SUMMARY ~~OF THE INVENTION~~

[0008] The present ~~invention~~disclosure provides a methods of treating a vascular disease comprising administering to a subject a composition comprising hemogenic endothelial cells (HEs) obtained by *in vitro* differentiation of pluripotent stem cells.

[0008a] In one aspect, the present disclosure provides the use of a composition in the manufacture of a medicament for treating a vascular disease in a subject suffering from, or suspected of suffering from, a vascular disease, wherein the composition comprises hemogenic endothelial cells (HEs) obtained by in vitro differentiation of pluripotent stem cells, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; and wherein the HE cells are CD73(+).

[0008b] In another aspect, the present disclosure provides a composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; wherein the HEs are obtained by *in vitro* differentiation of pluripotent stem cells in the absence of TGFβ inhibitors; and wherein the HEs are CD73(+), CD43(-), CD45(-), and CD146 (+).

[0008c] In another aspect, the present disclosure provides a composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; wherein the HEs are obtained by *in vitro* differentiation of pluripotent stem cells in the absence of TGFβ inhibitors; and wherein the HEs express CD144 (VECAD) and CD73.

[0008d] In another aspect, the present disclosure provides a pharmaceutical composition comprising the HEs as disclosed herein.

[0008e] In another aspect, the present disclosure provides a pharmaceutical composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells and a pharmaceutically acceptable carrier, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; wherein the HEs are obtained by *in vitro* differentiation of pluripotent stem cells in the absence of TGFβ inhibitors; and wherein the HEs express CD73, CD144 (VECAD), CD31, and CD309/KDR (FLK-1).

[0009] In an ~~embodiment~~example, the vascular disease is selected from the group consisting of coronary artery diseases (e.g., arteriosclerosis, atherosclerosis, and other diseases or injuries of the arteries, arterioles and capillaries or related complaint), myocardial infarction, (e.g. acute myocardial infarction), organizing myocardial infarct, ischemic heart disease, arrhythmia, left ventricular dilatation, emboli, heart failure, congestive heart failure, subendocardial fibrosis, left or right ventricular hypertrophy, myocarditis, chronic coronary

ischemia, dilated cardiomyopathy, restenosis, arrhythmia, angina, hypertension (e.g. pulmonary hypertension, glomerular hypertension, portal hypertension), myocardial hypertrophy, peripheral arterial disease including critical limb ischemia, cerebrovascular disease, renal artery stenosis, aortic aneurysm, pulmonary heart disease, cardiac dysrhythmias, inflammatory heart disease, congenital heart disease, rheumatic heart disease, diabetic vascular diseases, and endothelial lung injury diseases (e.g., acute lung injury (ALI), acute respiratory distress syndrome (ARDS)). In a specific ~~embodiment~~example, the vascular disease is pulmonary hypertension. In another ~~embodiment~~example, the vascular disease is pulmonary arterial hypertension.

[0010] In an ~~embodiment~~example of any of the methods disclosed herein, the mean pulmonary (artery) pressure is reduced in the subject.

[0011] The present ~~invention~~disclosure also provides a method of increasing blood flow in pulmonary arteries comprising administering to a subject a composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells. In an ~~embodiment~~example, the subject has pulmonary hypertension. In a specific ~~embodiment~~example, the subject has pulmonary arterial hypertension.

[0012] The present ~~invention~~disclosure further provides a method of reducing blood pressure in a subject comprising administering to the subject a composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells. In an ~~embodiment~~example, the subject has pulmonary hypertension. In a specific ~~embodiment~~example, the subject has pulmonary arterial hypertension. In another ~~embodiment~~example, the blood pressure is diastolic pressure. In yet another ~~embodiment~~example, the blood pressure is systolic pressure. In a further ~~embodiment~~example, the blood pressure is mean pulmonary (artery) pressure. Moreover, the blood pressure may be reduced by at least 20% in the subject by any of the methods of the present ~~invention~~disclosure.

[0013] In an ~~embodiment~~example, the pluripotent stem cells disclosed herein are embryonic stem cells. In another ~~embodiment~~example, the pluripotent stem cells disclosed herein are induced pluripotent stem cells.

[0014] In yet another ~~embodiment~~example, the HEs disclosed herein are obtained by culturing the pluripotent stem cells under adherent conditions in a differentiation medium in the absence of methylcellulose. In another ~~embodiment~~example, the HEs disclosed herein are obtained by *in vitro* differentiation of pluripotent stem cells without embryoid body formation.

