

1-Multi-targeted RNAi therapeutics for scarless wound healing of skin

US 8735567 B2

Abstract

The present invention provides small interfering RNA (siRNA) molecules, compositions containing them, and methods of using them for improvement of skin scarless wound healing and other skin conditions, such as psoriasis and lupus-caused cutaneous lesions. The invention includes siRNA molecules and compositions containing them that inhibit the expression of one or more genes that promote pathological or undesired processes in wound healing and methods of using them.

Claims (12)

What is claimed is:

1. A composition comprising at least three siRNA molecules and a pharmaceutically acceptable carrier, wherein each siRNA molecule binds an mRNA molecule that is encoded by a gene selected from the group consisting of TGF- β 1, Cox-2, and Hoxb13, wherein said molecules inhibit expression of said genes in both human and mouse cells, wherein said composition comprises a nanoparticle, and wherein said siRNA molecules comprise the following oligonucleotides:
 - (1) hmTF-2: sense, 5'-CCCAAGGGCUACCAUGCCAACUUCU-3' (SEQ ID NO: 11)
antisense, 5'AGAAGUUGGCAUGGUAGCCCUUGGG-3'; (SEQ ID NO: 12)
2. The composition of claim 1, wherein said pharmaceutically acceptable carrier comprises a branched histidine polypeptide or a branched lysine polypeptide.
3. A method for treating a dermal or epidermal wound in a subject, wherein said wound is characterized at least in part by inflammation and neovascularization, said method comprising administering to said subject a pharmaceutically effective amount of the composition of claim 1.
4. The method of claim 3 wherein said subject is a mammal.
5. The method of claim 3 wherein said subject is a human.
6. A composition comprising at least three siRNA molecules, wherein each siRNA molecule binds an mRNA molecule that is encoded by a gene selected from the group consisting of TGF- β 1, Cox-2, and Hoxb13, and a pharmaceutically acceptable carrier, wherein said siRNA molecules comprise the following oligonucleotides:
 - (1) hmTF-2: sense, 5'-CCCAAGGGCUACCAUGCCAACUUCU-3' (SEQ ID NO: 11)
antisense, 5'AGAAGUUGGCAUGGUAGCCCUUGGG-3'; (SEQ ID NO: 12)
7. The composition of claim 1, wherein said pharmaceutically acceptable carrier comprises a branched histidine-lysine peptide.
8. The composition of claim 6, wherein said pharmaceutically acceptable carrier comprises a branched histidine polypeptide or a branched lysine polypeptide.
9. The composition of claim 6, wherein said pharmaceutically acceptable carrier comprises a branched histidine-lysine peptide.
10. The composition of claim 6, wherein said composition comprises a nanoparticle.
11. The composition of claim 8, wherein said composition comprises a nanoparticle.

2-Inhibition of wound contraction with paclitaxel, colchicine and penicillamine

US 5916913 A

Abstract

The present invention uses Paclitaxel and/or Colchicine in an appropriate carrier to inhibit wound contraction. Paclitaxel is an antimicrotubule agent that is currently used as a cancer chemotherapeutic drug. Colchicine inhibits microtubule dependent processes such as cell contraction and motility. It has been given orally for decades to treat gout. Previous studies using Colchicine to control wound contraction have been unsuccessful because of both local and systemic toxicity. Studies using the present invention demonstrate that Paclitaxel and Colchicine, when applied to wounds locally (either topically or by injection) in concentrations which are much lower than those previously studied, inhibit wound contraction, collagen deposition and granulation tissue growth. When combined with D-penicillamine, a drug that inhibits collagen cross-linking, the combination inhibits wound contraction, granulation tissue growth (nascent tissue that forms in the wound immediately post-injury), and intramuscular collagen deposition; epithelialization (sealing of the wound) is promoted.

