CLAIMS

1. A medium for stem cell proliferation comprising a fibroblast growth factor (FGF), and a sulfated compound or a pharmaceutically acceptable salt thereof at a concentration promoting the growth of a stem cell in the presence of FGF, wherein the sulfated compound content is not more than 250 ng/ml when the sulfated compound is a sulfated polysaccharide, wherein the sulfated compound is a sulfated polymer, excluding sulfated saccharides; a sulfated saccharide; a sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound; a sulfated substance of sugar-lactone; or a sulfated substance of an organic acid,

wherein the aforementioned sulfated saccharide or a pharmaceutically acceptable salt thereof is at least one selected from the group consisting of cellulose SO_3Na, xanthan gum SO_3Na, pectin SO_3Na, alginate SO_3Na, inulin SO_3Na, maltoheptaose SO_3Na, maltotriose SO_3Na, maltitol SO_3Na, mannitol SO_3Na, xylitol SO_3Na and erythritol SO_3Na,

wherein the sulfated polymer is at least one selected from the group consisting of sulfo group-containing polyvinyl alcohol, sulfo group-containing polyvinyl amine, sulfo group-containing polyallylamine, sulfo group-containing α-poly methyl glutamate/α-5-hydroxynorvaline (2/8) copolymer, α-polyglutamic acid-γ-taurine, sulfo group-containing triserine, sulfo group-containing serine, sulfo group-containing branched-polyglycerol and a derivative thereof, and polyethylene sulfonate,

wherein the sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound or a pharmaceutically acceptable salt thereof is maltotriose-hexamethylene diisocyanate-SO3Na or dextran-hexamethylene

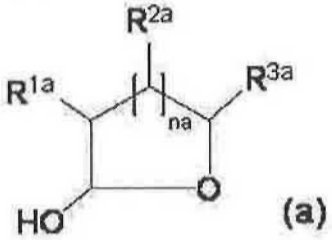
diisocyanate-SO3Na,

wherein the sulfated substance of sugar-lactone or a pharmaceutically acceptable salt thereof is gluconolactone-SO_3Na, and

wherein the sulfated substance of an organic acid or a pharmaceutically acceptable salt thereof is tartrate-SO3Na.

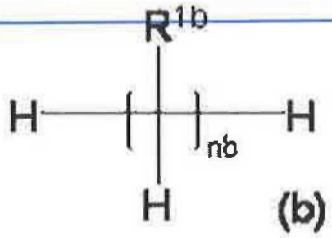
2. The medium according to claim 1, wherein the sulfated compound is sulfated saccharide, wherein the sulfated saccharide content is not more than 250 ng/ml when the sulfated saccharide is a sulfated polysaccharide.

3. The medium according to claim 2, wherein the aforementioned sulfated saccharide is at least one compound selected from the group consisting of
(I) a compound comprising one or more constitutional units induced from a compound represented by the following formula (a)



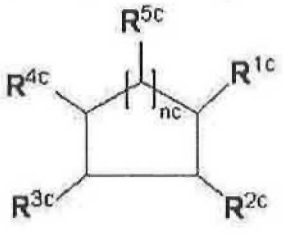
(a)

wherein
na is 1, 2 or 3,
R^{1a} and R^{3a} are the same or different and each is a functional group optionally having substituent(s), and
R^{2a} in the number of na are each independently a functional group optionally having substituent(s), and one or more sulfate groups,
(II) a compound represented b the following formula (b)



(b)

wherein
nb is an integer of 3 - 100, and
R^{1b} in the number of nb are each independently a functional group optionally having substituent(s) and containing one or more sulfate groups, and
(III) a compound represented by the following formula (c)



(c)

wherein
nc is 1, 2 or 3,
R^{1c} - R^{4c} are the same or different and each is a functional group optionally having substituent(s), and
R^{5c} in the number of nc are each independently a functional group optionally having substituent(s) and containing one or more sulfate groups.

4. The medium according to claim 2 or 3, wherein the sulfated saccharide is at least one selected from the group consisting of sulfated monosaccharide, sulfated disaccharide, sulfated polysaccharide, sulfated sugar alcohol and sulfated cyclitol.

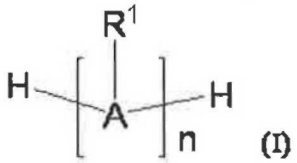
5. The medium according to any one of claims 2 to 4, wherein the content level of sulfur in the sulfated saccharide is not less than 5 wt%.

6. The medium according to any one of claims 1 to 5, wherein the aforementioned sulfated saccharide or a pharmaceutically acceptable salt thereof is at least one selected from the group consisting of xanthan gum SO_3Na, pectin SO_3Na, maltoheptaose SO_3Na, maltotriose SO_3Na, maltitol SO_3Na and sucrose $8SO_3K$.