[0015] In any of the methods provided herein, the subject may be a human. Additionally, the pluripotent stem cells disclosed herein may be human pluripotent stem cells. Furthermore, the HEs disclosed herein may be human HEs.

[0016] The HEs disclosed herein may be positive for at least one microRNA (miRNA) selected from the group consisting of miRNA-126, mi-RNA-24, miRNA-196-b, miRNA-214, miRNA-199a-3p, miRNA-335, hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p. In an ~~embodiment~~example, the HEs are positive for (i) miRNA-214, miRNA-199a-3p, and miRNA-335 and/or (ii) hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p. In another ~~embodiment~~example, the HEs are positive for (i) miRNA-126, miRNA-24, miRNA-196-b, miRNA-214, miRNA-199a-3p, and miRNA-335 and/or (ii) hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p. In an ~~embodiment~~example, the HEs are positive for miRNA-214.

[0017] In any of the ~~embodiment~~examples, the HEs disclosed herein may be negative for at least one miRNA selected from the group consisting of miRNA-367, miRNA-302a, miRNA-302b, miRNA-302c, miRNA-223, and miRNA-142-3p. In an ~~embodiment~~example, the HEs are negative for miRNA-223, and miRNA-142-3p. In another ~~embodiment~~example, the HEs are negative for miRNA-367, miRNA-302a, miRNA-302b, miRNA-302c, miRNA-223, and miRNA-142-3p.

[0018] In an ~~embodiment~~example, the HEs are positive for miRNA-214, miRNA-199a-3p, and miRNA-335, and negative for miRNA-223, and miRNA-142-3p.

[0019] In an ~~embodiment~~example, any of the HEs disclosed herein express at least one cell surface marker selected from the group consisting of CD31/PECAM1, CD309/KDR, CD144, CD34, CXCR4, CD146, Tie2, CD140b, CD90, CD271, and CD105. In an ~~embodiment~~example, the HEs of the ~~invention~~disclosure express CD146, CXCR4, CD309/KDR, CD90, and CD271. In another ~~embodiment~~example, the HEs of the ~~invention~~disclosure express CD146. In an ~~embodiment~~example, the HEs of the ~~invention~~disclosure express CD31/PECAM1, CD309/KDR, CD144, CD34, and CD105.

[0020] In an ~~embodiment~~example, the HEs exhibit limited or no detection of at least one cell surface marker selected from the group consisting of CD34, CXCR7, CD43 and CD45. In another

~~embodiment~~example, the HEs exhibit limited or no detection of CXCR7, CD43, and CD45. In another ~~embodiment~~example, the HEs exhibit limited or no detection of CD43 and CD45.

[0021] In an ~~embodiment~~example, the HEs of the ~~invention~~disclosure are CD43(-), CD45(-), and/or CD146 (+). In another ~~embodiment~~example, HEs express CD31, Calponin (CNN1), and NG2, and therefore have the potential to differentiate into endothelial (CD31+), smooth muscle (Calponin+) and /or pericyte (NG2+) cells.

[0022] In an ~~embodiment~~example, CD144 (VECAD)-expressing HEs are isolated from the HEs of the ~~invention~~disclosures. In an ~~embodiment~~example, the isolated CD144 (VECAD)-expressing HE cells further express CD31 and/or CD309/KDR (FLK-1). In another ~~embodiment~~example, the isolated CD144 (VECAD)-expressing HE cells further express at least one gene listed in Table 22 and Table 23. In another ~~embodiment~~example, the isolated CD144 (VECAD)-expressing HE cells further express at least one cell marker selected from the group consisting of PLVAP, GJA4, ESAM, EGFL7, KDR/VEGFR2, and ESAM. In an ~~embodiment~~example, the isolated CD144 (VECAD)-expressing HE cells further express at least one cell marker selected from the group consisting of SOX9, PDGFRA, and EGFRA. In another ~~embodiment~~example, the isolated CD144 (VECAD)-expressing HE cells further express at least one cell marker selected from the group consisting of KDR/VEGFR2, NOTCH4, collagen I, and collagen IV. In an ~~embodiment~~example, the composition comprising CD144 (VECAD)-expressing HEs isolated from the HEs of the ~~invention~~disclosure substantially lack CD144 (VECAD)-negative HEs.

