CLAIMS

What is claimed is:

1. A method for constructing a stem cell-derived embryo model, the method comprising:

culturing naïve stem cells *in vitro*, or injecting the naïve stem cells into an immunodeficient animal for *in vivo* differentiation, to obtain the stem cell-derived embryo model.

2. The method according to claim 1, wherein said culturing naïve stem cells *in vitro* comprises:

performing a first culture treatment on the naïve stem cells in a first culture medium and a second culture medium to obtain a first cell population;

performing a second culture treatment on the first cell population in a third culture medium to obtain a second cell population; and

performing a third culture treatment on the second cell population in a fourth culture medium and a fifth culture medium to obtain the stem cell-derived embryo model.

3. The method according to claim 2, wherein the naïve stem cells are subjected to a pre-culture treatment in advance, and coverage of the naïve stem cells subsequent to the pre-culture treatment ranges from 70% to 80% in a culture dish;

optionally, a digestion treatment is performed on the naïve stem cells subsequent to the pre-culture treatment; and

optionally, the digestion treatment is performed in the presence of TrypLE™ Express enzyme.

4. The method according to claim 2, wherein the first culture medium comprises a human primed pluripotent stem cell culture medium, penicillin-streptomycin, and a Rock pathway inhibitor;

optionally, the second culture medium comprises a human primed pluripotent stem cell culture medium and penicillin-streptomycin;

optionally, a mass-volume fraction of the penicillin-streptomycin in the first culture medium or the second culture medium ranges from 0.5% to 1.5%;

optionally, the Rock pathway inhibitor comprises Y27632;

optionally, a final concentration of Y27632 in the first culture medium ranges from 45 μM to 55 μM;

optionally, the first culture treatment is performed in a low-adhesion 96-well round-bottom plate, a 3D scaffold, or a microfluidic device;

optionally, the first culture treatment lasts for 5 days to 7 days, preferably 5 days;

optionally, the first culture treatment comprises a first-stage culture treatment in the first culture medium and a second-stage culture treatment in the second culture medium;

optionally, the first-stage culture treatment lasts for 3 days, and optionally, the first-stage culture treatment comprises: culturing the naïve stem cells in the first culture medium for 1 day, replacing the first culture medium, and further culturing the naïve stem cells in the first culture medium for 2 days; and

optionally, the second-stage culture treatment lasts for 2 days to 4 days, and preferably 2 days.

5. The method according to claim 2, wherein the third culture medium comprises a DMEM-F12 basal medium, an N2 supplement, glutamine, non-essential amino acids, heparin, and penicillin-streptomycin;

optionally, a mass-volume fraction of the N2 supplement in the third culture medium ranges from 0.5% to 1.5%;

optionally, a mass-volume fraction of the glutamine in the third culture medium ranges from 0.5% to 1.5%;

optionally, a mass-volume fraction of the non-essential amino acids in the third culture medium ranges from 0.5% to 1.5%;

optionally, a final concentration of the heparin in the third culture medium ranges from 0.5 μg/mL to 1.5 μg/mL;

optionally, a mass-volume fraction of the penicillin-streptomycin in the third culture medium ranges from 0.5% to 1.5%; and

optionally, the second culture treatment lasts for 3 days to 5 days.

6. The method according to claim 2, wherein, prior to the third culture treatment, the second cell population is mixed with a matrix gel.

7. The method according to any one of claims 2 to 6, wherein the fourth culture medium comprises a DMEM-F12 basal medium, a neural basal medium, an N2 supplement, glutamine, non-essential amino acids, insulin, β-mercaptoethanol, penicillin-streptomycin, and a vitamin A-free B27 supplement;

optionally, the fifth culture medium comprises a DMEM-F12 basal medium, a neural basal medium, an N2 supplement, glutamine, non-essential amino acids, insulin, β-mercaptoethanol, penicillin-streptomycin, and a vitamin A-containing B27 supplement;

optionally, a volume ratio of the DMEM-F12 basal medium to the neural basal medium ranges from 1: (0.8 to 1.2);

optionally, a mass-volume fraction of the N2 supplement in the fourth culture medium or the fifth culture medium ranges from 0.2% to 0.7%;

optionally, a mass-volume fraction of the glutamine in the fourth culture medium or the fifth culture medium ranges from 0.5% to 1.5%;

optionally, a mass-volume fraction of the non-essential amino acids in the fourth culture medium or the fifth culture medium ranges from 0.2% to 0.7%;

optionally, a final concentration of the insulin in the fourth culture medium or the fifth culture medium ranges from 1 μg/mL to 1.5 μg/mL;

optionally, a final concentration of the β-mercaptoethanol in the fourth culture medium or the fifth culture medium ranges from 0.1 μM to 0.25 μM;