Claims (13)

What is claimed is:

1. A method of treating a wound comprising:
providing a drug preparation containing Paclitaxel in a drug carrier; and
applying a therapeutically effective amount of the drug preparation locally to a wound site.
2. The method of claim 1 wherein the drug preparation further includes penicillamine.
3. The method of claim 1 wherein the drug preparation is applied either topically or by injection.
4. The method of claim 1 wherein the drug preparation further includes d-penicillamine.
5. The method of claim 1 wherein the drug preparation further includes Colchicine.
6. The method of claim 5 wherein the drug preparation further includes d-penicillamine.
7. A method of treating a wound comprising:
providing a drug preparation containing Paclitaxel and penicillamine and in a drug carrier; and
applying a therapeutically effective amount of the drug preparation locally to a wound site.
8. The method of claim 7 wherein the drug preparation further includes Colchicine.
9. The method of claim 7 wherein the drug preparation is applied either topically or by injection.
10. The method of claim 7 wherein said penicillamine is d-penicillamine.
11. A drug preparation for treating wounds, said preparation consisting essentially of a drug carrier, and effective amounts of Paclitaxel and penicillamine.
12. The drug preparation of claim 11 further including an effective amount of coichicine.
13. The drug preparation of claim 11 wherein said penicillamine is d-penicillamine.

3-Hydrogels for treating and ameliorating wounds and methods for making and using them

WO 2016004212 A1

Abstract

In alternative embodiments, provided are compositions, e.g., pharmaceutical compositions, formulations, kits and other products of manufacture, comprising a hydrogel and active ingredients, including mixed thickness skin micrografts, or full or split-thickness skin grafts, contained or mixed in or within the hydrogel; and methods for making and using them. In alternative embodiments, compositions and methods as provided herein are used for the treatment or amelioration of wounds and surgical sites, and include compositions and methods for micrografting, or for micrografting a wound, or for micrografting a wound for rapid re-epithelialization, or for micrografting a wound for rapid re-epithelialization of large non-healing wounds.

Claims (7)

WHAT IS CLAIMED IS:

1. A product of manufacture, a device, or a composition, comprising:
 - (a) a sterile hydrogel comprising a hydrogel material, wherein the hydrogel is:
 - (i) in a substantially liquid form capable of setting, gelling or self- assembling;
 - (ii) a partially assembled or gelled hydrogel, in a partially assembled or gelled form; or,
 - (iii) in a set, gelled or self-assembled state; or a substantially set, gelled or self-assembled state, and optionally the set, gelled or self-assembled state is in situ; and
 - (b)
 - (1)
 - (i) a mixed thickness skin micrograft, a split-thickness skin graft, or a full thickness skin graft, wherein the mixed thickness skin micrograft, split-thickness skin graft, or full thickness skin graft is dispersed in, or mixed into, or substantially evenly distributed throughout, the sterile hydrogel, and optionally the mixed thickness skin micrograft, split-thickness skin graft, or full thickness skin graft further comprises, or is dispersed in, or mixed into, or substantially evenly distributed throughout, a sterile pure water or a sterile isotonic solution or buffer, or equivalent, and optionally the micrograft or skin graft is an autologous micrograft;
 - (ii) a skin tissue column, a microscopic skin tissue column or a skin graft comprising a full-thickness column of skin tissue, a "fractional skin harvesting (FSH)" graft, an ultra-micrograft, a microscopic skin tissue column (MSTC), wherein optionally the skin tissue column, the micrograft, FSH or skin graft is an autologous graft, and optionally the skin tissue column, the micrograft, FSH or skin graft is derived from revertant Epidermolysis Bullosa (EB) skin tissue;
 - (2) a hemostatic agent, wherein optionally the hemostatic agent comprises a tranexamic acid, or a synthetic analog of the amino acid lysine;
 - (3) a growth factor or an accelerator of cell migration, wherein optionally the growth factor is an erythropoietin, a recombinant erythropoietin, or an epoetin alfa (e.g., PROCREDIT™ or EPOGEN™); a granulocyte colony-stimulating factor (G-CSF or GCSF), also known as colony- stimulating factor 3 (CSF 3); a filgrastin or a G-CSF analog, or a FILCAD™ (Cadila Pharmaceuticals), IMUMAX™ (Abbott Laboratories), GRAFEEL™ (Dr. Reddy's Laboratories), NEUKINE (Intas Biopharmaceuticals), EMGRAST™ (Emcure Pharmaceuticals), RELIGRAST™ (Reliance Life Sciences), ZARZIO™ (Sandoz), or a NUFIL™ (Biocon); a keratinocyte growth factor or a palifermin or a KEPIVANCE™ (Biovitrum); a gamma- aminobutyric acid (GABA); or ,any combination thereof, wherein

