Claims

1. An isolated population of cells, wherein greater than 85% of the cells in the population express markers characteristic of the definitive endoderm lineage, wherein the population of cells is obtained by differentiating pluripotent stem cells in medium lacking serum and supplemented with BSA and a factor selected from the group consisting of insulin and IGF-1.

2. The isolated population of claim 1, wherein the medium is supplemented with insulin.

3. The isolated population of claim 1 or claim 2, wherein the medium is supplemented with about 1 ng/ml to about 100 ng/ml of insulin.

4. The isolated population of claim 1, wherein the medium is supplemented with is IGF-1.

5. The isolated population of claim 1 or claim 4, wherein the medium is supplemented with from about 1 ng/ml to about 50 ng/ml of IGF-1.

6. The isolated population of any one of claims 1 to 5, wherein the cells expressing markers characteristic of the definitive endoderm lineage are definitive endoderm cells.

7. The isolated population of any of claims 1 to 6, wherein the medium is further supplemented with activin A and a Wnt ligand.

8. The isolated population of any of claims 1 to 6, wherein the medium is further supplemented with GDF-8 and at least one other factor is selected from the group consisting of: an aniline-pyridinotriazine, a cyclic aniline-pyridinotriazine, N-{[1-(Phenylmethyl)azepan-4-yl]methyl}-2-pyridin-3-ylacetamide, 4-{[4-(4-{[2-(Pyridin-2-ylamino)ethyl]amino}-1,3,5-triazin-2-yl)pyridin-2-yl]oxy}butan-1-ol, 3-({3-[4-({2-[Methyl(pyridin-2-yl)amino]ethyl}amino)-1,3,5-triazin-2-yl]pyridin-2-yl}amino)propan-1-ol, N~4~-[2-(3-Fluorophenyl)ethyl]-N~2~-[3-(4-methylpiperazin-1-yl)propyl]pyrido[2,3-d]pyrimidine-2,4-diamine, 1-Methyl-N-[(4-pyridin-3-yl-2-{[3-(trifluoromethyl)phenyl]amino}-1,3-thiazol-5-yl)methyl]piperidine-4-carboxamide, 1,1-Dimethylethyl {2-[4-({5-[3-(3-hydroxypropyl)phenyl]-4H-1,2,4-triazol-3-yl}amino)phenyl]ethyl}carbamate, 1,1-Dimethylethyl {[3-({5-[5-(3-hydroxypropyl)-2-(methyloxy)phenyl]-1,3-oxazol-2-yl}amino)phenyl]methyl}carbamate, 1-({5-[6-({4-[(4-Methylpiperazin-1-yl)sulfonyl]phenyl}amino)pyrazin-2-yl]thiophen-2-

yl}methyl)piperidin-4-ol, 1-({4-[6-({4-[(4-Methylpiperazin-1-yl)sulfonyl]phenyl}amino)pyrazin-2-yl]thiophen-2-yl}methyl)piperidine-4-carboxamide, and 2-{[4-(1-Methylethyl)phenyl]amino}-N-(2-thiophen-2-ylethyl)-7,8-dihydropyrido[4,3-d]pyrimidine-6(5H)-carboxamide.

9. The isolated population of any of claims 1 to 6, wherein the medium is further supplemented with GDF-8 and 14-Prop-2-en-1-yl-3,5,7,14,17,23,27-heptaazatetracyclo[19.3.1.1~2,6~.1~8,12~]heptacosa-1(25),2(27),3,5,8(26),9,11,21,23-nonaen-16-one.

10. A method for generating a population of cells wherein greater than 85% of the cells in the population express markers characteristic of the definitive endoderm lineage, comprising the steps of:

a. culturing a population of pluripotent stem cells,

b. differentiating the population of pluripotent stem cells to a population of cells wherein greater than 85% of the cells in the population express markers characteristic of the definitive endoderm lineage in medium lacking serum and supplemented with BSA and a factor selected from the group consisting of insulin and IGF-1.

