

the bone fracture site.

Based on these findings, the present application provides the following ~~inventions~~embodiments:

[1] a tissue regeneration-promoting agent, comprising any one of:

- (a) an HMGB1 protein;
- 5 (b) a cell that secretes an HMGB1 protein;
- (c) a vector into which a DNA encoding an HMGB1 protein is inserted;
- (d) an HMGB2 protein
- (e) a cell that secretes an HMGB2 protein;
- (f) a vector into which a DNA encoding an HMGB2 protein is inserted;
- 10 (g) an HMGB3 protein;
- (h) a cell that secretes an HMGB3 protein;
- (i) a vector into which a DNA encoding an HMGB3 protein is inserted;
- (j) an S100A8 protein;
- (k) a cell that secretes an S100A8 protein;
- 15 (l) a vector into which a DNA encoding an S100A8 protein is inserted;
- (m) an S100A9 protein;
- (n) a cell that secretes an S100A9 protein;
- (o) a vector into which a DNA encoding an S100A9 protein is inserted;
- (p) a cell or tissue extract; and
- 20 (q) a heparin-binding fraction of a cell or tissue extract;

wherein the agent is administered to a tissue other than a tissue in need of regeneration.

[2] the agent of [1], which is administered parenterally;

[3] the agent of [2], which is administered by injection;

[4] the agent of [1], which is administered intravascularly, intramuscularly, subcutaneously,
25 intradermally, or intraperitoneally;

[5] the agent of any one of [1] to [4], wherein the cell or tissue extract is produced by a method comprising the step of immersing a cell or tissue in a solvent;

[6] the agent of any one of [1] to [4], wherein the heparin-binding fraction of a cell or tissue extract is produced by a method comprising the steps of:

- 30 (a) immersing a cell or tissue in a solvent;
- (b) contacting immobilized heparin with the extract prepared in step (a); and
- (c) eluting a heparin-binding fraction from the immobilized heparin;

[7] the agent of any one of [1] to [6] for use in promoting the regeneration of a nerve, bone, or skin tissue;

35 [8] a kit for promoting tissue regeneration, which comprises a composition comprising any one of:

[21] the use of [18], wherein the agent is administered intravascularly, intramuscularly, subcutaneously, intradermally, or intraperitoneally;

[22] the use of any one of [18] to [21], wherein the agent is an agent for promoting the regeneration of a nerve, bone, or skin tissue;

- 5 [23] a composition for use in a method of promoting tissue regeneration, comprising any one of:
- (a) an HMGB1 protein;
 - (b) a cell that secretes an HMGB1 protein;
 - (c) a vector into which a DNA encoding an HMGB1 protein is inserted;
 - (d) an HMGB2 protein
 - 10 (e) a cell that secretes an HMGB2 protein;
 - (f) a vector into which a DNA encoding an HMGB2 protein is inserted;
 - (g) an HMGB3 protein;
 - (h) a cell that secretes an HMGB3 protein;
 - (i) a vector into which a DNA encoding an HMGB3 protein is inserted;
 - 15 (j) an S100A8 protein;
 - (k) a cell that secretes an S100A8 protein;
 - (l) a vector into which a DNA encoding an S100A8 protein is inserted;
 - (m) an S100A9 protein;
 - (n) a cell that secretes an S100A9 protein;
 - 20 (o) a vector into which a DNA encoding an S100A9 protein is inserted;
 - (p) a cell or tissue extract; and
 - (q) a heparin-binding fraction of a cell or tissue extract;

wherein the composition is administered to a tissue other than a tissue in need of regeneration;

[24] the composition of [23], which is administered parenterally;

- 25 [25] the composition of [24], which is administered by injection;

[26] the composition of [23], which is administered intravascularly, intramuscularly, subcutaneously, intradermally, or intraperitoneally; and

[27] the composition of any one of [23] to [26], wherein the method for promoting tissue regeneration is a method for promoting the regeneration of a nerve, bone, or skin tissue.

In an aspect, there is provided the use of a composition in producing nerve tissue regeneration-promoting agent, wherein the composition comprises any one of:

- (a) an S100A8 protein;
- (b) a cell that secretes an S100A8 protein;
- (c) a vector into which a DNA encoding an S100A8 protein is inserted;
- (d) an S100A9 protein;

- (e) a cell that secretes an S100A9 protein;
 - (f) a vector into which a DNA encoding an S100A9 protein is inserted;
 - (g) a cell or tissue extract, wherein the cell or tissue extract is produced by a method comprising the step of immersing a cell or tissue in a solvent; and
 - (h) a heparin-binding fraction of a cell or tissue extract, wherein the heparin-binding fraction of the cell or tissue extract is produced by a method comprising the steps of:
 - (a) immersing a cell or tissue in a solvent;
 - (b) contacting immobilized heparin with the extract prepared in step (a); and
 - (c) eluting a heparin-binding fraction from the immobilized heparin;
- wherein the cell or tissue to be immersed in a solvent is selected from the group consisting of tissue-derived cells, cells of cell lines established from tissue-derived cells, and cells transfected with DNA encoding S100A8, or S100A9 protein, live skin tissues and tissues obtained by internal biopsy (surgery); and
- wherein the agent is to be administered to a tissue other than a tissue in need of regeneration.

[Effects of the Invention]

Cell growth factors such as HGF, EGF, VEGF, and FGF are known as pharmaceutical agents for regenerating damaged tissues. These are used with an expectation that they will promote cell growth when administered directly to a damaged site and its surrounding tissues.

HMGB1, HMGB2, HMGB3, S100A8, and S100A9 have activity of recruiting bone marrow pluripotent stem cells. Bone marrow pluripotent stem cells can differentiate into

CLAIMS

1. Use of a composition in producing nerve tissue regeneration-promoting agent,
wherein the composition comprises ~~comprising~~ any one of:

- 5 (a) an S100A8 protein;
 - (b) a cell that secretes an S100A8 protein;
 - (c) a vector into which a DNA encoding an S100A8 protein is inserted;
 - (d) an S100A9 protein;
 - (e) a cell that secretes an S100A9 protein;
 - 10 (f) a vector into which a DNA encoding an S100A9 protein is inserted;
 - (g) a cell or tissue extract, wherein the cell or tissue extract is produced by a method comprising the step of immersing a cell or tissue in a solvent; and
 - (h) a heparin-binding fraction of a cell or tissue extract, wherein the heparin-binding fraction of the cell or tissue extract is produced by a method comprising the steps
 - 15 of:
 - (a) immersing a cell or tissue in a solvent;
 - (b) contacting immobilized heparin with the extract prepared in step (a); and
 - (c) eluting a heparin-binding fraction from the immobilized heparin;
- wherein the cell or tissue to be immersed in a solvent is selected from the group
- 20 consisting of tissue-derived cells, cells of cell lines established from tissue-derived cells, and cells transfected with DNA encoding ~~HMGB1, HMGB2, HMGB3,~~ S100A8, or S100A9 protein, live skin tissues and tissues obtained by internal biopsy (surgery);
and
~~in the manufacture of an agent for regenerating tissue,~~ wherein the agent is to be
 - 25 administered to a tissue other than a tissue in need of regeneration.

2. The use of claim 1, wherein the agent is to be administered parenterally.

3. The use of claim 2, wherein the administration is injection.

4. The use of claim 1, wherein the agent is to be administered intravascularly, intramuscularly, subcutaneously, intradermally, or intraperitoneally.

~~5. The use of any one of claims 1 to 4, wherein the agent is an agent for promoting the
 35 regeneration of a nerve, bone, or skin tissue.~~