7. The medium according to claim 1, wherein the sulfated compound is a sulfated polymer excluding sulfated saccharides.

8. The medium according to claim 7, wherein the

aforementioned sulfated polymer is a compound represented by the following formula (I)



(I)

wherein
A is a polymer constitutional unit,
n is an integer of 1 - 1500,
R^1 is a functional group optionally having substituent(s), which contains one or more sulfo groups.

9. The medium according to claim 7 or 8, wherein the content level of sulfur in the sulfated polymer is not less than 5 wt%.

10. The medium according to any one of claims 7 to 9, wherein the derivative of sulfo group-containing branched-polyglycerol or a pharmaceutically acceptable salt thereof is
branched-polyglycerol-monomethyltetraethyleneglycol-SO_3Na,
branched-polyglycerol-2-furfuryl-SO_3Na or
branched-polyglycerol-isopropyloxy-SO_3Na.

11. The medium according to claim 1, wherein the sulfated compound is a sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound.

12. The medium according to claim 1, wherein the sulfated compound is a sulfated substance of sugar-lactone.

13. The medium according to claim 1, wherein the sulfated compound is a sulfated substance of an organic acid.

14. The medium according to any one of claims 1 to 13, wherein the fibroblast growth factor is a basic fibroblast growth factor.

15. The medium according to any one of claims 1 to 14, wherein the aforementioned stem cell is a mesenchymal stem cell, an embryonic stem cell or an artificial pluripotent stem cell.

16. A culture method of a stem cell using a medium for stem cell proliferation comprising FGF, comprising adding a sulfated compound or a pharmaceutically acceptable salt thereof to the medium at a concentration promoting the growth of a stem cell in the presence of FGF, wherein the sulfated compound content is not more than 250 ng/ml when the sulfated compound is a sulfated polysaccharide

wherein the sulfated compound is a sulfated polymer, excluding sulfated saccharides; a sulfated saccharide; a sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound; a sulfated substance of sugar-lactone; or a sulfated substance of an organic acid,

wherein the aforementioned sulfated saccharide or a pharmaceutically acceptable salt thereof is at least one selected from the group consisting of dextran sulfate Na, cellulose SO_3Na, xanthan gum SO_3Na, pectin SO_3Na, alginate SO_3Na, inulin SO_3Na, maltoheptaose SO_3Na, maltotriose SO_3Na, maltitol SO_3Na, sucrose $8SO_3K$, mannitol SO_3Na, xylitol SO_3Na and erythritol SO_3Na,

wherein the sulfated polymer is at least one selected from the group consisting of sulfo group-containing polyvinyl alcohol, sulfo group-containing polyvinyl amine, sulfo group-containing polyallylamine, sulfo group-containing α-poly methyl glutamate/α-5-hydroxynorvaline (2/8) copolymer, α-polyglutamic acid-γ-taurine, sulfo group-containing triserine, sulfo group-containing serine, sulfo group-containing branched-polyglycerol and a derivative thereof, and polyethylene sulfonate,

wherein the sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound or a pharmaceutically acceptable salt thereof is maltotriose-hexamethylene diisocyanate-SO3Na or dextran-hexamethylene

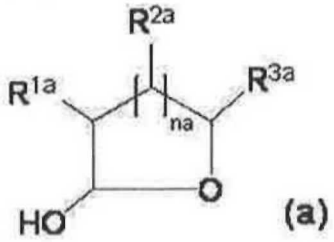
diisocyanate-SO3Na,

wherein the sulfated substance of sugar-lactone or a pharmaceutically acceptable salt thereof is gluconolactone-SO_3Na, and

wherein the sulfated substance of an organic acid or a pharmaceutically acceptable salt thereof is tartrate-SO3Na.

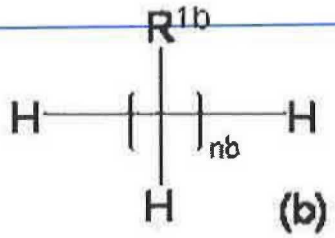
17. The method according to claim 16, wherein the sulfated compound is a sulfated saccharide wherein sulfated saccharide content is not more than 250 ng/ml when the sulfated saccharide is a sulfated polysaccharide.