optionally the accelerator of cell migration comprises an inhibitor of a microtubule-severing enzyme, an inhibitor of microtubule degradation or an accelerator of microtubule formation, and *optionally the microtubule-severing enzyme comprises an fidgetin-like 2 (FL2) enzyme and the inhibitor of a microtubule-severing enzyme comprises an inhibitor of FL2, and optionally the FL2 inhibitor comprises an FL2-inhibiting antisense nucleotide (e.g., an antisense RNA) or an FL2-inhibiting siRNA*; (4) an anti-oxidant, wherein optionally the anti-oxidant comprises: a glycyrrhetic acid (GA) (also known as enoxolone), a nicotinamide (also known as vitamin B3), a niacin, a vitamin A, a vitamin C, a vitamin E or any tocopherol or tocotrienol, or a deferoxamine (also known as desferoxamine B, desferoxamine B, DFO, DFO-B, DFOA, DFB or desferal), and optionally the deferoxamine is at a concentration of about 0.1%, and optionally the nicotinamide is at a concentration of about 0.1 %;

(5) an aminoglycoside, wherein optionally the aminoglycoside comprises a gentamicin; or

(6) a combination of (1), (2), (3) and (4); and others. Too many to list.

2. The product of manufacture, device, or composition of claim 1 , wherein:

(a) the mixed thickness skin micrograft, split-thickness skin graft, or full thickness skin graft of 1 (b) is a minced mixed thickness skin micrograft, split-thickness skin graft, or full thickness skin graft;

3. The product of manufacture, device, or composition of claim 1, wherein:

(a) the hydrogel is capable of self-assembling, gelling or setting when exposed to an environment comprising a salt concentrations > 1 mM (or gelation, self-assembly or setting is initiated by salt concentrations > 1 mM);

(b) the hydrogel is capable of self-assembling, gelling or setting into a 3D hydrogel having a nanometer scale and/or a fibrous structure with an average pore size of between about 50 to 200 nm

4. The product of manufacture, device, or composition of any of claims 1 to 3, wherein:

(a) the hydrogel or hydrogel material comprises a self-assembling peptide; (b) the hydrogel or hydrogel material comprises a plurality of synthetic peptides characterized by stable B-sheet structure with ionic side-chain interactions after setting, gelling or self-assembling;

5. A method for treating and/or micrografting, or for micrografting a wound, wound site, a disease lesion or surgical site; or, for micrografting a wound, a wound site, a disease lesion or a surgical site or any micrograft application site, for rapid re-epithelialization, or for micrografting a wound, wound site, a disease lesion or a surgical site for rapid re-epithelialization of large non-healing wounds,

6. The method of claim 5, wherein the amount of mixed thickness skin micrograft, split-thickness skin graft, or full thickness skin graft is based on a 10X to 100X, or 5X to 125X, expansion over the micrograft application site, surgical site, wound, wound site, or skin disease site (e.g., EB skin wound or lesion, or an infected biofilm).

7. The method of claim 5 or claim 6, wherein:

the product of manufacture, device, or composition as set forth in the mixture of claim 5(a) or claim 6, is applied to: or

the micrograft application site is:

(a) a refractory large wound, a wound >10 cm², a chronic wound, a diabetic foot ulcer, a venous leg ulcer, a pressure ulcer, a burn a third degree burn, or a large >10% total body surface area burn or wound;

(b) a skin disease wound, a wound site or a skin disease lesion, and optionally the treated or micrografted skin disease wound, wound site or skin disease lesion is or comprises or is caused by a genetic blistering disease, optionally an

Epidermolysis Bullosa (EB) or related condition, optionally a simplex EB, a junctional EB, a dystrophic EB, indler syndrome, a revertant EB or a non-revertant EB.

4-A pharmaceutical preparation for the treatment of wounds

translated from [German](#)

DE 10140623 A1

Abstract

The invention relates to a novel pharmaceutical preparation for treating wounds, which comprises a proportion of platelet-derived growth factor (PDGF).

