application for the assessment of physiological and pathological states of connective tissues. J Chromatogr B. 2002;781:21-38.). The resulting disaccharide mixtures can be analyzed by PAGE (Hampson IN, Gallagher JT. Separation of radiolabeled glycosaminoglycan oligosaccharides by polyacrylamide-gel electrophoresis Biochem J. 1984;221:697-705.), SAX-HPLC (Skidmore M AA, Yates E and Turnbull JE. Labelling heparan sulfate saccharides with chromophore, fluorescence and mass tag for HPLC and MS separations. Methods in Molecular biology. 2009;534:157-69.), or highly sensitive capillary electrophoresis (CE) (Lamari F, Militsopoulou M, Gioldassi X, Karamanos NK. Capillary electrophoresis: a superior miniaturized tool for analysis of the mono-, di-, and oligosaccharide constituents of glycan moieties in proteoglycans. Fresenius J Anal Chem. 2001;371:157-67.; Karamanos NK, Vanky P, Tzanakakis GN, Hjerpe A. High performance capillary electrophoresis method to characterize heparin and heparan sulfate disaccharides. Electrophoresis. 1996;17:391-5.; Sudhalter J, Folkman J, Svahn CM, Bergendal K, Damore PA. Importance of size, sulfation, and anticoagulant activity in the potentiation of acidic fibroblast growth-factor by heparin J Biol Chem. 1989;264:6892-7.; Militsopoulou M, Lamari FN, Hjerpe A, Karamanos NK. Determination of twelve heparin- and heparan sulfate-derived disaccharides as 2-aminoacridone derivatives by capillary zone electrophoresis using ultraviolet and laser-induced fluorescence detection. Electrophoresis. 2002;23:1104-9) by comparison to known disaccharides standards.

Summary

In one aspect, the present invention refers to an isolated or substantially purified heparan sulphate HS6, wherein the heparan sulphate HS6 is capable of binding a peptide or polypeptide having, or consisting of, the amino acid sequence RAKTPQTRVTIRTVRVRRPPKGKHRKFKHTHDK (SEQ ID NO:1). In another aspect, the present invention refers to a composition comprising isolated or substantially purified heparan sulphate HS6 according to the present invention and a growth factor, preferably PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B. In still another aspect, the present invention refers to the use of isolated or substantially purified heparan sulphate HS6 according to the present invention in the manufacture of a medicament for the treatment of a disease, condition or injury to tissue, wherein the method involves the repair and/or regeneration of tissue. In one aspect, the present invention refers to a biocompatible implant or prosthesis comprising a biomaterial and isolated or substantially purified heparan sulphate HS6 according to the present invention In one aspect, the present invention refers to the use of isolated or substantially purified heparan sulphate HS6 according to the present invention in the manufacture of a medicament for use in a therapeutic method of repair and/or

regeneration of skin. In one aspect, the present invention refers to a method of stabilising PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B, the method comprising contacting PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B with isolated or substantially purified heparan sulphate HS6 according to the present invention. In one other aspect, the present invention refers to a method of preserving biological material, the method comprising contacting the biological material *in vitro* with isolated or substantially purified heparan sulphate HS6 according to the present invention. In one other aspect, the present invention refers to a preparation comprising biological material and a preservative, wherein the preservative comprises isolated or substantially purified heparan sulphate HS6 according to the present invention. In one aspect, the present invention refers to a method of isolating, processing, culturing or expanding stem cells, the method comprising contacting the stem cells with isolated or substantially purified heparan sulphate HS6 according to the present invention.

The present disclosure concerns a heparan sulphate species and heparan sulphate preparations comprising or consisting of the heparan sulphate species. The heparan sulphate species is called HS6 (or HS6+). HS6 refers to a novel class of structurally and functionally related isolated heparan sulphate.

HS6 has been found to bind PDGF-B and/or PDGF-BB. HS6 has also been found to enhance the proliferation of human dermal fibroblasts *in vitro*, enhance migration of human dermal fibroblasts in an *in vitro* model of wound healing, and enhance wound healing *in vivo*. HS6 has also been found to increase/enhance binding of PDGF-BB to PDGFRβ.