[0023] Accordingly, the present ~~invention~~disclosure also provides a composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells disclosed herein. The present ~~invention~~disclosure further provides a pharmaceutical composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells disclosed herein and a pharmaceutically acceptable carrier.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] **FIG. 1** is an overview of an exemplary method for producing HEs.

[0025] **FIG. 2** is an overview of an exemplary method for producing hemangioblasts (HBs).

[0026] **FIG. 3** are bar graphs of PDGFRa, HAND1, FOXF1, APLNR, PECAM/CD31 expression in cells over the course the differentiation process from ES cells (day -1). Time points tested were at day -1 (ES cells), day 2 (D2), day 4 (D4), and day 6 (D6).

[0027] **FIG. 4A** shows a graph of CD31, CD43, CD34, KDR, CXCR4, CD144, CD146, and CD105 expression in J1-HE cells (red, left bar) and GMP1-HE cells (blue, right bar) obtained at day 6 of the differentiation process.

CLAIMS

What is claimed is:

1. Use of a composition in the manufacture of a medicament for ~~A method of~~ treating a vascular disease in a subject suffering from, or suspected of suffering from, a vascular disease, ~~comprising administering to the subject~~wherein the~~a~~ composition ~~comprising~~ comprises hemogenic endothelial cells (HEs) obtained by *in vitro* differentiation of pluripotent stem cells, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; and wherein the HE cells are CD73(+).

2. The ~~method~~ use of claim 1, wherein the vascular disease is selected from the group consisting of coronary artery diseases (e.g., arteriosclerosis, atherosclerosis, and other diseases or injuries of the arteries, arterioles and capillaries or related complaint), myocardial infarction, (e.g. acute myocardial infarction), organizing myocardial infarct, ischemic heart disease, arrhythmia, left ventricular dilatation, emboli, heart failure, congestive heart failure, subendocardial fibrosis, left or right ventricular hypertrophy, myocarditis, chronic coronary ischemia, dilated cardiomyopathy, restenosis, arrhythmia, angina, hypertension (eg. pulmonary hypertension, glomerular hypertension, portal hypertension), myocardial hypertrophy, peripheral arterial disease including critical limb ischemia, cerebrovascular disease, renal artery stenosis, aortic aneurysm, pulmonary heart disease, cardiac dysrhythmias, inflammatory heart disease, congenital heart disease, rheumatic heart disease, diabetic vascular diseases, endothelial lung injury diseases (e.g., acute lung injury (ALI), and acute respiratory distress syndrome (ARDS)).

3. The ~~method~~ use of claim 1, wherein the vascular disease is pulmonary hypertension or pulmonary arterial hypertension.

~~4. The method of claim 1, wherein the vascular disease is pulmonary arterial hypertension.~~

~~5~~4. The ~~method~~ use of any one of claims 1-~~4~~3, wherein the mean pulmonary (artery) pressure is reduced in the subject.

~~6~~5. Use of a composition in the manufacture of a medicament for ~~A method of~~ increasing blood flow in pulmonary arteries in a subject suffering from, or suspected of suffering from, a vascular disease, wherein the ~~comprising administering to the subject a~~ composition ~~comprising~~ comprises HEs obtained by *in vitro* differentiation of pluripotent stem cells, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; and wherein the HE cells are CD73(+).

~~7~~6. The ~~method~~ use of claim ~~6~~5, wherein the subject has pulmonary hypertension or pulmonary arterial hypertension.

~~8. The method of claim 6, wherein the subject has pulmonary arterial hypertension.~~

~~9~~7. Use of a composition in the manufacture of a medicament for ~~A method of~~ reducing blood pressure in a subject suffering from, or suspected of suffering from, a vascular disease, wherein the ~~comprising administering to the subject a~~ composition ~~comprising~~ comprises HEs obtained by *in vitro* differentiation of pluripotent stem cells, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; and wherein the HE cells are CD73(+).

~~10~~8. The ~~method~~ use of claim ~~9~~7, wherein the subject has pulmonary hypertension or pulmonary arterial hypertension.

~~11. The method of claim 9, wherein the subject has pulmonary arterial hypertension.~~

~~9~~12. The ~~method~~ use of claim ~~9~~7, wherein the blood pressure is diastolic pressure, systolic pressure, and/or mean pulmonary (artery) pressure.

