Claims:

1. A method of isolating glycosaminoglycans capable of binding to a protein having a heparin-binding domain, the method comprising:

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

(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.

2. A method of identifying glycosaminoglycans capable of stimulating or inhibiting the growth and/or differentiation of cells and/or tissues, the method comprising:

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

(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;

(vi) adding the collected glycosaminoglycans to cells or tissues in which a protein containing the amino acid sequence of the heparin-binding domain is present;

(vii) measuring one or more of: proliferation of the cells, differentiation of the cells, expression of one or more protein markers.

3. The method of claim 1 or 2 wherein the mixture comprising glycosaminoglycans contains extracellular matrix material.

4. The method of claim 3 wherein the extracellular matrix material is derived from connective tissue or connective tissue cells.

5. The method of any one of claims 1 to 4 wherein the mixture comprising glycosaminoglycans contains one or more of a dextran sulphate, a chondroitin sulphate, a heparan sulphate.

6. The method of any one of claims 1 to 5 wherein the mixture comprising glycosaminoglycans has been enriched for one of dextran sulphate, chondroitin sulphate, heparan sulphate.

7. The method of any one of claims 1 to 6 wherein the method further comprises subjecting the collected glycosaminoglycans to further analysis in order to determine structural characteristics of the GAG.

8. The method of any one of claims 1 to 7 wherein the glycosaminoglycan-polypeptide complexes are contacted with a lyase.

9. The method of any one of claims 1 to 8 wherein the polypeptide is, or comprises, one of SEQ ID NO.s: 1-13 or 17.

10. Heparan sulphate HS/BMP2.

11. Culture media comprising HS/BMP2.

12. A pharmaceutical composition or medicament comprising HS/BMP2.

13. The pharmaceutical composition or medicament of claim 12 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

14. The pharmaceutical composition or medicament of claim 12 or 13 further comprising BMP2 protein.

15. A pharmaceutical compositions or medicament according to any one of claims 12 to 14 for use in the prevention or treatment of injury or disease.

16. Use of HS/BMP2 in the manufacture of a medicament for the prevention or treatment of injury or disease.

17. The pharmaceutical composition or use of claim 15 or 16 wherein the prevention or treatment is chosen from: repair, regeneration or replacement of connective tissue and wound healing.

18. A method of preventing or treating injury or disease in a patient in need of treatment thereof, the method comprising administering an effective amount of HS/BMP2 to the patient.

19. The method of claim 18 wherein the administered HS/BMP2 is formulated as a pharmaceutical composition or medicament.

20. The method of claim 19 wherein the pharmaceutical composition or medicament further comprises BMP2 protein.

21. A method of promoting or inhibiting osteogenesis comprising administering HS/BMP2 to bone precursor cells or bone stem cells.

22. The method of claim 21 wherein the bone precursor cells or bone stem cells are contacted with HS/BMP2 in vitro.

23. The method of claim 21 wherein the bone precursor cells or bone stem cells are contacted with HS/BMP2 in vivo.

24. The method of any one of claims 21 to 23 wherein the bone precursor cells or bone stem cells are contacted with BMP2 simultaneously with HS/BMP2.

25. A method of promoting or inhibiting the formation of cartilage tissue comprising administering HS/BMP2 to cartilage precursor cells or cartilage stem cells.

26. The method of claim 25 wherein the cartilage precursor cells or cartilage stem cells are contacted with HS/BMP2 in vitro.

27. The method of claim 25 wherein the cartilage precursor cells or cartilage stem cells are contacted with HS/BMP2 in vivo.

28. The method of any one of claims 25 to 27 wherein the cartilage precursor cells or cartilage stem cells are contacted with BMP2 simultaneously with HS/BMP2.

29. A method for the repair, replacement or regeneration of connective tissue in a human or animal patient in need of such treatment, the method comprising:

(i) culturing mesenchymal stem cells in vitro in contact with HS/BMP2 for a period of time sufficient for said cells to form connective tissue;

(ii) collecting said connective tissue;

(iii) implanting said connective tissue into the body of the patient at a site of injury or disease to repair, replace or regenerate connective tissue in the patient.

30. The method of claim 29 further comprising contacting the mesenchymal cells in culture with exogenous BMP2.

31. Connective tissue obtained by in vitro culture of mesenchymal stem cells in the presence of HS/BMP2.

32. Connective tissue as claimed in claim 31, wherein the mesenchymal cells are cultured in the presence of exogenous BMP2, and optionally in the presence of BMP2.

33. A pharmaceutical composition comprising stem cells and HS/BMP2.

34. The pharmaceutical composition of claim 32 wherein the stem cells are mesenchymal stem cells.

35. The pharmaceutical composition of claims 33 or 34 wherein the composition further comprises BMP2.

36. A pharmaceutical composition according to any of claims 33 to 35 for use in the treatment of injury or disease.

37. A method for the treatment of injury or disease in a patient in need of treatment thereof comprising administering to the patient a pharmaceutical composition comprising stem cells and HS/BMP2.

38. The method of claim 37 wherein the stem cells are mesenchymal stem cells.

39. The method of claim 37 or 38 wherein the method further comprises administering BMP2 to the patient.

40. Use of HS/BMP2 in the growth of connective tissue in vitro.

41. A method for growing connective tissue in vitro comprising culturing mesenchymal stem cells in contact with exogenously added HS/BMP2.

42. A biological implant comprising a solid or semi-solid matrix material impregnated with HS/BMP2.

43. The biological implant of claim 42 further impregnated with BMP2.

44. The biological implant of claim 42 or 43 further impregnated with mesenchymal stem cells.

45. A kit comprising a predetermined amount of a glycosaminoglycan having high affinity for a protein having a heparin-binding domain and a predetermined amount of said protein.