In one example of the present disclosure a heparan sulphate HS6 is provided. HS6 may be provided in isolated form or in substantially purified form. This may comprise providing a composition in which the heparan sulphate component is at least 80% HS6, more preferably one of at least 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%.

In preferred examples, HS6 is capable of binding a peptide or polypeptide having the amino acid sequence of RAKTPQTRVTIRTVRVRRPPKGKHRKFKHTHDK (SEQ ID NO: 1). The peptide may have one or more additional amino acids at one or both ends of this sequence. For example, the peptide may have any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more amino acids at one or both end of this sequence.

In other examples the polypeptide is a PDGF-B or PDGF-BB protein. In some examples HS6 binds to a peptide having or consisting of the amino acid sequence of SEQ ID NO:1 or PDGF-B or PDGF-BB protein with a K_D of less than 100μM, more preferably less than one of 50μM, 40μM, 30μM, 20μM, 10μM, 1μM, 100nM, 50nM, 10nM or 1nM.

HS6 may be obtained, identified, isolated or enriched according to the inventors' methodology described herein, which may comprise the following steps:

(i) providing a solid support having polypeptide molecules adhered to the support, wherein the polypeptide comprises a heparin-binding domain having the amino acid sequence of RAKTPQTRVTIRTVRVRRPPKGKHRKFKHTHDK (SEQ ID NO: 1);

(ii) contacting the polypeptide molecules with a mixture comprising glycosaminoglycans such that polypeptide-glycosaminoglycan complexes are allowed to form;

(iii) partitioning polypeptide-glycosaminoglycan complexes from the remainder of the mixture;

(iv) dissociating glycosaminoglycans from the polypeptide-glycosaminoglycan complexes;

(v) collecting the dissociated glycosaminoglycans.

In the inventors' methodology the mixture may comprise glycosaminoglycans obtained from commercially available sources. One suitable source is a heparan sulphate fraction, e.g. a commercially available heparan sulphate. One suitable heparan sulphate fraction can be obtained during isolation of heparin from porcine intestinal mucosa, another is heparan sulphate from porcine mucosa [HS^{PM}] (e.g. from Celsus Laboratories Inc. – sometimes called "Celsus HS").

Other suitable sources of heparan sulphate include heparan sulphate from any mammal (human or non-human), particularly from the kidney, lung or intestinal mucosa. In some examples the heparan sulphate is from pig (porcine) or cow (bovine) intestinal mucosa, kidney or lung.

In another example of the present disclosure a composition comprising HS6 according to any one of the examples above and PDGF-B or PDGF-BB protein is provided. The composition may comprise isolated PDGF-B, PDGF-BB, or a heterodimer comprising PDGF-B, and isolated HS6. The composition may be a PDGF-B preparation comprising PDGF-B, PDGF-BB, or a heterodimer comprising PDGF-B, and isolated HS6 in a container. A suitable container may be a bottle, vial, tube or syringe, and may optionally be sterile.

In one example of the present disclosure a pharmaceutical composition or medicament is provided comprising HS6 in accordance with the examples described above. The pharmaceutical composition or medicament may further comprise a pharmaceutically acceptable carrier, adjuvant or diluent. In some examples the pharmaceutical composition or medicament may further comprise PDGF-B or PDGF-BB protein.

In some examples the pharmaceutical composition is for use in a method of medical treatment. The method may comprise wound healing *in vivo*, the repair and/or regeneration of tissue, e.g. skin, dermal or epithelial tissue, or the repair and/or regeneration of skin.

In another example of the present disclosure HS6 is provided for use in a method of medical treatment. The method of medical treatment may comprise a method of wound healing *in vivo*, the repair and/or regeneration of tissue, or the repair and/or regeneration of skin. Such repair and/or regeneration may be in a mammal or a human.

In a related example of the present disclosure the use of HS6 in the manufacture of a medicament for use in a method of medical treatment is provided. In some examples the method of medical treatment comprises wound healing *in vivo* or the repair and/or regeneration of tissue as described above.

