Claims

1. Use of a molecule comprising a payload linked to a gamma-carboxyglutamic acid component (GLA-component)
   wherein said GLA-component comprises a GLA domain, and said molecule does not comprise an active catalytic domain from a GLA protein, in the manufacture of a medicament for targeting a stem cell *in vivo*.
2. An *in vitro* method of targeting a stem cell, said method comprising the step of contacting the stem cell with a molecule comprising a payload linked to a gamma-carboxyglutamic acid component (GLA-component), wherein said GLA-component comprises a GLA domain, and said molecule does not comprise an active catalytic domain from a GLA protein.
3. Use or method according to claims 1 or 2, wherein the GLA domain or active fragment thereof is from thrombin, factor VII, factor IX, factor X, protein C, protein S, protein Z, osteocalcin, matrix GLA protein (MGP), GAS6, transthyretin (TTR), inter-alpha-trypsin-inhibitor, periostin, proline rich gla 1 (PRRG1), proline rich gla 2 (PRRG2), proline rich gla 3(PRRG3), or proline rich gla 4 (PRRG4).
4. Use or method according to claim 3, wherein the GLA domain or active fragment thereof is from protein S.
5. Use or method according to any one of claims 1 to 4, wherein the GLA-component further comprises an EGF domain, for example a calcium binding EGF domain.
6. Use or method according to any one of claims 1 to 5, 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.
7. Use or method according to claim 6, wherein the EGF domain is from protein S.
8. Use or method according to any of claims 1 to 7, wherein the GLA-domain component further comprises a Kringle domain.
9. Use or method according to claim 8, 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).
10. Use or method according to any one of claims 1 to 9, wherein the GLA-component comprises a sequence shown in SEQ ID NO: 6.

11. Use or method according to any one of claims 1 to 10, wherein the molecule targets the exterior of the stem cell.
12. Use or method according to any one of claims 1 to 11, wherein the molecule is internalised in the stem cell.
13. Use or method according to any one of claims 1 to 13, wherein the cell is non-apoptotic.
14. Use or method according to any one of claims 1 to 13, wherein the cell is apoptotic, for example a diseased stem cell.
15. Use or method according to any one of claims 1 to 14, wherein the stem cell is an embryonic stem cell or an adult stems cells including progenitor cells, and haemotopoietic stem cells, myogenic stem cells, osteoprogenitor stem cells, neural stem cells, mesenchymal stem cell, such as satellite cells, radial glial cells, bone marrow stromal cells, periosteum, pancreatic progenitor cells, endothelial progenitor cells, blast cells and trophoblast stem cells.
16. Use or method according to any one of claims 1 to 15, wherein the stem cell expresses a surface marker CD34.
17. Use or method according to any one of claims 1 to 16, wherein the stem cell is negative for lineage positive surface markers (i.e. is Lin-).
18. Use or method according to any one of claims 1 to 17, wherein the stem cell is CD90+, CD133+, CD105+, CD45+, Lin-, CD48-, and CD244-.
19. Use or method according to any one of claims 1 to 18, wherein the stem cell is Lin-, CD34+, CD38-, CD45RA-, CD90+ and CD49f+.
20. Use or method according to any one of claims 1 to 19, wherein the stem cell is non-cancerous.
21. Use or method according to any one of claims 1 to 20, wherein the stem cell is a cancer stem cell.
22. Use or method according to claim 21, wherein the cancer stem cell is of epithelial origin.
23. Use or method according to claim 21 or 22, wherein cancer stem cell expresses a surface marker selected from CD44 (which is over expressed in at least breast, ovary, prostate, pancreatic, squamous, and bladder cancer), CD133 (which is over expressed in at least brain, colon, lung, prostate cancer and medulloblastoma), CD24, CD90, CD271, CD4f, CD13 and combinations of two or more of the same.
24. Use or method according to any one of claims 1 to 23, wherein the stem cell is of haemotopoietic origin.
25. Use or method according to any one of claims 1 to 24, wherein the payload comprises a therapeutic agent, a targeting agent and/or a label.
26. Use or method according to claim 25, wherein the therapeutic agent is a chemical entity or biological molecule (such as a protein).

