, IFNG, STAT1, ICAM1-5, VCAM-1, JAK1, JAK2, CCR5, HLA-DRA, CXCR6, TIGIT, CD27, CD274, PDCD1LG2 (PD-L2), LAG3, NKG7, PSMB10, CMKLR1, CD8A, CD8B, HLA-DB1, HLA-E, CD276, CD3D, CD3E, CD3G, CD247, ZAP70, CD2, CD28, ICOS, IL12Rb1, GZMM, FLTSLG, IL-15, Eotazin, GRO-1, VEGF, HGF, AFP, BCR-ABL, BRCA1/BRCA2, B-Raf V600E, CA-125, CA19-9, CEA, EGFR, HER-2/neu, KIT, PSA, S100, KRAS, UGT1A1, CD20, TNF-alpha, IL-16, IL-17, IL-21, IL-22, IL-33, CD86, CD80, CRP, IL-1, IL-1alpha, IL-1beta, IL-2, IL-6, IL-8, IL-12, IFN-gamma, serum amyloid (SAA), COX2, NK-kappaB, CCL2, CXCL10, CCL2, CXCL5, CXCL9, CXCL6, MMP-7, MMP-2, MMP-9, CSFIR, CD3, CD4, CD8, CD40L, CD45RO, CD45RA, sCD40L, Fas/CD95, CD14, APP, CD19, CD69, IL-2, IFN-alpha, sCD40, CD11b, CD14, Iba1, CD11b, CD11c, RCA-1, MHCI (including HLA-DR), ferritin, IL-1alpha, CD68, CD163, Ricinus communis agglutinin-1 (RCA-1), translocator protein (TSPO), triggering receptor expressed on myeloid cells 2 (TREM2), CR3 or CD33.~~