18. The method according to claim 17, wherein the aforementioned sulfated saccharide is at least one compound selected from the group consisting of
(I) a compound comprising one or more constitutional units induced from a compound represented by the following formula (a)



(a)

wherein
na is 1, 2 or 3,
R^{1a} and R^{3a} are the same or different and each is a functional group optionally having substituent(s), and
R^{2a} in the number of na are each independently a functional group optionally having substituent(s), and one or more sulfate groups,
(II) a compound represented by the following formula (b)



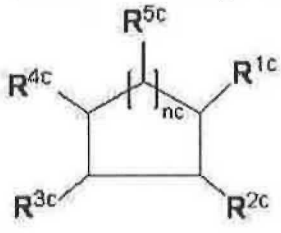
(b)

wherein

nb is an integer of 3 - 100, and

R^{1b} in the number of nb are each independently a functional group optionally having substituent(s) and containing one or more sulfate groups, and

(III) a compound represented by the following formula (c)



(c)

wherein

nc is 1, 2 or 3,

R^{1c} - R^{4c} are the same or different and each is a functional group optionally having substituent(s), and

R^{5c} in the number of nc are each independently a functional group optionally having substituent(s) and containing one or more sulfate groups.

19. The method according to claim 17 or 18, wherein the sulfated saccharide is at least one selected from the group consisting of sulfated monosaccharide, sulfated disaccharide, sulfated polysaccharide, sulfated sugar alcohol and sulfated cyclitol.

20. The method according to any one of claims 17 to 19, wherein the content level of sulfur in the sulfated saccharide is not less than 5 wt%.

21. The method according to any one of claims 16 to 20, wherein the aforementioned sulfated saccharide or a pharmaceutically acceptable salt thereof is at least one selected from the group consisting of dextran sulfate Na, xanthan gum SO_3Na, pectin SO_3Na, maltoheptaose SO_3Na, maltotriose SO_3Na, maltitol SO_3Na and sucrose $8SO_3K$.

22. The method according to any one of claims 17 to 21, wherein the aforementioned sulfated saccharide or a pharmaceutically acceptable salt thereof is dextran sulfate Na having an average molecular weight of 2,500 - 7,500.

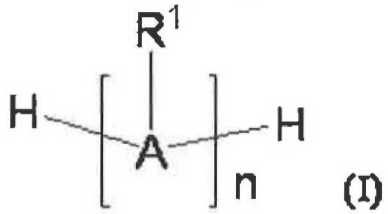
23. The method according to any one of claims 17 to 21, wherein the aforementioned sulfated saccharide or a pharmaceutically acceptable salt thereof is sucrose $8SO_3K$.

24. The method according to claim 23, wherein the content of the aforementioned sucrose $8SO_3K$ is 25 pg/ml - 10 μg/ml.

25. The method according to claim 16, wherein the sulfated compound is a sulfated polymer excluding sulfated saccharides.

26. The method according to claim 25, wherein the

aforementioned sulfated polymer is a compound represented by the following formula (I)



(I)

wherein
A is a polymer constitutional unit,
n is an integer of 1 - 1500,
R^1 is a functional group optionally having substituent(s), which contains one or more sulfo groups.

27. The method according to claim 25 or 26, wherein the content level of sulfur in the sulfated polymer is not less than 5 wt%.

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28. The method according to any one of claims 25 to 27, wherein the derivative of the sulfo group-containing branched-polyglycerol or a pharmaceutically acceptable salt thereof is branched-polyglycerol-monomethyltetraethyleneglycol-SO_3Na, branched-polyglycerol-2-furfuryl-SO_3Na or branched-polyglycerol-isopropyloxy-SO_3Na.

29. The method according to claim 16, wherein the sulfated compound is a sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound.

30. The method according to claim 16, wherein the sulfated compound is a sulfated substance of sugar-lactone.

31. The method according to claim 16, wherein the sulfated compound is a sulfated substance of an organic acid.

32. The method according to any one of claims 16 to 31, wherein the fibroblast growth factor is a basic fibroblast growth factor.

33. The method according to any one of claims 16 to 32, wherein the aforementioned stem cell is a mesenchymal stem cell, an embryonic stem cell or an artificial pluripotent stem cell.

34. A sulfated compound selected from the group consisting of xylitol SO_3Na, maltotriose-hexamethylene diisocyanate-SO_3Na and gluconolactone-SO_3Na or a pharmaceutically acceptable salt thereof.

35. A sulfated compound selected from the group consisting of an α-poly methyl glutamate/α-5-hydroxynorvaline (5-SO_3Na) (2/8) copolymer, triserine-SO_3Na and branched-polyglycerol-isopropyloxy-SO_3Na or a pharmaceutically acceptable salt thereof.