In one example of the present disclosure Heparan Sulphate HS6 is provided for use in a therapeutic method of repair and/or regeneration of skin. In another example of the present disclosure the use of Heparan Sulphate HS6 in the manufacture of a medicament for use in a therapeutic method of repair and/or regeneration of skin is provided. In another example of

the present disclosure a therapeutic method of repair and/or regeneration of skin is provided, the method comprising administering Heparan Sulphate HS6 to a subject in need of treatment thereof.

In some examples the therapeutic method may involve treatment of a skin wound or scar, optionally selected from skin burns, ulcers, excisional wounds, cut, stab or puncture wounds. In some examples the therapeutic method may involve skin graft healing, skin reconstruction, or skin plastic surgery.

In another example of the present disclosure a method of healing a skin wound is provided, the method comprising contacting the skin wound with an effective amount of a pharmaceutical composition comprising HS6. In another example of the present disclosure heparan sulphate HS6 is provided for use in a method of healing a skin wound, the method comprising contacting the skin wound with an effective amount of a pharmaceutical composition comprising HS6. In another example of the present disclosure the use of heparan sulphate HS6 in the manufacture of a medicament for use in a method of healing a skin wound, the method comprising contacting the skin wound with an effective amount of a pharmaceutical composition comprising HS6 is provided.

In another example of the present disclosure a method of treating a subject having a skin wound is provided, the method comprising administration of a therapeutically effective amount of heparan sulphate HS6 to the subject leading to repair and/or regeneration of skin at the wound. In another example of the present disclosure heparan sulphate HS6 is provided for use in a method of treating a subject having a skin wound, the method comprising administration of a therapeutically effective amount of heparan sulphate HS6 to the subject leading to repair and/or regeneration of skin at the wound. In another example of the present disclosure the use of heparan sulphate HS6 in the manufacture of a medicament for use in a method of treating a subject having a skin wound, the method comprising administration of a therapeutically effective amount of heparan sulphate HS6 to the subject leading to repair and/or regeneration of skin at the wound, is provided.

In some examples the skin wound is a skin burn, ulcer, excisional wound, cut, stab or puncture wound

In another example of the present disclosure a method of skin grafting, skin reconstruction, or skin plastic surgery is provided, the method comprising contacting the skin at or adjacent the

region of grafting, reconstruction or plastic surgery with an effective amount of a pharmaceutical composition comprising HS6. In another example of the present disclosure heparan sulphate HS6 is provided for use in a method of skin grafting, skin reconstruction, or skin plastic surgery, the method comprising contacting the skin at or adjacent the region of grafting, reconstruction or plastic surgery with an effective amount of a pharmaceutical composition comprising HS6. In another example of the present disclosure the use of heparan sulphate HS6 in the manufacture of a medicament for use in a method of skin grafting, skin reconstruction, or skin plastic surgery is provided, the method comprising contacting the skin at or adjacent the region of grafting, reconstruction or plastic surgery with an effective amount of a pharmaceutical composition comprising HS6.

In another example of the present disclosure HS6 is provided for use in a method of scarless wound healing in skin. In another example of the present disclosure the use of HS6 in the manufacture of a medicament for use in a method of scarless wound healing in skin is provided. In another example of the present disclosure a method of scarless wound healing in skin is provided, the method comprising administering heparan sulphate HS6 to a subject in need of treatment thereof.

In another example of the present disclosure HS6 is provided for use in the treatment of wounds and/or injured tissues. In some examples, the tissue is a soft tissue, and in some examples the tissue is bone. In some examples the tissue is connective tissue, such as skin, tendon, ligament, fascia, fibrous tissues, fat or synovial membrane. In some examples the tissue is muscle, nerve or blood vessel tissue. In particular examples, the tissue is skin, tendon, ligament or bone. In some examples the skin wound is a skin burn, ulcer, excisional wound, cut, stab or puncture wound.

In another example of the present disclosure HS6 is provided for use to prevent or inhibit scarring, and/or to promote or facilitate healing or repair. In some examples the use is to prevent scarring and/or to promote or facilitate healing or repair of wounds or damaged tissue. In some examples, the damaged tissue or wound is a result of surgical intervention (e.g. a surgical wound), in particular incision. Wound healing may be *in vivo* repair and/or regeneration of tissue, e.g. skin, dermal or epithelial tissue.

