Claims

1. Use of a molecule comprising:
    - a gamma-carboxyglutamic acid component (GLA-component) comprising a GLA domain, which does not comprise an active catalytic domain from a GLA protein, and
    - linked to a payload,

    in the manufacture of a medicament targeting surface exposed phosphatidylserine on an extracellular vesicle to deliver a functional molecule to the vesicle thereby allowing tracking and/or treatment.
2. An *in vitro* method for targeting extracellular vesicles with surface exposed phosphatidylserine, said method comprising the step of introducing a molecule comprising:

    a gamma-carboxyglutamic acid component (GLA-component) said GLA-component comprises a GLA domain, and which does not comprise an active catalytic domain from a GLA protein, for example linked to a payload,

    into a fluid which may comprise the extracellular vesicle.
3. Use or method according to claims 1 or 2, wherein the extracellular vesicle is an exosome.
4. Use or method according to claim 3, wherein the exosome has a diameter in the range 30nm to 100nm.
5. Use or method according to any one of claims 1 to 4, wherein the vesicle has a density in the range 1 to 1.5g/ml, such as 1 to 1.2g/ml, in particular 1.13 to 1.19g/ml.
6. Use or method according to any one of claims 1 to 5, wherein the vesicle comprises one or more transmembrane proteins independently selected from Lamp-1, Lamp-2, CD 13, CD86, Flotillin, Syntaxin-3, CD2, CD36, CD40, CD40L, CD41a, CD44, CD45, ICAM-1, Integrin alpha4, LiCAM, LFA-1, Mac-1 alpha and beta, Vti-IA and B, CD3 epsilon and zeta, CD9, CD18, CD37, CD53, CD63, CD81, CD82, CXCR4, FcR, GluR2/3, HLA-DM (MHC II), immunoglobulins, MHC-I or MHC-II components, TCR beta, tetraspanins and combinations of two or more of the same.
7. Use or method according to any one of claims 1 to 6, wherein the vesicle was released from an unhealthy cell, for example an apoptotic cell, a necrotic cell, a cancer cell, a pathogen infected cell (such as a virus infected cell, a bacteria infected cell or a parasite infected cells).
8. Use or method according to claim 7, wherein the pathogen infected cell is a bacteria infected cell or a parasite infected cell.
9. Use or method according to claim 7, wherein the cell is a cancer cell.

10. Use or method according to claim 9, wherein the cancer cell is a haematological cancer cell.
11. Use or method according to claims 9 or 10, wherein the cell is a cancer stem cell.
12. The method according to any one of claims 2 to 6, wherein the extracellular vesicle is from a healthy stem cell.
13. The method according to any one of claims 2 to 12, wherein the fluid comprises an *ex vivo* patient sample, for example a blood sample, fluid drawn from a cyst or tumor, or a homogenised biopsy.
14. Use or method according to any one of claims 1 to 13, wherein GLA domain or active fragment thereof is independently selected from thrombin, factor VII, factor IX, factor X, protein C, protein S, protein Z, Osteocalcin, Matrix GLA protein, GAS6, Transthretin, Periostin, Proline rich GLA 1, Proline rich GLA 2, Proline rich GLA 3 and Proline rich GLA 4.
15. Use or method according to any one of claims 1 to 14, wherein GLA domain or active fragment thereof is from, protein S, for example comprises a sequence shown in SEQ ID NO: 1.
16. Use or method according to any one of claims 1 to 5, wherein the GLA-domain-component further comprises an EGF domain, for example a calcium binding EGF domain.
17. Use or method according to claim 16, wherein the construct comprises an EGF domain selected from thrombin, factor VII, factor IX, factor X, protein C, protein S, protein Z, Osteocalcin, Matrix GLA protein, GAS6, Transthretin, Periostin, Proline rich GLA 1, Proline rich GLA 2, Proline rich GLA 3 and Proline rich GLA 4.
18. Use or method according to claim 16, wherein the construct comprises an EGF domain selected from protein S.
19. Use or method according to any one of claims 1 to 18, wherein the GLA-component comprises a sequence shown in SEQ ID NO: 6 or a derivative thereof wherein the His-tag is absent, in particular SEQ ID NO: 6.
20. Use or method according to any of claims 1 to 19, wherein the GLA-domain component further comprises a Kringle domain.
21. Use or method according to claim 20, wherein the Kringle domain is from a protein selected from the group comprising Activating transcription factor 2 (ATF); Factor XII (F12); thrombin (F2); Hyaluronan-binding protein 2 (HABP2); Hepatocyte growth factor (HGF); Hepatocyte growth factor activator (HGFAC); Kremen protein 1 (KREMEN1); KREMEN2; Lipoprotein(a) (LPA); LPAL2; Macrophage-stimulating protein (MSP or MST1); Phosphoinositide-3-kinase-interacting protein 1 (PIK3IP1); Tissue plasminogen activator (PLAT); Urokinase (PLAU); Plasmin (PLG); PRSS12;

Tyrosine-protein kinase transmembrane receptor ROR1 (ROR1); and Tyrosine-protein kinase transmembrane receptor ROR2 (ROR2).

22. Use or method according to any one of claims 1 to 21, wherein the GLA-component is conjugated to the payload.
23. Use or method according to any one of claims 1 to 21, wherein the GLA-component is part of a fusion protein.
24. Use or method according to any one of claims 1 to 23, wherein the payload comprises a detectable label.
25. Use or method according to claim 24, wherein the label is selected from a fluorescent protein (including where the, a fluorescent probe (such as rhodamine dye, FITC, FAM, CY5), biotin, an enzyme, a tag (for example a HIS-tag, FLAG-tag, myc-tag), a radionuclides (particularly radioiodide, radioisotopes, such as ^{99m}Tc), luminescent labels or compounds which may be detected by NMR or ESR spectroscopy including wherein the detectable label is in a Molecular Beacons.
26. Use or method according to any one of claims 22 to 25, wherein the payload is a bead, plate or a tag, for example an isolatable bead, such as a magnetic bead.
27. Use or method according to any one of claims 1 to 26, wherein the payload is linked to the GLA-component via a linker.
28. Use or method according to claim 27, wherein the linker is cleavable.
29. The method according to any one of claims 2 to 28, wherein the method comprises a further step of providing an enriched population of the vesicles.
30. The method according to any one of claims 2 to 29, wherein the method comprises the step of isolating the vesicles.
31. Use or method according to any one of claims 1 to 30, wherein the molecule comprising the GLA-component is a therapeutic.
32. Use or method according to any one of claims 1 to 31, wherein the payload comprises a drug, a chemotherapeutic agent, a peptide (including stapled peptides) or biological therapeutic, for example, an anti-viral drug, anti-bacterial drug, anti-parasitic agent, anti-cancer drug, an anti-cancer therapy or an oncolytic virus or viral vector.
33. Use or method according to claim 32, wherein the payload comprises a chemotherapeutic agent, an anti-cancer drug, an anti-cancer therapy or an oncolytic virus or viral vector.
34. Use or method according to any one of claims 1 to 32, wherein the payload comprises a toxin, a polymer (for example synthetic or naturally occurring polymers), biologically active proteins (for example enzymes, other antibody or antibody fragments), a drug (small molecule (chemical entity), nucleic acids and fragments thereof (for example DNA, RNA and fragments thereof) a metal chelating agent, nanoparticles or a combination of two or more of the same.

35. An extracellular vesicle obtained or obtainable from the method according to any one of claims 2 to 34.
36. An extracellular vesicle according to claim 35 for use in treatment and/or diagnosis.