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

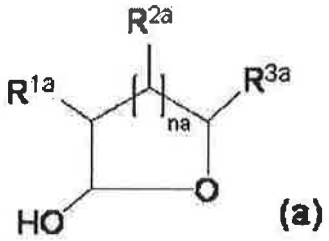
diisocyanate-SO3Na,

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)

~~6. The medium according to any one of claims 2 to 5, 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, fucoidan, alginate SO_3Na, inulin SO_3Na, maltoheptaose SO_3Na, stachyose SO_3Na, maltotriose SO_3Na, maltitol SO_3Na, sucrose $8SO_3K$, glucose SO_3Na, myo-6 inositol SO_3K, α-cyclodextrin SO_3Na, mannitol SO_3Na, xylitol SO_3Na and erythritol SO_3Na.~~

~~7~~6. The medium according to any one of claims ~~6~~1 to 5, wherein the aforementioned sulfated saccharide or a pharmaceutically acceptable salt thereof is at least one selected from the group consisting of ~~dextran sulfate Na, fucoidan,~~ xanthan gum SO_3Na, pectin SO_3Na, maltoheptaose SO_3Na, maltotriose SO_3Na, maltitol SO_3Na and sucrose $8SO_3K$.

~~8. The medium according to any one of claims 2 to 7, 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.~~

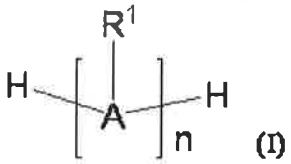
~~9. The medium according to any one of claims 2 to 7, wherein the aforementioned sulfated saccharide or a pharmaceutically acceptable salt thereof is sucrose $8SO_3K$.~~

~~10. The medium according to claim 9, wherein the content of the aforementioned sucrose $8SO_3K$ is 25 pg/ml - 10 μg/ml.~~

~~11~~7. The medium according to claim 1, wherein the sulfated compound is a sulfated polymer ~~(~~excluding sulfated saccharides~~)~~.

~~12~~8. The medium according to claim ~~11~~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.

~~13~~9. The medium according to claim ~~11~~7 or ~~12~~8, wherein the content level of sulfur in the sulfated polymer is not less than 5 wt%.

~~14. The medium according to any one of claims 11 to 13, 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 polyethyleneimine, sulfo group-containing α-polylysine, 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 sulfonic acid.~~

~~15~~10. The medium according to any one of claims 7 to ~~14~~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.

~~16~~11. The medium according to claim 1, wherein the sulfated compound is a sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound.

~~17. The medium according to claim 16, wherein the sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound or a pharmaceutically acceptable salt thereof is maltotriose-hexamethylene diisocyanate-SO_3Na or dextran-hexamethylene diisocyanate-SO_3Na.~~

~~18~~12. The medium according to claim 1, wherein the sulfated compound is a sulfated substance of sugar-lactone.

~~19. The medium according to claim 18, wherein the sulfated substance of sugar-lactone or a pharmaceutically acceptable salt thereof is gluconolactone-SO_3Na.~~

~~20~~13. The medium according to claim 1, wherein the sulfated compound is a sulfated substance of an organic acid.

~~21. The medium according to claim 20, wherein the sulfated substance of an organic acid or a pharmaceutically acceptable salt thereof is tartrate-SO_3Na.~~

~~22~~14. The medium according to any one of claims 1 to ~~21~~13, wherein the fibroblast growth factor is a basic fibroblast growth factor.

~~23~~15. The medium according to any one of claims 1 to ~~22~~14, wherein the aforementioned stem cell is a mesenchymal stem cell, an embryonic stem cell or an artificial pluripotent stem cell.

~~24~~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

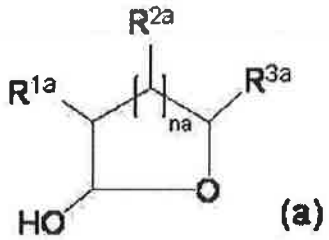
diisocyanate-SO3Na,

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

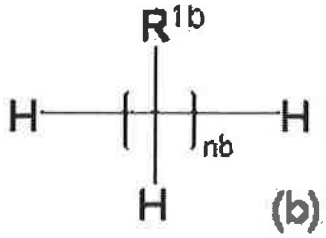
wherein the sulfated substance of an organic acid or a pharmaceutically acceptable salt thereof is tartrate-SO3Na.

