Specificity studies on the heparin lyases from Flavobacterium-heparinum Biochemistry. 1993;32:8140-5.; Shriver Z, Sundaram M, Venkataraman G, Fareed J, Linhardt R, Biemann K, et al. Cleavage of the antithrombin III binding site in heparin by heparinases and its implication in the generation of low molecular weight heparin. Proc Natl Acad Sci U S A. 2000;97:10365-70) using the *Flavobacterium heparinium* enzymes heparinase I, II and III to cleave the glycosidic bonds. More than 90 % depolymerization of heparin or HS is possible when all 3 heparinases are used in combination (Karamanos NK, Vanky P, Tzanakakis GN, Tsegenidis T, Hjerpe A. Ion-pair high-performance liquid chromatography for determining disaccharide composition in heparin and heparan sulphate. J Chromatogr A. 1997;765:169-79.; Vynios DH, Karamanos NK, Tsiganos CP. Advances in analysis of glycosaminoglycans: its 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 disaccharide standards.

Summary

In one aspect, the present invention refers to an isolated heparan sulphate HS16, wherein the HS16 is capable of binding a peptide consisting of the amino acid sequence RKDLGWKWIHEPKGYH (SEQ ID NO: 1). In another aspect, the present invention refers to a composition comprising isolated heparan

sulphate HS16 according to the present invention, optionally further comprising a growth factor, preferably TGFβ1. In another aspect, the present invention refers to a method for obtaining isolated heparan sulphate HS16 according to the present invention, the method comprising: (i) providing a solid support having polypeptide molecules adhered to the support, wherein the polypeptide comprises a heparin-binding domain consisting of the amino acid sequence RKDLGWKWIHEPKGYH (SEQ ID NO:1); (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. In still another aspect, the present invention refers to a cosmetic composition, pharmaceutical composition or medicament comprising isolated heparan sulphate HS16 according to the present invention, optionally wherein the pharmaceutical composition or medicament further comprises TGFβ1 protein and/or mesenchymal stem cells. In yet another aspect, the present invention refers to a pharmaceutical composition or medicament of the present invention for use in a method of medical treatment. In one other aspect, the present invention refers to an isolated heparan sulphate HS16 according to the present invention for use in a method of medical treatment. In another aspect, the present invention refers to the use of isolated Heparan sulphate HS16 according to the present invention in the manufacture of a medicament for the treatment of a disease, condition or injury to tissue, wherein the treatment involves the repair and/or regeneration of tissue, preferably connective tissue. In another aspect, the present invention refers to a biocompatible implant or prosthesis comprising a biomaterial and isolated heparan sulphate HS16 according to the present invention for use in a method of treating a disease, condition or injury to tissue in a patient, the method comprising surgically implanting the biocompatible implant or prosthesis into tissue of the patient at or surrounding the site of the disease, condition or injury leading to repair and/or regeneration of the tissue. In another aspect, the present invention refers to a biocompatible implant or prosthesis comprising a biomaterial and isolated heparan sulphate HS16 according to the present invention. In another aspect, the present invention refers to a method of forming a biocompatible implant or prosthesis, the method comprising the step of coating or impregnating a biomaterial with isolated heparan sulphate HS16 according to the present invention. In

another aspect, the present invention refers to a method of culturing stem cells *in vitro*, the method comprising culturing stem cells *in vitro* in contact with isolated heparan sulphate HS16 according to the present invention. In another aspect, the present invention refers to a culture media comprising isolated heparan sulphate HS16 according to the present invention, optionally further comprising TGFβ1. In another aspect, the present invention refers to a kit of parts, the kit comprising a predetermined amount of isolated heparan sulphate HS16 according to the present invention and a predetermined amount of TGFβ1. In another aspect, the present invention refers to products containing therapeutically effective amounts of: (i) isolated heparan sulphate HS16 according to the present invention; and one or both of (ii) TGFβ1 protein; (iii) mesenchymal stem cells, or cells in the fibroblastic lineage, for simultaneous, separate or sequential use in a method of medical treatment. In another aspect, the present invention refers to a method of increasing the stability of a growth factor, preferably TGFβ1, the method comprising contacting a growth factor, preferably TGFβ1, with isolated heparan sulphate HS16 according to the present invention. In another aspect, the present invention refers to a cosmetic method comprising administering heparan sulphate HS16 according to the present invention to a subject. In another aspect, the present invention refers to a preparation comprising a blood derived product and a predetermined quantity of heparan sulphate HS16 according to the present invention. In another aspect, the present invention refers to a method of preserving biological material, the method comprising contacting biological material with a predetermined quantity of heparan sulphate HS16 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

Claims:

1. Isolated heparan sulphate HS16, wherein the HS16 is capable of binding a peptide consisting of the amino acid sequence RKDLGWKWIHEPKGYH (SEQ ID NO: 1).