In examples of the present disclosure HS6 is provided for use to promote skin graft healing, in skin reconstruction, or in skin plastic surgery.

In this and other examples of the present disclosure, administration of HS6 may be at the point of care or later. For example, HS6 may be administered at the time of surgery, or later.

In another example of the present disclosure HS6 is provided for use as a stabilising agent. In some examples, HS6 is used as an agent for stabilising a growth factor. In some examples stabilising comprises promoting the activity of the growth factor. In some examples stabilising comprises prolonging the half-life or inhibiting degradation of the growth factor. The growth factor is preferably a protein growth factor, more preferably PDGF-B or PDGF-BB or a heterodimer comprising PDGF-B.

Accordingly, in one example of the present disclosure a method of stabilising PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B, optionally in isolated and/or recombinant form, is provided the method comprising contacting PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B with HS6, preferably a predetermined quantity of HS6, e.g. in the range 1nM to 100mM, or 1µM to 100mM, or 1µM to 10mM, or 1µM to 1mM. The method may comprise mixing the growth factor and HS6.

In another example of the present disclosure a method of increasing the stability of a growth factor is also provided, the method comprising contacting a growth factor with isolated HS6. In some examples the growth factor is PDGF-B or PDGF-BB or a heterodimer comprising PDGF-B.

In another example of the present disclosure HS6 is provided for use as a preserving agent and/or preservative. In some examples, HS6 is provided as a preserving agent or preservative for use to preserve biological material. In some examples HS6 is used as a preserving agent and/or preservative for biological material in storage.
In some examples, the biological material is cellular material or tissue. In some examples the cellular material or tissue is animal cellular material or animal tissue. In some examples the material has been obtained from an animal. In some examples the animal is a mammal, and in particular examples the mammal is a human.

In some examples, the cellular material or tissue is for use as source material for graft or transplant. In some examples the tissue is skin for use in a skin graft, skin reconstruction, or in skin plastic surgery.

In some examples HS6 is used as a preserving agent and/or preservative during the production of blood-derived products. In some examples the blood-derived products include platelets, platelet products, platelet lysates and platelet-rich plasma (PRP).

In accordance with the above, a method of preserving biological material is provided, preferably biological material comprising PDGF-B or PDGF-BB or a heterodimer comprising PDGF-B, the method comprising contacting the biological material with a predetermined quantity of HS6. In some examples the biological material may be selected from cellular material, tissue, blood-derived products, cells, or stem cells.

Accordingly, in one example of the present disclosure a method of preserving biological material is provided, the method comprising contacting the biological material with HS6, preferably a predetermined quantity of HS6, e.g. in the range 1nM to 100mM, or 1μM to 100mM, or 1μM to 10mM, or 1μM to 1mM.

In one example of the present disclosure a preparation comprising biological material and a preservative is provided, wherein the preservative comprises HS6, preferably a predetermined quantity of HS6, e.g. in the range 1nM to 100mM, or 1μM to 100mM, or 1μM to 10mM, or 1μM to 1mM. The biological material may be cellular material, tissue, blood, a blood-derived product, cells, or stem cells. The preparation may be an *in vitro* or *ex vivo* preparation.

In another example of the present disclosure HS6 is provided for use during isolation and/or processing of stem cells. In some examples, HS6 is provided as a reagent for use during culture and/or expansion of stem cells. Accordingly, a method of isolating, processing, culturing or expanding stem cells may be provided, the method comprising contacting the stem cells with a predetermined quantity of HS6, e.g. in the range 1nM to 100mM, or 1μM to 100mM, or 1μM to 10mM, or 1μM to 1mM.. The stem cells may optionally express PDGF-B or PDGF-BB or a heterodimer comprising PDGF-B.

In another example of the present disclosure HS6 is provided for use to promote angiogenesis. Accordingly, a method of promoting angiogenesis is provided, the method comprising contacting cells or tissue, *in vitro* or *in vivo*, with a predetermined quantity of HS6. The tissue may be vascular tissue. The cells may be stem cells, e.g. hematopoietic stem cells.