~~13. The method of claim 9, wherein the blood pressure is systolic pressure.~~

~~14. The method of claim 9, wherein the blood pressure is mean pulmonary (artery) pressure.~~

~~15~~10. The ~~method~~ use of any one of claims ~~9-14~~7-9, wherein the blood pressure is reduced by at least 20% in the subject.

~~16~~11. The ~~method~~ use of any one of claims 1-~~15~~10, wherein

(a) the HEs are positive for at least one microRNA (miRNA) selected from the group consisting of miRNA-126, miRNA-24, miRNA-196-b, miRNA-214, miRNA-199a-3p, miRNA-335, hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p;~~.~~

(b) ~~17. The method of claim 16, wherein~~ the HEs are positive for (i) miRNA-214, miRNA-199a-3p, and miRNA-335 and/or (ii) hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p;~~.~~

(c) ~~18. The method of claim 16, wherein~~ the HEs are positive for (i) miRNA-126, miRNA-24, miRNA-196-b, miRNA-214, miRNA-199a-3p, and miRNA-335 and/or (ii) hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p;~~.~~

(d) ~~19. The method of claim 16, wherein~~ the HEs are positive for miRNA-214;~~.~~

(e) ~~20. The method of any one of claims 1-19, wherein~~ the HEs are negative for at least one miRNA selected from the group consisting of miRNA-367, miRNA-302a, miRNA-302b, miRNA-302c, miRNA-223, and miRNA-142-3p;~~.~~

(f) ~~21. The method of claim 20, wherein~~ the HEs are negative for miRNA-223, and miRNA-142-3p;~~.~~

(g) ~~22. The method of claim 20, wherein~~ the HEs are negative for miRNA-367, miRNA-302a, miRNA-302b, miRNA-302c, miRNA-223, and miRNA-142-3p;~~.~~

(h) ~~23. The method of any one of claims 1-22, wherein~~ the HEs further express at least one cell surface marker selected from the group consisting of CD24, CD31/PECAM1, CD309/KDR, CD144, CD34, CXCR4, CD146, Tie2, CD140b, CD90, CD271, and CD105;~~.~~

(i) ~~24. The method of claim 23, wherein~~ the HEs express CD146, CXCR4, CD309/KDR, CD90, and CD271;~~.~~

(j)~~25. The method of claim 23, wherein~~ the HEs express CD146;~~.~~

(k) ~~26. The method of claim 23, wherein~~ the HEs express CD144 (VECAD);~~.~~

(l)~~27. The method of claim 26, wherein~~ the HEs further express at least one cell marker selected from the group consisting of CD24, CD31, CD309/KDR (FLK-1), PLVAP, GJA4, EGFL7, KDR/VEGFR2, and ESAM;~~.~~

(m) ~~28. The method of claim 26 or 27, wherein~~ the HEs further express at least one cell marker selected from the group consisting of SOX9, PDGFRA, and EGFRA;~~.~~

(n) ~~29. The method of any one of claims 26-28, wherein~~ the HEs further express at least one cell marker selected from the group consisting of KDR/VEGFR2, NOTCH4, collagen I, and collagen IV;~~.~~

(o) ~~30. The method of claim 23, wherein~~ the HEs express CD31/PECAM1, CD309/KDR, CD144, CD34, and CD105;~~.~~

(p) ~~31. The method of any one of claims 1-29, wherein~~ the HEs exhibit limited or no detection of at least one cell surface marker selected from the group consisting of CD34, CXCR7, CD43 and CD45;~~.~~

(q) ~~32. The method of any one of claims 1-31, wherein~~ the HEs exhibit limited or no detection of CXCR7, CD43, and CD45;~~.~~

(r) ~~33. The method of any one of claims 1-31, wherein~~ the HEs exhibit limited or no detection of CD43 and CD45;~~.~~

(s) ~~34. The method of any one of claims 1-33, wherein~~ the HEs are CD73(+), CD43(-), CD45(-), and CD146 (+);

(t) the HEs express (i) CD144 (VECAD) and (ii) CD73 and (iii) CD31 and/or CD309/KDR (FLK-1);

(u) the HEs express at least one gene listed in Table 22 and Table 23; and/or

(v) the HE further express CD24.