optionally, a mass-volume fraction of the penicillin-streptomycin in the fourth culture medium or the fifth culture medium ranges from 0.5% to 1.5%;

optionally, a mass-volume fraction of the vitamin A-free B27 supplement in the fourth culture medium ranges from 0.2% to 0.7%;

optionally, a mass-volume fraction of the vitamin A-containing B27 supplement in the fifth culture medium ranges from 0.2% to 0.7%;

optionally, the third culture treatment comprises a third-stage culture treatment in the fourth culture medium and a fourth-stage culture treatment in the fifth culture medium;

optionally, the third-stage culture treatment lasts for 3 days to 5 days, and preferably 4 days;

optionally, the fourth-stage culture treatment lasts for 13 days to 18 days, and preferably

16 days;

optionally, the fourth-stage culture treatment is performed on a shaker; and

optionally, a rotational speed of the shaker ranges from 60 RPM to 80 RPM.

8. The method according to claim 1, wherein, prior to said injecting the naïve stem cells into an immunodeficient animal for differentiation, the naïve stem cells are mixed with a DMEM-F12 basal medium containing a matrix gel;

optionally, a volume ratio of the DMEM-F12 basal medium to the matrix gel ranges from 1: (0.8 to 1.2); and

optionally, a ratio of the number of the naïve stem cells to a volume of the DMEM-F12 basal medium containing the matrix gel ranges from 5^4 cells: (0.8 to 1.2) μL.

9. The method according to claim 1 or 8, wherein the immunodeficient animal is selected from an immunodeficient mouse, an immunodeficient rabbit, an immunodeficient cow, an immunodeficient pig, or an immunodeficient monkey;

optionally, the naïve stem cells are selected from at least one of pluripotent stem cells, totipotent stem cells, primitive endoderm cells, or trophectoderm cells;

optionally, a source of the naïve stem cells is selected from human, cow, monkey, pig, or mouse;

optionally, said injecting is performed subcutaneously; and

optionally, the *in vivo* differentiation lasts for 13 days to 70 days.

10. A stem cell-derived embryo model, comprising an extraembryonic tissue and an intraembryonic tissue,

optionally the extraembryonic tissue comprises: visceral endoderm, anterior visceral endoderm, yolk sac endoderm, extraembryonic mesoderm, mesothelial cells, allantois cells, mesoderm progenitor cells of hematopoietic precursor cells from extraembryonic mesoderm, hemangioblasts from extraembryonic mesoderm, endothelial cells from extraembryonic mesoderm, arterial endothelial cells from extraembryonic mesoderm, hematopoietic precursor cells from extraembryonic mesoderm, megakaryocytes from extraembryonic mesoderm, erythrocytes from extraembryonic mesoderm, myeloid precursor cells from extraembryonic mesoderm, amniotic ectoderm cells, and amniotic/non-neural ectoderm progenitor cells;

optionally, the intraembryonic tissue comprises epiblast, committed epiblast, primordial

germ cell-like cells, definitive endoderm, primitive streak, emergent mesoderm, advanced mesoderm, neuroepithelium, and neural crest-derived cells.

11. The stem cell-derived embryo model according to claim 10, wherein genes expressed in the visceral endoderm comprise *HNF4A* and *SOX17*; genes expressed in the anterior visceral endoderm comprise *OTX2* and *CXCR4*; genes expressed in the yolk sac endoderm comprise *HNF4A*, and the yolk sac endoderm exhibits low or no expression of *SOX17*; genes expressed in the extraembryonic mesoderm cells comprise *ANXA1*, *LUM*, *NID2*, and *FRZB*; genes expressed in the mesothelial cells comprise *AQP1*; genes expressed in the allantois cells comprise *TBX4* and *HOXA13*; genes expressed in the mesoderm progenitor cells of hematopoietic precursor cells from the extraembryonic mesoderm comprise *BMP4* and *WNT5A*; genes expressed in the hemangioblasts from the extraembryonic mesoderm comprise *ETV2*, *TAL1*, *BMP4*, and *WNT5A*; genes expressed in the endothelial cells from the extraembryonic mesoderm comprise *CDH5* and *CD34*; genes expressed in the arterial endothelial cells from the extraembryonic mesoderm comprise *GJA4* and *GJA5*; genes expressed in the hematopoietic precursor cells from the extraembryonic mesoderm comprise *RUNX1* and *SPN*; genes expressed in the megakaryocytes from the extraembryonic mesoderm comprise *PPBP*; genes expressed in the erythrocytes from the extraembryonic mesoderm comprise *GATA1* and *HBE1*; genes expressed in the myeloid precursor cells from the extraembryonic mesoderm comprise *CSF1R*; genes expressed in the amniotic ectoderm cells comprise *ISL1* and *GABRP*; genes expressed in the amniotic/non-neural ectoderm progenitor cells comprise *CLDN10*, *AMR2*, *PCAT14*, and *VGLL1*; genes expressed in the epiblast comprise *POU5F1* and *DPPA4*; genes expressed in the committed epiblast comprise *TNFRSF12A* and *JUND*; genes expressed in the primordial germ cell-like cells comprise *NANOG*, *NANOS3*, *TFAP2C*, and *SOX17*; genes expressed in the definitive endoderm comprise *HHEX*; genes expressed in the primitive streak comprise *TBXT*; genes expressed in the emergent mesoderm comprise *LHX1*; genes expressed in the advanced mesoderm comprise *MYL7*, and the advanced mesoderm exhibits low or no expression of *TBXT*; genes expressed in the neuroepithelium comprise *PAX6*; and genes expressed in the neural crest-derived cells comprise *SOX10* and *MPZ*;