11. The method of claim 10, wherein the population of pluripotent stem cells is differentiated in the medium lacking serum and supplemented with BSA and a factor selected from the group consisting of insulin and IGF-1 for a period of at least 6 days.

12. The method of claim 10, wherein the population of pluripotent stem cells is differentiated in the medium lacking serum and supplemented with BSA and a factor selected from the group consisting of insulin and IGF-1 for a period of at least 7 days.

13. The method of any one of claims 10 to 12, wherein the population of pluripotent stem cells is differentiated in the medium lacking serum and supplemented with BSA and insulin.

14. The method of any one of claims 10 to 13, wherein the medium is supplemented with about 1 ng/ml to about 100 ng/ml of insulin.

15. The method of any one of claims 10 to 12, wherein the population of pluripotent stem cells is differentiated in the medium lacking serum and supplemented with BSA and IGF-1.

16. The method of any one of claims 10 to 12 or claim 15, wherein the medium is supplemented with from about 1 ng/ml to about 50 ng/ml of IGF-1.

17. The method of any one of claims 10 to 16, wherein the cells expressing markers characteristic of the definitive endoderm lineage are definitive endoderm cells.

18. The method of any of claims 10 to 17, wherein the population of pluripotent stem cells are differentiated to a population of cells wherein greater than 85% of the cells in the population express markers characteristic of the definitive endoderm lineage using activin A and a Wnt ligand.

19. The method of claims 10 to 17, wherein the population of pluripotent stem cells are differentiated to a population of cells wherein greater than 85% of the cells in the population express markers characteristic of the definitive endoderm lineage using GDF-8 and at least one other factor is selected from the group consisting of: an aniline-pyridinotriazine, a cyclic aniline-pyridinotriazine, N-{[1-(Phenylmethyl)azepan-4-yl]methyl}-2-pyridin-3-ylacetamide, 4-{[4-(4-{[2-(Pyridin-2-ylamino)ethyl]amino}-1,3,5-triazin-2-yl)pyridin-2-yl]oxy}butan-1-ol, 3-({3-[4-({2-[Methyl(pyridin-2-yl)amino]ethyl}amino)-1,3,5-triazin-2-yl]pyridin-2-yl}amino)propan-1-ol, N~4~-[2-(3-Fluorophenyl)ethyl]-N~2~-[3-(4-methylpiperazin-1-yl)propyl]pyrido[2,3-d]pyrimidine-2,4-diamine, 1-Methyl-N-[(4-pyridin-3-yl-2-{[3-(trifluoromethyl)phenyl]amino}-1,3-thiazol-5-yl)methyl]piperidine-4-carboxamide, 1,1-Dimethylethyl {2-[4-({5-[3-(3-hydroxypropyl)phenyl]-4H-1,2,4-triazol-3-yl}amino)phenyl]ethyl}carbamate, 1,1-Dimethylethyl {[3-({5-[5-(3-hydroxypropyl)-2-(methyloxy)phenyl]-1,3-oxazol-2-yl}amino)phenyl]methyl}carbamate, 1-({5-[6-({4-[(4-Methylpiperazin-1-yl)sulfonyl]phenyl}amino)pyrazin-2-yl]thiophen-2-yl}methyl)piperidin-4-ol, 1-({4-[6-({4-[(4-Methylpiperazin-1-yl)sulfonyl]phenyl}amino)pyrazin-2-yl]thiophen-2-yl}methyl)piperidine-4-carboxamide, and 2-{[4-(1-Methylethyl)phenyl]amino}-N-(2-thiophen-2-ylethyl)-7,8-dihydropyrido[4,3-d]pyrimidine-6(5H)-carboxamide.

20. The method of any of claims 10 to 17, wherein the population of pluripotent stem cells are differentiated to a population of cells wherein greater than 85% of the cells in the population express markers characteristic of the definitive endoderm lineage using GDF-8 and 14-Prop-2-en-1-yl-3,5,7,14,17,23,27-heptaazatetracyclo[19.3.1.1~2,6~.1~8,12~]heptacosa-1(25),2(27),3,5,8(26),9,11,21,23-nonaen-16-one.