CLAIMS

1. A medium for stem cell proliferation comprising a fibroblast growth factor (FGF), and a sulfated compound or a pharmaceutically acceptable salt thereof at a concentration promoting the growth of a stem cell in the presence of FGF, wherein the sulfated compound is a sulfated polymer or a sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound,

wherein the content level of sulfur in the sulfated compound is not less than 5 wt%,

wherein the sulfated polymer or a pharmaceutically acceptable salt thereof at a concentration promoting the growth of a stem cell in the presence of FGF is selected from the group consisting of:

polyvinyl alcohol SO_3Na, 250 pg/mL - 100 ng/mL;

polyvinyl amine SO_3Na, 25 ng/mL - 250 ng/mL;

polyallylamine SO_3Na, 25 pg/mL - 250 pg/mL or 25 ng/mL;

α-poly methyl glutamate/α-5-hydroxynorvaline (5-SO_3Na)(2/8) copolymer, 25 pg/mL - 250 pg/mL, or 25 ng/mL - 2.5 μg/mL;

α-polyglutamic acid-γ-taurine Na, 25 pg/mL - 250 pg/mL, or 25 ng/mL - 2.5 μg/mL;

triserine SO_3Na, 250 pg/mL - 2.5 ng/mL;

branched-polyglycerol SO_3Na, 25 pg/mL - 250 ng/mL;

branched-polyglycerol-monomethyltetraethyleneglycol -SO_3N, 25 pg/mL - 2.5 ng/mL;

branched-polyglycerol-isopropyloxy-SO_3Na, 25 pg/mL - 25 ng/mL; and

polyethylene sulfonate Na, 25 ng/mL - 250 ng/mL, and

wherein the sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound or a pharmaceutically acceptable salt thereof at a concentration promoting the

growth of a stem cell in the presence of FGF is selected from the group consisting of:

maltotriose-hexamethylene diisocyanate-SO3Na, 25 pg/mL - 250 pg/mL, or 250 ng/mL; and

dextran-hexamethylene diisocyanate-SO3Na, 25 pg/mL - 250 pg/mL, or 25 ng/mL.

2. The medium according to claim 1, wherein the fibroblast growth factor is a basic fibroblast growth factor.

3. The medium according to claim 1 or 2, wherein the aforementioned stem cell is a mesenchymal stem cell, an embryonic stem cell or an artificial pluripotent stem cell.

4. A method of culturing a stem cell using a medium for stem cell proliferation comprising FGF, comprising adding a sulfated compound or a pharmaceutically acceptable salt thereof to the medium at a concentration promoting the growth of a stem cell in the presence of FGF, wherein the sulfated compound is a sulfated polymer or a sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound,

wherein the content level of sulfur in the sulfated compound is not less than 5 wt%,

wherein the sulfated polymer or a pharmaceutically acceptable salt thereof at a concentration promoting the growth of a stem cell in the presence of FGF is selected from the group consisting of:

polyvinyl alcohol SO_3Na, 250 pg/mL - 100 ng/mL;

polyvinyl amine SO_3Na, 25 ng/mL - 250 ng/mL;

polyallylamine SO_3Na, 25 pg/mL - 250 pg/mL or 25 ng/mL;

α-poly methyl glutamate/α-5-hydroxynorvaline (5-SO_3Na)(2/8) copolymer, 25 pg/mL - 250 pg/mL, or 25 ng/mL - 2.5 μg/mL;

α-polyglutamic acid-γ-taurine Na, 25 pg/mL - 250 pg/mL,

or 25 ng/mL - 2.5 μg/mL;

triserine SO_3Na, 250 pg/mL - 2.5 ng/mL;

branched-polyglycerol SO_3Na, 25 pg/mL - 250 ng/mL;

branched-polyglycerol-monomethyltetraethyleneglycol -SO_3N, 25 pg/mL - 2.5 ng/mL;

branched-polyglycerol-isopropyloxy-SO_3Na, 25 pg/mL - 25 ng/mL; and

polyethylene sulfonate Na, 25 ng/mL - 250 ng/mL, and

wherein the sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound or a pharmaceutically acceptable salt thereof at a concentration promoting the growth of a stem cell in the presence of FGF is selected from the group consisting of:

maltotriose-hexamethylene diisocyanate-SO3Na, 25 pg/mL - 250 pg/mL, or 250 ng/mL; and

dextran-hexamethylene diisocyanate-SO3Na, 25 pg/mL - 250 pg/mL, or 25 ng/mL.

5. The method according to claim 4, wherein the fibroblast growth factor is a basic fibroblast growth factor.

6. The method according to claim 4 or 5, wherein the aforementioned stem cell is a mesenchymal stem cell, an embryonic stem cell or an artificial pluripotent stem cell.

7. The medium according to claim 1, wherein the sulfated polymer or the sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound is maltotriose-hexamethylene diisocyanate-SO3Na.

8. The method according to claim 4, wherein the sulfated polymer or the sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound is maltotriose-hexamethylene diisocyanate-SO3Na.