Claims(11)

1. A pharmaceutical preparation for the treatment of wounds, with a portion of the growth factor PDGF, **characterized by** at least two components, of which a first component contains the growth factor PDGF and a second component is an aqueous solution which in addition to water 10-100 mg Zn, from 6.5 to 65 mg Fe as well as acid contains in a proportion such that the pH value of the second component forming solution is in the range between about 2.5-3.5, preferably about 2.8.
2. A preparation according to claim 1, characterized in that the second component per liter of solution, about 15-45 mg Zn, and contains about 10-30 mg Fe.
3. A preparation according to claim 1 or 2, characterized in that the acid is sulfuric acid, preferably 95-97% strength sulfuric acid.
4. A preparation according to one of the preceding claims, characterized in that the constituent of zinc of $ZnCl_2$ is formed, preferably in an amount of 10-100 mg per liter of solution, for example 46 to 80 mg per liter of solution.
5. A preparation according to one of the preceding claims, characterized in that the proportion of iron is formed of the second component of $FeSO_4$, preferably in an amount of 32-325 mg per liter of solution, for example 80 to 114 mg per liter of solution.
6. A preparation according to one of the preceding claims, characterized in that the second component per liter of solution, 63 mg of $ZnCl_2$ and about 97 mg $FeSO_4$ contains.
7. A preparation according to one of the preceding claims, characterized in that the aqueous solution of the second component in addition to zinc and iron contains only distilled water and acid.
8. A preparation according to one of the preceding claims, characterized in that the first component contains the growth factor PDGF in a concentration of 0.005 weight percent to 0.04 weight percent, preferably in a concentration of 0.01 weight percent.
9. A preparation according to one of the preceding claims, characterized in that the first component contains the PDGF growth factor in admixture with a base, for example in the form of a gel.
10. A preparation according to one of the preceding claims, characterized in that the first and the second component are used in a ratio such that the combination of the first and second component has a pH below 7.
11. A preparation according to one of the preceding claims, characterized by a mixture of the first and second component.

5-Methods for heart regeneration

US 20140221463 A1

Abstract

Methods for heart regeneration are provided. The invention provided herein includes methods of modulating proliferation of cardiomyocytes using small molecules and microRNAs. In embodiments, the methods provided may be used to increase proliferation of cardiomyocytes. Further provided are methods to be used for the treatment of myocardial infarction.

Claims (20)

What is claimed is:

1. A method of modulating proliferation of a cardiomyocyte, said method comprising:
 - (i) transfecting a cardiomyocyte with a nucleic acid encoding a microRNA modulator, thereby forming a transfected cardiomyocyte; and
 - (ii) allowing said transfected cardiomyocyte to divide, thereby modulating proliferation of said cardiomyocyte.
2. The method of claim 1, wherein said nucleic acid is a lentiviral vector.
3. The method of claim 1, wherein said microRNA modulator is an antagonist of a mir 99 micro RNA, a let-7a microRNA, a mir 100 microRNA, a mir 4458 micro RNA, a mir 4500 micro RNA or a mir 89 microRNA.
4. The method of claim 1, wherein said nucleic acid comprises a nucleic acid sequence as set forth in SEQ ID NO:1124 or SEQ ID NO:1125.
5. The method of claim 4, wherein said proliferation of said cardiomyocyte is increased compared to a control cardiomyocyte lacking said nucleic acid encoding said RNA modulator.
6. A method of modulating proliferation of a cardiomyocyte, said method comprising:
 - (i) contacting a cardiomyocyte with a small molecule, thereby forming a treated cardiomyocyte; and
 - (ii) allowing said treated cardiomyocyte to divide, thereby modulating proliferation of said cardiomyocyte.
7. The method of claim 6, wherein said proliferation of said cardiomyocyte is increased compared to a control cardiomyocyte lacking said small molecule.
8. The method of claim 7, wherein said small molecule modulates expression of a mir 99 micro RNA-regulated protein, a let-7a micro RNA-regulated protein, a mir 100 micro RNA-regulated protein, a mir 4458 micro RNA-regulated protein, a mir 4500 micro RNA-regulated protein or a mir 89 micro RNA-regulated protein.
9. The method of claim 6, wherein said small molecule is a synthetic micro RNA molecule.
10. The method of claim 9, wherein said synthetic micro RNA molecule is an antagonist of a mir 99 micro RNA, a let-7a micro RNA, a mir 100 micro RNA, a mir 4458 micro RNA, a mir 4500 micro RNA or a mir 89 micro RNA.
11. The method of claim 6, wherein said synthetic micro RNA molecule comprises a nucleic acid sequence as set forth in SEQ ID NO:1124 or SEQ ID NO:1125.
12. A method of treating myocardial infarction in a subject in need thereof, said method comprising administering to said subject a therapeutically effective amount of a nucleic acid encoding a micro RNA modulator, wherein said RNA modulator increases cardiomyocyte proliferation thereby treating said myocardial infarction.
13. The method of claim 12, wherein said micro RNA modulator is an antagonist of a mir 99 micro RNA, a let-7a micro RNA, a mir 100 micro RNA, a mir 4458 micro RNA, a mir 4500 micro RNA or a mir 89 micro RNA.
14. The method of claim 12, wherein said nucleic acid comprises a nucleic acid sequence as set forth in SEQ ID NO:1124 or SEQ ID NO:1125.
15. The method of claim 12, wherein said administering to said subject a therapeutically effective amount of a nucleic acid comprises administering a first nucleic acid and a second nucleic acid, wherein said first nucleic acid encodes an antagonist of a mir 99 micro RNA and said second nucleic acid encodes an antagonist of a let-7a micro RNA.