3512. The ~~method~~ use of any one of claims 1-3411, wherein the HEs are obtained (i) by culturing the pluripotent stem cells under adherent conditions in a differentiation medium in the absence of methylcellulose; and/or (ii) by in vitro differentiation of pluripotent stem cells without embryoid body formation.

~~36. The method of any one of claims 1-35, wherein the HEs are obtained by *in vitro* differentiation of pluripotent stem cells without embryoid body formation.~~

3713. The ~~method~~ use of any one of claims 1-3612, wherein the subject is a human.

~~38. The method of any one of claims 1-37, wherein the pluripotent stem cells are human pluripotent stem cells.~~

~~39. The method of any one of claims 1-38, wherein the HEs are human HEs.~~

4014. A composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; wherein the HEs are obtained by *in vitro* differentiation of pluripotent stem cells in the absence of TGFβ inhibitors; and wherein the HEs are CD73(+), CD43(-), CD45(-), and CD146 (+).

4115. The composition of claim 4014, wherein
(a) the HEs are positive for at least one microRNA (miRNA) selected from the group consisting of miRNA-126, mi-RNA-24, miRNA-196-b, miRNA-214, miRNA-199a-3p, miRNA-335, hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p;~~.~~

(b) ~~42. The composition of claim 41, wherein~~ the HEs are positive for (i) miRNA-214, miRNA-199a-3p, and miRNA-335 and/or (ii) hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p;~~.~~

(c) ~~43. The composition of claim 41, wherein~~ the HEs are positive for (i) miRNA-126, mi-RNA-24, miRNA-196-b, miRNA-214, miRNA-199a-3p, and miRNA-335 and/or (ii) hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p;~~.~~

(d) ~~44. The composition of claim 41, wherein~~ the HEs are positive for miRNA-214;~~.~~

(e) ~~45. The composition of any one of claims 40-44, wherein~~ the HEs are negative for at least one miRNA selected from the group consisting of miRNA-367, miRNA-302a, miRNA-302b, miRNA-302c, miRNA-223, and miRNA-142-3p;~~.~~

(f) ~~46. The composition of claim 45, wherein~~ the HEs are negative for miRNA-223, and miRNA-142-3p;~~.~~ and/or

(g) ~~47. The composition of claim 45, wherein~~ the HEs are negative for miRNA-367, miRNA-302a, miRNA-302b, miRNA-302c, miRNA-223, and miRNA-142-3p.

~~48~~16. A composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; wherein the HEs are obtained by *in vitro* differentiation of pluripotent stem cells in the absence of TGFβ inhibitors; and wherein the HEs express CD144 (VECAD) and CD73.

~~49~~17. The composition of claim ~~48~~16, wherein

(a) the HEs further express at least one cell marker selected from the group consisting of CD24, CD31, CD309/KDR (FLK-1), PLVAP, GJA4, EGFL7, KDR/VEGFR2, and ESAM~~.~~;

(b) ~~50. The composition of claim 48 or 49, wherein~~ the HEs further express at least one cell marker selected from the group consisting of SOX9, PDGFRA, and EGFRA~~.~~;

(c) ~~51. The composition of any one of claims 48-50, wherein~~ the HEs further express at least one cell marker selected from the group consisting of KDR/VEGFR2, NOTCH4, collagen I, and collagen IV;~~.~~ and/or

(d) ~~52. The composition of any one of claims 48-51, wherein~~ the composition substantially lacks CD73-negative and CD144 (VECAD)-negative HE cells; and/or

(e) the HEs express (i) CD144 (VECAD) and (ii) CD73 and (iii) CD31 and/or CD309/KDR (FLK-1);

(f) the HEs express at least one gene listed in Table 22 and Table 23; and/or

(g) the HE further express CD24.

~~53~~18. A pharmaceutical composition comprising the HEs of any one of claims 14-17~~obtained by *in vitro* differentiation of pluripotent stem cells and a pharmaceutically acceptable carrier, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; wherein the HEs are obtained by *in vitro* differentiation of pluripotent stem cells in the absence of TGFβ inhibitors; and wherein the HEs are CD73(+), CD43(-), CD45(-), and CD146 (+)~~.