optionally, the definitive endoderm, the visceral endoderm, the anterior visceral endoderm, and the yolk sac endoderm co-express *FOXA2*.

12. The stem cell-derived embryo model according to claim 10, wherein a proportion of respective cell types in the extraembryonic tissue is: the visceral endoderm 0.46% to 11.57%, the anterior visceral endoderm 0.14% to 33.17%, the yolk sac endoderm 1.19% to 4.24%, the extraembryonic mesoderm 0.33% to 32.35%, the mesothelial cells 4.22% to 4.33%, the allantois cells 0.14% to 4.26%, the mesoderm progenitor cells of hematopoietic precursor cells from extraembryonic mesoderm 0.1% to 0.5%, the hemangioblasts 0.1% to 0.5%, the endothelial cells 1.40% to 4.79%, the arterial endothelial cells 0.04% to 0.1%, the hematopoietic precursor cells 0.01% to 0.1%, the megakaryocytes 0.01% to 0.1%, the erythrocytes 0.1% to 0.5%, the myeloid precursor cells 0.01% to 0.1%, the amniotic ectoderm cells 0.21% to 10.23%, and the amniotic/non-neural ectoderm progenitor cells 0.09% to 3.00%;

optionally, a proportion of respective major cell types in the intraembryonic tissue is: the epiblast 2.18% to 33.61%, the committed epiblast 2.57% to 2.86%, the primordial germ cell-like cells 0.02% to 0.19%, the definitive endoderm 0.48% to 1.63%, the primitive streak 0.31% to 0.90%, the emergent mesoderm 0.15% to 1.83%, the advanced mesoderm 1.61% to 12.81%, the neuroepithelium 0.18% to 3.13%, and the neural crest-derived cells 0.18% to 2.84%,

optionally, the proportions of respective cell types in the extraembryonic tissue and the intraembryonic tissue are as represented in FIG. 5,

optionally, the stem cell-derived embryo model is capable of simulating cell types during a gastrulation stage.

13. A method for producing specific lineage progenitor cells, the method comprising:

culturing and expanding a specific lineage in the stem cell-derived embryo model according to any one of claims 10 to 12 to obtain the specific lineage progenitor cells,

optionally, further comprising performing gene editing or cell differentiation on the specific lineage subjected to said culturing and expanding, or using the specific lineage subjected to said culturing and expanding for cell therapy.

14. A method for constructing a specific organoid model or a cellular 3D aggregate, the method comprising:

inducing the stem cell-derived embryo model according to any one of claims 10 to 12 into the specific organoid model or the cellular 3D aggregate using induction means,

optionally, the induction means comprises addition of a small molecule compound, co-

culture with cells, or addition of a cytokine.

15. A method for screening a drug for intervening in embryonic development during a gastrulation stage, the method comprising:

adding a candidate drug to a culture process of the method for constructing the stem cell-derived embryo model according to any one of claims 1 to 9, or bringing a candidate drug into contact with the stem cell-derived embryo model according to any one of claims 10 to 12; and

determining, when the stem cell-derived embryo model obtained by the method according to any one of claims 1 to 9 or the stem cell-derived embryo model according to any one of claims 10 to 12 undergoes an expected change, the candidate drug as a target drug,

optionally, wherein an indicator that the candidate drug is the target drug is that the stem cell-derived embryo model obtained by the method according to any one of claims 1 to 9 undergoes the expected change subsequent to said adding the candidate drug, as compared with prior to said adding the candidate drug, or

wherein an indicator that the candidate drug is the target drug is that the stem cell-derived embryo model according to any one of claims 10 to 12 undergoes the expected change subsequent to the contact, as compared with prior to the contact.