16. A method of treating myocardial infarction in a subject in need thereof, said method comprising administering to said subject a therapeutically effective amount of a nucleic acid encoding an antagonist of a mir 99 micro RNA and a nucleic acid encoding an antagonist of a let-7a micro RNA, thereby treating said myocardial infarction.
17. A method of treating myocardial infarction in a subject in need thereof, said method comprising administering to said subject a therapeutically effective amount of a small molecule, wherein said small molecule increases cardiomyocyte proliferation thereby treating said myocardial infarction.
18. The method of claim 17, wherein said small molecule modulates expression of a mir 99 micro RNA-regulated protein and a let-7a micro RNA-regulated protein.
19. The method of claim 17, wherein said small molecule is a synthetic micro RNA molecule.
20. The method of claim 19, wherein said synthetic micro RNA molecule comprises a nucleic acid sequence as set forth in SEQ ID NO:1124 or SEQ ID NO:1125.

6-Blood plasma based hydrogels for tissue regeneration and wound healing applications

WO 2014035721 A1

Abstract

The present disclosure generally relates to tissue engineering and wound healing. More particularly, the present disclosure relates to the modification of plasma with a stability conferring agent to create a hydrogel for use in regenerative medicine and other tissue engineering applications.

Claims (23)

What is claimed is:

1. A composition comprising plasma in which at least a portion of the fibrinogen present in the plasma is co-polymerized with polyethylene glycol.
2. The composition of claim 1 wherein the plasma is from an allogenic source.
3. The composition of claim 1 wherein the plasma is platelet free plasma.
4. The composition of claim 1 wherein the plasma is platelet rich plasma.
5. The composition of claim 1 further comprising one or more components chosen from growth factors, extracellular matrix proteins, therapeutic drugs, and antibiotics.
6. The composition of claim 1 further comprising therapeutic cells.
7. The composition of claim 1 further comprising adipose derived stem cells.
8. The composition of claim 1 further comprising a fibrinogen-converting agent.
9. The composition of claim 1 further comprising a fibrinolytic inhibitor.
10. The composition of claim 1 wherein the composition is a hydrogel.
11. The composition of claim 1 wherein the polyethylene glycol is bifunctional.
12. The composition of claim 1 wherein the polyethylene glycol is SG-PEG-SG.
13. A method comprising providing a PEGylated plasma and initiating crosslinking of the PEGylated plasma to form a hydrogel.
14. The method of claim 13, wherein the PEGylated plasma is formed by co- polymerizing polyethylene glycol to at least a portion of fibrinogen present in a plasma.
15. The method of claim 13, wherein the initiating crosslinking of the PEGylated plasma comprises introducing a fibrinogen-converting agent to the PEGylated plasma.
16. The method of claim 13 wherein the PEGylated plasma is formed from platelet free plasma.
17. The method of claim 13 wherein the PEGylated plasma is formed from platelet rich plasma.
18. The method of claim 13 wherein the plasma is from an allogenic source.
19. A method comprising introducing a PEGylated plasma hydrogel to a patient in need thereof.
20. The method of claim of claim 19, wherein the PEGylated plasma hydrogel forms at the site of implantation.
21. A kit comprising PEGylated plasma and fibrinogen-converting agent.
22. A system comprising PEGylated plasma disposed in a first container and fibrinogen-converting agent disposed in a second container, wherein the first and second container are operably connected to allow mixing.
23. A system comprising: a PEGylated plasma hydrogel; and therapeutic cells in contact with the PEGylated plasma hydrogel, wherein the therapeutic cells are capable of differentiating into vascular-like structures.