27. Use or method according to claims 25 or 26, wherein the therapeutic agent is selected from an anti-cancer drug, an anti-cancer therapy, a chemotherapeutic agent, virus or viral vector, such as an oncolytic virus.
28. Use or method according to any one of claims 1 to 24, wherein the payload is selected from a toxin, a polymer(for example synthetic or naturally occurring polymers), biologically active proteins (for example enzymes, other antibody or antibody fragments), a drug (for example, small molecule (chemical entity) or chemotherapeutic agent), nucleic acids and fragments thereof (for example DNA, RNA such as shRNA and siRNA and fragments thereof, including gRNA for CRISPRCas9 and CRISPRa/i, radionuclides (particularly radioiodide, radioisotopes) a metal chelating agent, nanoparticles and reporter groups (such as fluorescent or luminescent labels or compounds which may be detected by NMR or ESR spectroscopy).
29. Use or method according to claim 28, wherein the toxin is selected from an auristatin (for example MMAE (monomethyl auristatin E), MMAF (monomethyl auristatin F)), pyrrolobenzodiazepine (PBD), doxorubicin, duocarmycin, a maytansinoid (for example N 2'-deacetyl-N 2'-(3-mercapto-1-oxopropyl)-maytansine (DM1), N 2'-deacetyl-N2'-(4-mercapto-1-oxopentyl)-maytansine (DM3) and N 2'-deacetyl-N 2'(4-methyl-4-mercapto-1-oxopentyl)-maytansine (DM4)), calocheamicin, dolastatin, maytansine, α-amanitin, Pseudomonas exotoxin (PE38), ricin A chain, diphtheria toxin, Pokeweed antiviral protein (PAP), saporin, gelonin and a tubulysin.
30. Use or method according to claim 27, wherein the chemotherapeutic is selected from temozolomide, epothilones, melphalan, carmustine, busulfan, lomustine, cyclophosphamide, dacarbazine, polifeprosan, ifosfamide, chlorambucil, mechlorethamine, busulfan, cyclophosphamide, carboplatin, cisplatin, thiotepa, capecitabine, streptozocin, bicalutamide, flutamide, nilutamide, leuprolide acetate, doxorubicin hydrochloride, bleomycin sulfate, daunorubicin hydrochloride, dactinomycin, liposomal daunorubicin citrate, liposomal doxorubicin hydrochloride, epirubicin hydrochloride, idarubicin hydrochloride, mitomycin, doxorubicin, valrubicin, anastrozole, toremifene citrate, cytarabine, fluorouracil, fludarabine, floxuridine, interferon α-2b, plicamycin, mercaptopurine, methotrexate, interferon α-2a, medroxyprogersterone acetate, estramustine phosphate sodium, estradiol, leuprolide acetate, megestrol acetate, octreotide acetate, deithylstilbestrol diphosphate, testolactone, goserelin acetate, etoposide phosphate, vincristine sulfate, etoposide, vinblastine, etoposide, vincristine sulfate, teniposide, trastuzumab, gemtuzumab ozogamicin, rituximab, exemestane, irinotecan hydrocholride, asparaginase, gemcitabine hydrochloride, altretamine, topotecan hydrochloride, hydroxyurea, cladribine, mitotane, procarbazine hydrochloride, vinorelbine tartrate, pentrostatin sodium, mitoxantrone, pegaspargase, denileukin diftitix, altretinoin,

porfimer, bexarotene, paclitaxel, docetaxel, arsenic trioxide, tretinoin and combinations of two or more of the same.

31. Use or method according to claim 27, wherein the chemotherapeutic is selected from an alkylating agent, an antimetabolite including thymidylate synthase inhibitors, a taxane, an anthracycline, an anti-microtubule agent including plant alkaloids, and combinations of two or more of the same.
32. Use or method according to claim 27, wherein the chemotherapeutic is selected from paclitaxel, docetaxel, abraxane, carbazitaxel, derivatives of any one of the same, and combinations of two or more of any of the aforementioned.
33. Use or method according to claim 31, wherein the alkylating agent is selected from a nitrogen mustard, a nitrosourea (such as carmustine), a tetrazine, a aziridine, a platin and derivatives thereof, a non-classical alkylating agent and a combination of two or more of the same.
34. Use or method according to claim 33, wherein the platin is selected from cisplatin, carboplatin, oxaliplatin, satraplatin, picoplatin, nedaplatin, triplatin, lipoplatin and a combination of two or more of the same.
35. Use or method according to claim 31, wherein the alkylating agent is an antimetabolite selected from anti-folates (for example methotrexate and pemetrexed), purine analogues (for example thiopurines, such as azathiopurine, mercaptopurine, thiopurine, fludarabine (including the phosphate form), pentostatin and cladribine), pyrimidine analogues (for example fluoropyrimidines, such as 5-fluorouracil and prodrugs thereof such as capecitabine [Xeloda®]), floxuridine, gemcitabine, cytarabine, decitabine, raltitrexed(tomudex) hydrochloride, cladribine and 6-azauracil and combination of two or more thereof.
36. Use or method according to claim 31, wherein the anthracycline is selected from daunorubicin (Daunomycin), daunorubicin (liposomal), doxorubicin (Adriamycin), doxorubicin (liposomal), epirubicin, idarubicin, mitoxantrone and a combination of two or more thereof, in particular doxorubicin.
37. Use or method according to claim 27, wherein the anti-cancer drug is selected from a topoisomerase inhibitor, a PARP inhibitor and a combination of or more of the same.
38. Use or method according to claim 28, wherein the radionuclide is selected from Y-90, P-32, I-131, In-111, Sr-89, Re-186, Sm-153, Sn-117m and a combination of two or more of the same.