~~54. The pharmaceutical composition of claim 53, wherein the HEs are positive for at least one microRNA (miRNA) selected from the group consisting of miRNA-126, mi-RNA-24, miRNA-196-b, miRNA-214, miRNA-199a-3p, miRNA-335, hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p.~~

~~55. The pharmaceutical composition of claim 54, wherein the HEs are positive for (i) miRNA-214, miRNA-199a-3p, and miRNA-335 and/or (ii) hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p.~~

~~56. The pharmaceutical composition of claim 54, wherein the HEs are positive for (i) miRNA-126, mi-RNA-24, miRNA-196-b, miRNA-214, miRNA-199a-3p, and miRNA-335 and/or (ii) hsa-miR-11399, hsa-miR-196b-3p, hsa-miR-5690, and hsa-miR-7151-3p.~~

~~57. The pharmaceutical composition of claim 54, wherein the HEs are positive for miRNA-214.~~

~~58. The pharmaceutical composition of any one of claims 54-57, wherein the HEs are negative for at least one miRNA selected from the group consisting of miRNA-367, miRNA-302a, miRNA-302b, miRNA-302c, miRNA-223, and miRNA-142-3p.~~

~~59. The pharmaceutical composition of claim 58, wherein the HEs are negative for miRNA-223, and miRNA-142-3p.~~

~~60. The pharmaceutical composition of claim 58, wherein the HEs are negative for miRNA-367, miRNA-302a, miRNA-302b, miRNA-302c, miRNA-223, and miRNA-142-3p.~~

~~61~~19. A pharmaceutical composition comprising HEs obtained by *in vitro* differentiation of pluripotent stem cells and a pharmaceutically acceptable carrier, wherein the pluripotent stem cells comprise embryonic stem cells and/or induced pluripotent stem cells; wherein the HEs are obtained by *in vitro* differentiation of pluripotent stem cells in the absence of TGFβ inhibitors; and wherein the HEs express CD73, CD144 (VECAD), CD31, and CD309/KDR (FLK-1).

~~62~~20. The pharmaceutical composition of claim ~~61~~19, wherein
(a) the HEs further express at least one cell marker selected from the group consisting of CD24, CD31, CD309/KDR (FLK-1), PLVAP, GJA4, EGFL7, KDR/VEGFR2, and ESAM;~~.~~

(b) ~~63. The pharmaceutical composition of claim 61 or 62, wherein~~ the HEs further express at least one cell marker selected from the group consisting of SOX9, PDGFRA, and EGFRA;~~.~~

(c) ~~64. The pharmaceutical composition of any one of claims 61-63, wherein~~ the HEs further express at least one cell marker selected from the group consisting of KDR/VEGFR2, NOTCH4, collagen I, and collagen IV;~~.~~

(d) ~~65. The pharmaceutical composition of any one of claims 61-64, wherein~~ the composition substantially lacks CD73-negative and CD144 (VECAD)-negative HE cells;

(e) the HEs express (i) CD144 (VECAD) and (ii) CD73 and (iii) CD31 and/or CD309/KDR (FLK-1);

(f) the HEs further express at least one gene listed in Table 22 and Table 23; and/or

(g) the HEs further express CD24.

~~66. The method of any one of claims 26-39, wherein the HEs express (i) CD144 (VECAD) and (ii) CD73 and (iii) CD31 and/or CD309/KDR (FLK-1).~~

~~67. The method of any one of claims 26-49 or 66, wherein the HEs further express at least one gene listed in Table 22 and Table 23.~~

~~68. The composition of any one of claims 48-51, wherein the HEs express (i) CD144 (VECAD) and (ii) CD73 and (iii) CD31 and/or CD309/KDR (FLK-1).~~

~~69. The composition of any one of claims 48-41 or 68, wherein the HEs further express at least one gene listed in Table 22 and Table 23.~~

~~70. The pharmaceutical composition of any one of claims 61-65, wherein the HEs express (i) CD144 (VECAD) and (ii) CD73 and (iii) CD31 and/or CD309/KDR (FLK-1).~~

~~71. The pharmaceutical composition of any one of claims 61-65 or 70, wherein the HEs further express at least one gene listed in Table 22 and Table 23.~~

~~72~~21. The ~~method~~ use of any one of claims 1-~~36~~12, wherein the HEs are obtained by *in vitro* differentiation of pluripotent stem cells in the absence of TGFβ inhibitors.

~~73. The method of claim 67, wherein the HEs further express CD24.~~

~~74. The composition of claim 69, wherein the HEs further express CD24.~~

~~75. The pharmaceutical composition of claim 71, wherein the HEs further express CD24.~~