7-Molecules with effects on cellular development and function

WO 2006015368 A2

Abstract

This invention relates to methods to stabilize and/or improve the function of parenchymal cells. Also provided are systems of co-cultures of hepatocyte-stabilizing non-parenchymal cells used in bioreactor microenvironments to identify hepatic stabilizing factors by gene-expression profiling.

Claims (8)

WHAT IS CLAIMED IS:

1. A method of identifying molecular mediators of parenchymal and non-parenchymal cell interactions, comprising: (a) obtaining a first profile of a co-culture of a parenchymal cell population and a first non-parenchymal cell population, comprising measuring a tissue-specific function of the parenchymal cells and correlating the tissue-specific function with a gene expression profile of the first non-parenchymal cell population; (b) obtaining a second profile of a co-culture of the parenchymal cell population and a second non-parenchymal cell population, comprising measuring the tissue-specific function of the parenchymal cells and correlating the tissue-specific function with a gene expression profile of the second non-parenchymal cell population; (c) generating a functional profile, comprising: (i) identifying a change in the tissue-specific function; (ii) comparing the first and second gene expression profiles to identify one or more gene expression differences; and (iü) correlating the one or more genes with the change in the tissue specific function; wherein the function profile comprises the identity of candidate molecular mediators.
2. The method of claim 1, wherein the non-parenchymal cell is a stromal cell.
3. The method of claim 2, wherein the stromal cell is a fibroblast cell.
4. The method of claim 3, wherein the fibroblast comprises a cell line selected from the group consisting of 3T3- J2 fibroblasts, mouse embryonic fibroblasts, and NIH-3T3 fibroblasts.
5. The method of claim 1, wherein the parenchymal cell population comprises cells selected from the group consisting of liver cells, bone marrow cells, skin cells, pancreas cells, kidney cells, neuronal cells, and adrenal gland cells.
6. The method of claim 1, wherein the liver cells are hepatocytes.
7. The method of claim 6, wherein the tissue specific function is selected from the group consisting of: albumin production, fibrinogen production, TCDD-inducible cP450 activity, and urea production.
7. The method of claim 6, wherein the functional profile comprises genes selected from the group consisting of Delta-like 1 homolog; Endothelial differentiation, sphingolipid G-protein- coupled receptor, 3; Aquaporin 1; T-cadherin (Cdh13) ; vascular cadherin-2; tight junction protein 2; Insulin-like growth factor II (IGF-II); Connective tissue growth factor; Follistatin; Secreted phosphoprotein 1; C-fos induced growth factor (VEGF-D) ; Small inducible cytokine A9; Ceruloplasmin; Adiponectin (Acrp30); fibroblast inducible secreted protein; osteoblast specific factor 2 (fasciclin I-like) ; Mouse insulin-like growth factor II (IGF- II); Tnf receptor associated factor 4 (Traf4); apolipoprotein D; Haptoglobin; Follistatin; Interleukin-6; Connective Tissue Growth Factor; small inducible cytokine B subfamily, member 5 (Scyb5) ; Decorin; laminin alpha 4 chain; Jun-B oncogene; Early growth response 1; Notch gene homolog 1 (Drosophila) ; FBJ osteosarcoma oncogene; Interferon regulatory factor 1; 204 interferon- activatable protein; Splicing factor, arginine/serine-rich 3; Heterogeneous nuclear ribonucleoprotein D-like protein JKTBP; Autoantigen Ia (ss-b) ; High mobility group box 1; DNA polymerase delta small subunit (pold2); Esk kinase; Mouse dihydrofolate reductase gene: 3' end; Pml protein; B-cell translocation gene 2; Thymidine kinase 1; She SH2-domain binding protein 1; Guanylate nucleotide binding protein 4; Interferon-induced protein 44; Spindle pole body component 25 homolog; Baculoviral IAP repeat- containing 5; Aurora kinase A; Solute carrier family 1 (glial high affinity glutamate transporter) , member 3; Leucine rich repeat containing 17; Interferon, alpha-inducible protein; Minichromosome maintenance deficient 5, cell division cycle 46; Cysteine rich protein 61; Apolipoprotein D; Interferon-induced protein with tetratricopeptide repeats 3; Interferon-induced protein with tetratricopeptide

repeats 1; 2'-5' oligoadenylate synthetase-like 2; fidgetin-like 1; Rac gtpase-activating protein 1; and Translocase of inner mitochondrial membrane 8 homolog a.