~~25~~17. The method according to claim ~~24~~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~~)~~.

~~26~~18. The method according to claim ~~25~~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)



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)



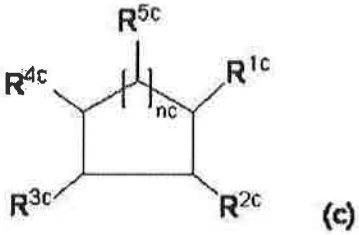
(b)

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.

~~27~~19. The method according to claim ~~25~~ 17 or ~~26~~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.

~~28~~20. The method according to any one of claims ~~25~~ 17 to ~~27~~19, wherein the content level of sulfur in the sulfated saccharide is not less than 5 wt%.

~~29. The method according to any one of claims 25 to 28, 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, fucoidan, alginate SO_3Na, inulin SO_3Na, maltoheptaose SO_3Na, stachyose SO_3Na, maltotriose SO_3Na, maltitol SO_3Na, sucrose $8SO_3K$, glucose SO_3Na, myo-6 inositol SO_3K, α-cyclodextrin SO_3Na, mannitol SO_3Na, xylitol SO_3Na and erythritol SO_3Na.~~

~~30~~21. The method according to any one of claims ~~29~~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, ~~fucoidan,~~ xanthan gum SO_3Na, pectin SO_3Na, maltoheptaose SO_3Na, maltotriose SO_3Na, maltitol SO_3Na and sucrose $8SO_3K$.

~~31~~22. The method according to any one of claims ~~25~~17 to ~~30~~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.

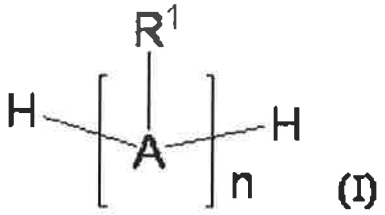
~~32~~23. The method according to any one of claims ~~25~~17 to ~~30~~21, wherein the aforementioned sulfated saccharide or a pharmaceutically acceptable salt thereof is sucrose $8SO_3K$.

~~33~~24. The method according to claim ~~32~~23, wherein the content of the aforementioned sucrose $8SO_3K$ is 25 pg/ml - 10 μg/ml.

~~34~~25. The method according to claim ~~24~~16, wherein the sulfated compound is a sulfated polymer ~~(~~excluding sulfated saccharides~~)~~.

~~35~~26. The method according to claim ~~34~~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.

~~36~~27. The method according to claim ~~34~~ 25 or 26~~35~~, wherein the content level of sulfur in the sulfated polymer is not less than 5 wt%.

~~37. The method according to any one of claims 34 to 36, 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 polyethyleneimine, sulfo group-containing α-polylysine, 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 sulfonic acid.~~

~~38~~28. The method according to any one of claims 25 to 27~~37~~, 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.

~~39~~29. The method according to claim 16~~24~~, wherein the sulfated compound is a sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound.

~~40. The method according to claim 39, wherein the sulfated substance of a saccharide polymer crosslinked by a diisocyanate compound or a pharmaceutically acceptable salt thereof is maltotriose-hexamethylene diisocyanate-SO_3Na or dextran-hexamethylene diisocyanate-SO_3Na.~~

~~41~~30. The method according to claim ~~24~~16, wherein the sulfated compound is a sulfated substance of sugar-lactone.

~~42. The method according to claim 41, wherein the sulfated substance of sugar-lactone or a pharmaceutically acceptable salt thereof is gluconolactone-SO_3Na.~~

~~43~~31. The method according to claim ~~24~~16, wherein the sulfated compound is a sulfated substance of an organic acid.

~~44. The method according to claim 43, wherein the sulfated substance of an organic acid or a pharmaceutically acceptable salt thereof is tartrate-SO_3Na.~~

~~45~~32. The method according to any one of claims ~~24~~ 16 to ~~44~~31, wherein the fibroblast growth factor is a basic fibroblast growth factor.

~~46~~33. The method according to any one of claims ~~24~~16 to ~~45~~32, wherein the aforementioned stem cell is a mesenchymal stem cell, an embryonic stem cell or an artificial pluripotent stem cell.

~~47~~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.

~~48~~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.