46. The kit of claim 45 wherein the glycosaminoglycan is HS/BMP2 and the protein is BMP2.

Claims:

1. A method of isolating heparan sulphate capable of specific and high affinity binding to a protein having a heparin-binding domain, the method comprising:

(i) providing a solid support having peptide molecules adhered to the support, wherein the peptide molecules comprise the heparin-binding domain and optionally one or more additional amino acids at one or each of the N- and C-terminal ends wherein the number of such additional amino acids is 1-20;

(ii) contacting the peptide molecules with a glycosaminoglycan mixture enriched for heparan sulphate such that peptide-heparan sulphate complexes form;

(iii) partitioning peptide-heparan sulphate complexes from the remainder of the mixture which does not bind the heparin-binding domain, or does not specifically bind the heparin-binding domain;

(iv) dissociating heparan sulphate from the peptide-heparan sulphate complexes; and

(v) collecting the dissociated heparan sulphate, wherein the dissociated heparan sulfate is enriched for molecules that are capable of specific and high affinity binding to the heparin binding domain.

2. A method of identifying heparan sulphate capable of stimulating or inhibiting growth and/or differentiation of cells and/or tissues, the method comprising:

(i) providing a solid support having peptide molecules adhered to the support, wherein the peptide molecules comprise a heparin-binding domain and optionally one or more additional amino acids at one or each of the N- and C-terminal ends wherein the number of such additional amino acids is 1-20;

(ii) contacting the peptide molecules with a glycosaminoglycan mixture enriched for heparan sulphate such that peptide-heparan sulphate complexes form;

(iii) partitioning peptide-heparan sulphate complexes from the mixture remainder which does not bind the heparin-binding domain, or does not specifically bind the heparin-binding domain;

(iv) dissociating heparan sulphate from the polypeptide-heparan sulphate complexes;

(v) collecting the dissociated heparan sulphate, wherein the dissociated heparan sulfate is enriched for molecules that are capable of specific and high affinity binding to the heparin binding domain;

(vi) adding the collected heparan sulphate to cells or tissues in which a protein comprising the heparin-binding domain amino acid sequence is present; and

(vii) measuring one or more of: proliferation of the cells, differentiation of the cells, expression of one or more protein markers.

3. The method of claim 1 or claim 2 wherein the method comprises selecting heparan sulphate having the highest affinity and/or specificity for the heparin-binding domain by varying a salt concentration present at the surface of the solid support.

4. The method of any one of claims 1 to 3 wherein the method comprises obtaining heparan sulphate having a binding affinity for the peptide molecules of less than 1μM.

5. The method of any one of claims 1 to 4 wherein the method further comprises subjecting the collected heparan sulphate to further analysis in order to determine structural characteristics of the heparan sulphate.

6. The method of any one of claims 1 to 5 wherein the peptide-heparan sulphate complexes are contacted with a lyase.

7. An isolated heparan sulphate when obtained by the method of any one of claims 1 to 4.

Claims:

1. A method of isolating heparan sulphate capable of specific and high affinity binding to a protein having a heparin-binding domain, the method comprising:

(i) providing a solid support having peptide molecules adhered to the support, wherein the peptide molecules comprise the heparin-binding domain and optionally one or more additional amino acids at one or each of the N- and C-terminal ends wherein the number of such additional amino acids is 1-20;

(ii) contacting the peptide molecules with a glycosaminoglycan mixture enriched for heparan sulphate such that peptide-heparan sulphate complexes form;

(iii) partitioning peptide-heparan sulphate complexes from the remainder of the mixture which does not bind the heparin-binding domain, or does not specifically bind the heparin-binding domain;

(iv) dissociating heparan sulphate from the peptide-heparan sulphate complexes; and

(v) collecting the dissociated heparan sulphate, wherein the dissociated heparan sulfate is enriched for molecules that are capable of specific and high affinity binding to the heparin binding domain.

2. A method of identifying heparan sulphate capable of stimulating or inhibiting growth and/or differentiation of cells and/or tissues, the method comprising:

(i) providing a solid support having peptide molecules adhered to the support, wherein the peptide molecules comprise a heparin-binding domain and optionally one or more additional amino acids at one or each of the N- and C-terminal ends wherein the number of such additional amino acids is 1-20;

(ii) contacting the peptide molecules with a glycosaminoglycan mixture enriched for heparan sulphate such that peptide-heparan sulphate complexes form;

(iii) partitioning peptide-heparan sulphate complexes from the mixture remainder which does not bind the heparin-binding domain, or does not specifically bind the heparin-binding domain;

(iv) dissociating heparan sulphate from the polypeptide-heparan sulphate complexes;

(v) collecting the dissociated heparan sulphate, wherein the dissociated heparan sulfate is enriched for molecules that are capable of specific and high affinity binding to the heparin binding domain;

(vi) adding the collected heparan sulphate to cells or tissues in which a protein comprising the heparin-binding domain amino acid sequence is present; and

(vii) measuring one or more of: proliferation of the cells, differentiation of the cells, expression of one or more protein markers.

3. The method of claim 1 or claim 2 wherein the method comprises selecting heparan sulphate having the highest affinity and/or specificity for the heparin-binding domain by varying a salt concentration present at the surface of the solid support.

4. The method of any one of claims 1 to 3 wherein the method comprises obtaining heparan sulphate having a binding affinity for the peptide molecules of less than 1μM.

5. The method of any one of claims 1 to 4 wherein the method further comprises subjecting the collected heparan sulphate to further analysis in order to determine structural characteristics of the heparan sulphate.

6. The method of any one of claims 1 to 5 wherein the peptide-heparan sulphate complexes are contacted with a lyase.

7. An isolated heparan sulphate when obtained by the method of any one of claims 1 to 4.