8. The method of claim 6, wherein the functional profile comprises genes selected from the group consisting of Thrombin receptor (PAR-I) ; Hyaluronic acid receptor (CD44) ; Junction plakoglobin (cadherin associated) ; N-cadherin; Beta-catenin; Alpha-catenin 1; BH-Protocadherin-a (Pcdh7); Protocadherin-13; Catenin src; Catenin (cadherin-associated protein) , delta 2 (neural plakophilin-related arm-repeat protein) ; integral membrane glycoprotein; Stomatin; transforming growth factor, beta receptor I (Tgfb1); gap junction membrane channel protein alpha 1; thrombospondin 2; Mesothelin; Dickkopf homolog 3; Inhibin beta-A; FISP-12 protein; Adrenomedullin; Procollagen, type VIII, alpha 1; Tissue inhibitor of metalloproteinase 2; Matrix Metalloproteinase 14; Actin, alpha 1, skeletal muscle; Rho- associated coiled-coil forming kinase 2; Rho interacting protein 2; Myosin Va; Cyclin-dependent kinase inhibitor IA (P21) ; Necdin; General transcription factor HH, polypeptide 1; Kruppel-like factor 9; basonuclein; Src homology 2 domain-containing transforming protein C1; PDZ and LIM domain 1 (elfin) ; SH3 domain 103 protein 5; LIM and SH3 protein 1; Dihydropyrimidinase-like 3.

8-Treatment of skin, and wound repair, with thymosin beta 4

US 8143218 B2

Abstract

Compositions and methods for treatment of skin utilizing thymosin β 4.

Claims (21)

1. A composition for topical administration to skin, comprising a tissue regeneration promoting amount of human thymosin β 4 of SEQ ID NO:3; human transforming growth factor β 1, and a pharmaceutically acceptable topical vehicle.
2. A composition for topical administration to skin comprising a tissue regeneration promoting amount of human thymosin β 4 of SEQ ID NO:3; human vascular endothelial growth factor and a pharmaceutically acceptable topical vehicle.
3. The composition according to claim 2, wherein said vehicle is an oil in water, or water in oil emulsion.
4. A method for improving damage to the skin, the method comprising:
applying topically to said damaged skin a composition comprising a tissue regeneration promoting amount of human thymosin β 4 of SEQ ID NO:3; and a pharmaceutically acceptable topical vehicle.
5. A method for improving damage to the skin, the method comprising:
applying topically a composition comprising a tissue regeneration promoting amount of human thymosin β 4 of SEQ ID NO:3, human transforming growth factor β 1, and a pharmaceutically acceptable topical vehicle.
6. A method for improving damage to the skin, the method comprising:
applying topically a composition comprising a tissue regeneration promoting amount of human thymosin β 4 of SEQ ID NO:3, human vascular endothelial growth factor, and a pharmaceutically acceptable topical vehicle.
7. The method according to claim 6, wherein said skin damaged by irradiation or contains scar tissue.
8. The method according to claim 7, wherein said cosmetically acceptable vehicle is an oil in water, or water in oil emulsion.
9. A composition for topical treatment of skin, comprising a thymosin beta 4 of SEQ ID NO:3 and a vehicle acceptable for topical administration, further comprising transforming growth factor beta, vascular endothelial growth factor, or both.
10. The composition of claim 9, further comprising transforming growth factor beta.
11. The composition of claim 10, wherein said transforming growth factor beta is transforming growth factor beta 1.
12. The composition of claim 9, further comprising vascular endothelial growth factor.
13. The composition of claim 9, wherein said vehicle is a lotion, cream, suspension, dispersion or oil.
14. A method of treating damaged skin tissue in a subject comprising topically administering the composition of claim 9, to said subject.
15. A method of regenerating or revitalizing skin tissue in a subject comprising topically administering the composition of claim 9, to said subject.
16. The method of claim 14, wherein said vehicle is a lotion, cream, suspension, dispersion or oil.
17. The composition of claim 1 wherein said skin is in need of repair.
18. The composition of claim 2 wherein said skin is in need of repair.
19. The method of claim 4 wherein said skin is in need of repair.
20. The method of claim 5 wherein said skin is in need of repair.
21. The method of claim 6 wherein said skin is in need of repair.