In another example of the present disclosure a method for treating a dermal or epidermal wound in a subject is provided, the method comprising administering to the subject a pharmaceutical composition comprising HS6. In another example of the present disclosure heparan sulphate HS6 is provided for use in a method for treating a dermal or epidermal wound in a subject. In another example of the present disclosure, the use of heparan sulphate HS6 in the manufacture of a medicament for use in a method for treating a dermal or epidermal wound in a subject is provided.

In some examples HS6, or medicaments or pharmaceutical compositions containing HS6 may be formulated for topical or transdermal administration. In some examples HS6, or medicaments or pharmaceutical compositions containing HS6 may be formulated as a gel, spray, paste, ointment, cream, lotion, salve, oil, aqueous solution, suspension, dispersion, patch, adhesive plaster, bandage, dressing, depot, or reservoir.

In some examples, the method/treatment may further comprise administration of a growth factor, preferably PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B. In some examples the HS6, or medicament or pharmaceutical composition is formulated as a combined preparation together with a growth factor, preferably PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B.

In a further example of the present disclosure a biocompatible implant or prosthesis comprising a biomaterial and HS6 is provided. In some examples the implant or prosthesis is coated with HS6. In some examples the implant or prosthesis is impregnated with HS6. The implant or prosthesis may be further coated or impregnated with PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B.

In another example of the present disclosure a method of forming a biocompatible implant or prosthesis is provided, the method comprising the step of coating or impregnating a biomaterial with HS6. In some examples the method further comprises coating or impregnating the biomaterial with PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B.

Preferably, the HS6, and optionally PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B, are respectively provided in therapeutically effective amounts. In some examples the method of treatment further comprises the step of formulating therapeutically effective amounts of HS6, and optionally PDGF-B, or PDGF-BB, or a

heterodimer comprising PDGF-B, as a pharmaceutical composition comprising the HS6, and optionally PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B, and a pharmaceutically acceptable carrier, adjuvant or diluent, wherein the pharmaceutical composition is administered to the patient.

In another example of the present disclosure a method of treatment of a patient is provided, the method comprising surgically implanting a biocompatible implant or prosthesis, which implant or prosthesis comprises a biomaterial and HS6, into tissue of the patient at or surrounding a site at which wound healing is required.

In some examples the implant or prosthesis is coated with HS6. In some examples the implant or prosthesis is impregnated with HS6. In some examples the implant or prosthesis is further impregnated with PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B.

In yet a further example of the present disclosure a kit of parts is provided, the kit comprising a predetermined amount of HS6 and a predetermined amount of PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B. The kit may comprise a first container containing the predetermined amount of HS6 and a second container containing the predetermined amount of PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B. The kit may be provided for use in a method of medical treatment. The method of medical treatment may comprise a method of wound healing *in vivo*, the repair and/or regeneration of tissue, as described herein. The repair and/or regeneration may be in a mammal or a human. The kit may be provided together with instructions for the administration of the HS6 and PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B separately, sequentially or simultaneously in order to provide the medical treatment.

In a further example of the present disclosure products are provided, the products containing therapeutically effective amounts of:

(i) HS6; and

(ii) PDGF-B, or PDGF-BB, or a heterodimer comprising PDGF-B;

for simultaneous, separate or sequential use in a method of medical treatment. The method of medical treatment may comprise a method of wound healing *in vivo* or the repair and/or regeneration of tissue as described herein. The repair and/or regeneration may be in a mammal or a human. The products may optionally be formulated as a combined preparation for co-administration.

Claims:

1. Isolated or substantially purified heparan sulphate HS6, wherein the heparan sulphate HS6 is capable of binding a peptide or polypeptide having, or consisting of, the amino acid sequence RAKTPQTRVTIRTVRVRRPPKGKHRKFKHTHDK (SEQ ID NO:1).

