Claims:

1. A heart organoid of at least 60% cardiac cells irrespective of optional additional cells of a vascular system of the organoid, or comprising at least 50% cardiac cells; wherein the cardiac cells surround an inner cavity, wherein the cardiac cells are selected from the group of cardiomyocytes, endocardial cells and epicardial cells, and wherein the heart organoid comprises cardiomyocytes or endocardial cells that directly face the inner cavity.

2. The heart organoid of claim 1 comprising at least 30% cardiomyocytes, preferably further comprising at least 2% endocardial cells.

3. The heart organoid of claim 1 or 2 comprising cardiomyocytes and endocardial cells in different tissue layers.

4. The heart organoid of any one of claims 1 to 3 comprising at most 5%, preferably at most 3%, or no foregut endodermal cells and/or at most 3% or no hemogenic cells.

5. The heart organoid of any one of claims 1 to 4 comprising epicardium smooth muscle cells and/or epicardium cardiac fibroblasts; and/or comprising at most 3% or no non-epicardium-derived smooth muscle cells and/or at most 3% or no non-epicardium-derived fibroblasts.

6. The heart organoid of any one of claims 1 to 5 having a size in its largest dimension of 0.3 mm to 15 mm; and/or wherein the size of the inner cavity at its largest dimension is at least 30% of the size of the heart organoid at its largest dimension.

7. A method of generating a heart organoid comprising the steps of
a) providing pluripotent stem cells,
b) inducing mesoderm differentiation in the presence of a WNT activator and/or GSK3-beta inhibitor, and further in the presence of a PI3 kinase inhibitor, in a 3D culture in a low attachment culture, wherein the cells bind to each other instead of a

culturing vessel to form aggregates of the cells, thereby producing an aggregate of mesoderm cells, or
inducing mesoderm differentiation in the presence of a WNT activator and/or GSK3-beta inhibitor, wherein the WNT activator and/or GSK3-beta inhibitor and/or an optional PI3 kinase inhibitor are in an amount sufficient to differentiate the pluripotent stem cells to exit pluripotency in an amount at least 90% of the pluripotent stem cells within 40 hours of starting induction, thereby producing an aggregate of mesoderm cells, wherein the cells are treated with fibroblast growth factor and/or albumin,
c) differentiating the mesoderm cells of step b) into cardiac cells in a 3D culture in a low attachment culture, wherein the cells aggregate with each other instead of binding to a culturing vessel to form aggregates of the cells, in the presence of cardiac differentiation factors and in the absence of a WNT activator and/or in the presence of a WNT antagonist, for at least 3 days, preferably for 3-7 days, for cardiac mesoderm formation and formation of an inner cavity.

8. The method of claim 7, wherein the WNT activator in step b) is a WNT ligand, such as WNT-3a, or CHIR99021; preferably wherein
in case the WNT activator is in an amount sufficient to differentiate the pluripotent stem cells to exit pluripotency in an amount at least 90% of the pluripotent stem cells within 40 hours of starting induction then the amount of CHIR99021 as WNT activator is in a concentration of at least 1µM, preferably at least 6µM, or at least 12µM;
in case the PI3 kinase inhibitor is present then CHIR99021 as WNT activator is in a concentration of at least, 0.5 µM, preferably 0.5 µM to 12µM µM.

9. The method of 7 or 8, wherein the pluripotent stem cells are induced pluripotent stem cells or cells from a cell line and/or wherein the provided pluripotent stem cells of step a) have been passaged, preferably in a medium comprising albumin and/or a fibroblast growth factor, and preferably further comprising BMP and/or Insulin; and/or wherein the provided pluripotent stem cells of step a) have been grown in a medium comprising at least 1.5% (w/v), albumin, preferably BSA, and/or at least 100 ng/ml

fibroblast growth factor, preferably FGF2, more preferred further comprising BMP and/or Insulin.

10. The method of any one of claims 7 to 9, wherein mesoderm differentiation is induced in a medium comprising activin A and/or bone morphogenetic protein, preferably further fibroblast growth factor, preferably wherein mesoderm differentiation is induced in a medium comprising at least 1 ng/ml bone morphogenetic protein, preferably BMP4.

11. The method of any one of claims 7 to 10, further comprising d) further differentiating the aggregate with cardiac mesoderm into a tissue with a cardiomyocyte layer with cardiac differentiation factors for a further one day or more.

12. A kit for performing a method of any one of claims 7 to 11 comprising i) WNT activator and/or GSK3-beta inhibitor, ii) a PI3 kinase inhibitor, iii) a low-attachment cell culturing vessel, iv) albumin, preferably further comprising a WNT inhibitor.

13. A vessel plate comprising at least 10 compartments, wherein in each compartment a organoid according to any one of claims 1 to 6 is present at substantially the same stage of development.

14. The method of any one of claims 7 to 11 for screening or testing a candidate compound on its effects on heart development or functionality comprising generating a heart organoid according to any one of claim 7 to 11 while treating the cells with the candidate compound and comparing development or functionality of the heart organoid with development of a heart organoid that was not treated with the candidate compound.

15. The method of observing the effects of suppressed or overexpressed genes during on heart development comprising generating a heart organoid according to any one of claim 7 to 11 wherein the cells have a supressed candidate gene or overexpress a candidate gene and comparing development of the heart organoid with development of a heart organoid that was not generated with a supressed or overexpressed gene.