2. Isolated heparan sulphate HS16 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 HS16 has a disaccharide composition comprising:

Disaccharide	Normalised weight percentage
ΔUA,2S-GlcNS,6S	14.75±3.0
ΔUA,2S-GlcNS	4.58±2.0
ΔUA-GlcNS,6S	12.98±3.0
ΔUA-GlcNS	22.24±3.0
ΔUA,2S-GlcNAc	0.56±0.5
ΔUA-GlcNAc,6S	12.63±3.0
ΔUA-GlcNAc	32.26±3.0

3. Isolated heparan sulphate HS16 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 HS16 has a disaccharide composition comprising:

Disaccharide	Normalised weight percentage
ΔUA,2S-GlcNS,6S	14.75±1.0
ΔUA,2S-GlcNS	4.58±0.4
ΔUA-GlcNS,6S	12.98±1.0
ΔUA-GlcNS	22.24±1.6
ΔUA,2S-GlcNAc	0.56±0.4
ΔUA-GlcNAc,6S	12.63±1.0
ΔUA-GlcNAc	32.26±1.6

4. A method for obtaining isolated heparan sulphate HS16 according to any one of claims 1 to 3, the method comprising:

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

(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.

5. The method of claim 4, wherein the mixture comprising glycosaminoglycans is a heparan sulphate preparation obtained from porcine mucosa (HS^{PM}).

6. A composition comprising isolated heparan sulphate HS16 according to any one of claims 1 to 3, optionally further comprising a growth factor, preferably TGFβ1.

7. A cosmetic composition, pharmaceutical composition or medicament comprising isolated heparan sulphate HS16 according to any one of claims 1 to 3, optionally wherein the pharmaceutical composition or medicament further comprises TGFβ1 protein and/or mesenchymal stem cells.

8. The pharmaceutical composition or medicament of claim 7 for use in a method of medical treatment.

9. Isolated heparan sulphate HS16 according to any one of claims 1 to 3 for use in a method of medical treatment.

10. Isolated heparan sulphate HS16 for use according to claim 9 wherein the method of medical treatment comprises a method of wound healing

in vivo; or wherein the method of medical treatment comprises the repair and/or regeneration of tissue, preferably connective tissue, optionally wherein the method comprises administration of a therapeutically effective amount of isolated heparan sulphate HS16 to the patient leading to repair and/or regeneration of the tissue, preferably connective tissue.

11. Isolated heparan sulphate HS16 for use according to claim 9 or 10 wherein the method of medical treatment further comprises administration of TGFß1 protein to the patient.

12. Use of isolated Heparan sulphate HS16 according to any one of claims 1 to 3 in the manufacture of a medicament for the treatment of a disease, condition or injury to tissue, wherein the treatment involves the repair and/or regeneration of tissue, preferably connective tissue.

13. A biocompatible implant or prosthesis comprising a biomaterial and isolated heparan sulphate HS16 according to any one of claims 1 to 3 for use in a method of treating a disease, condition or injury to tissue in a patient, the method comprising that the biocompatible implant or prosthesis is to be surgically implanted into tissue of the patient at or surrounding the site of the disease, condition or injury leading to repair and/or regeneration of the tissue.

14. A biocompatible implant or prosthesis comprising a biomaterial and isolated heparan sulphate HS16 according to any one of claims 1 to 3.

15. A method of forming a biocompatible implant or prosthesis, the method comprising the step of coating or impregnating a biomaterial with isolated heparan sulphate HS16 according to any one of claims 1 to 3.

16. A method of culturing stem cells *in vitro*, the method comprising culturing stem cells *in vitro* in contact with isolated heparan sulphate HS16 according to any one of claims 1 to 3.

17. Culture media comprising isolated heparan sulphate HS16 according to any of claims 1 to 3, optionally further comprising TGFβ1.

18. A kit of parts, the kit comprising a predetermined amount of isolated heparan sulphate HS16 according to any one of claims 1 to 3 and a predetermined amount of TGFβ1.

19. Products containing therapeutically effective amounts of:

(i) Isolated heparan sulphate HS16 according to any one of claims 1 to 3; and one or both of

(ii) TGFβ1 protein;

(iii) Mesenchymal stem cells, or cells in the fibroblastic lineage,

for simultaneous, separate or sequential use in a method of medical treatment.

20. A method of increasing the stability of a growth factor, preferably TGFβ1, the method comprising contacting a growth factor, preferably TGFβ1, with isolated heparan sulphate HS16 according to any one of claims 1 to 3.

21. A cosmetic method comprising administering heparan sulphate HS16 according to any one of claims 1 to 3 to a subject.

22. A preparation comprising a blood derived product and a predetermined quantity of heparan sulphate HS16 according to any one of claims 1 to 3.

23. The preparation of claim 22, wherein the preparation is a platelet preparation.

24. A method of preserving biological material, the method comprising contacting biological material with a predetermined quantity of heparan sulphate HS16 according to any one of claims 1 to 3.

25. The cosmetic method, preparation or method of any one of claims 21 to 24 wherein the heparan sulphate HS16 is isolated heparan sulphate HS16 according to any one of claims 1 to 3.