2. Isolated or substantially purified heparan sulphate HS6 according to claim 1, wherein following digestion with heparin lyases I, II and III and then subjecting the resulting disaccharide fragments to HPLC analysis the heparan sulphate HS6 has a disaccharide composition comprising:

Disaccharide	Normalised weight percentage
ΔUA,2S-GlcNS,6S	12.9 ±3.0
ΔUA,2S-GlcNS	6.8 ±2.0
ΔUA-GlcNS,6S	11.7 ±3.0
ΔUA-GlcNS	24.5 ±3.0
ΔUA,2S-GlcNAc	0.5 ±0.5
ΔUA-GlcNAc,6S	12.1 ±3.0
ΔUA-GlcNAc	31.6 ±3.0

3. Isolated or substantially purified heparan sulphate HS6 according to claim 1 or claim 2, obtained by a method comprising:

(i) providing a solid support having polypeptide molecules adhered to the support, wherein the polypeptide comprises a heparin-binding domain having the amino acid sequence RAKTPQTRVTIRTVRVRRPPKGKHRKFKHTHDK;

(ii) contacting the solid support with a mixture comprising glycosaminoglycan, preferably a heparan sulphate preparation, such that polypeptide-glycosaminoglycan complexes are allowed to form;

(iii) partitioning polypeptide-glycosaminoglycan complexes from the remainder of the mixture;

(iv) dissociating glycosaminoglycans, preferably heparan sulphate species, from the polypeptide-glycosaminoglycan complexes;

(v) collecting the dissociated glycosaminoglycans, preferably one or more heparan sulphate species.

4. Isolated or substantially purified heparan sulphate HS6 according to claim 3 wherein the mixture comprising glycosaminoglycans is a heparan sulphate preparation obtained from porcine mucosa (HS^{PM}).

5. A composition comprising isolated or substantially purified heparan sulphate HS6 according to any one of claims 1 to 4 and a growth factor, preferably PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B.

6. Use of isolated or substantially purified heparan sulphate HS6 according to any one of claims 1 to 4 in the manufacture of a medicament for the treatment of a disease, condition or injury to tissue, wherein the method involves the repair and/or regeneration of tissue.

7. A biocompatible implant or prosthesis comprising a biomaterial and isolated or substantially purified heparan sulphate HS6 according to any one of claims 1 to 4.

8. Use of isolated or substantially purified heparan sulphate HS6 according to any one of claims 1 to 4 in the manufacture of a medicament for use in a therapeutic method of repair and/or regeneration of skin.

9. The use of claim 8 wherein the therapeutic method involves treatment of a skin wound or scar, optionally selected from skin burns, ulcers, excisional wounds, cut, stab or puncture wounds.

10. The use of claim 8 wherein the therapeutic method involves skin graft healing, skin reconstruction, or skin plastic surgery.

11. The use of any one of claims 8 to 10 wherein the isolated or substantially purified heparan sulphate HS6 is formulated for topical or transdermal administration.

12. The use of any one of claims 8 to 11 wherein the isolated or substantially purified heparan sulphate HS6 is formulated as a gel, spray, paste, ointment, cream, lotion, salve, oil, aqueous solution, suspension, dispersion, patch, adhesive plaster, bandage, dressing, depot, or reservoir.

13. The use of any one of claims 8 to 12 wherein the method further comprises administration of a growth factor, preferably PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B.

14. The use of any one of claims 8 to 13, wherein the isolated or substantially purified heparan sulphate HS6 is formulated as a combined preparation with a growth factor, preferably PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B.

15. A method of stabilising PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B, the method comprising contacting PDGF-B, PDGF-BB or a heterodimer comprising PDGF-B with isolated or substantially purified heparan sulphate HS6 according to any one of claims 1 to 4.

16. A method of preserving biological material, the method comprising contacting the biological material *in vitro* with isolated or substantially purified heparan sulphate HS6 according to any one of claims 1 to 4.

17. The method of claim 16, wherein the biological material is cellular material, tissue, blood, a blood-derived product, cells, or stem cells.

18. A preparation comprising biological material and a preservative, wherein the preservative comprises isolated or substantially purified heparan sulphate HS6 according to any one of claims 1 to 4.

19. The preparation of claim 18, wherein the biological material is cellular material, tissue, blood, a blood-derived product, cells, or stem cells.

20. A method of isolating, processing, culturing or expanding stem cells, the method comprising contacting the stem cells with isolated or substantially purified heparan sulphate HS6 according to any one of claims 1 to 4.