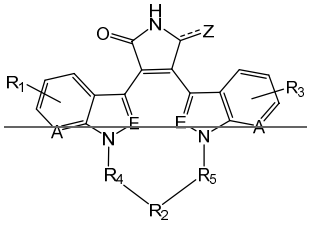
Claims

1. A method to expand and differentiate ~~human~~ pluripotent cells, comprising the steps of ~~culturing:~~

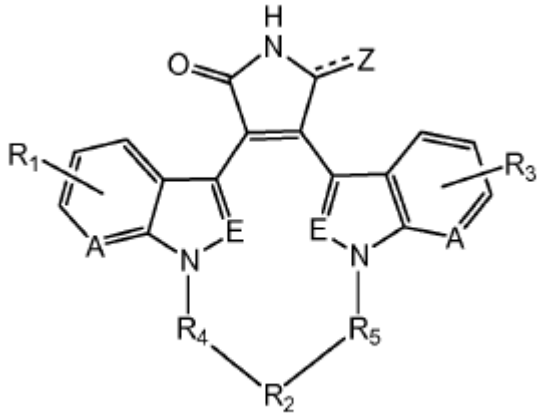
a) Culturing pluripotent cells, and ~~treating~~

~~1.~~ b) Treating the pluripotent cells with an inhibitor of GSK--3B enzyme activity ~~having~~, wherein



Formula (III)

the inhibitor is a compound of the Formula ~~(~~III~~:~~ ~~,~~):~~



Formula (III).

---

2. The method of claim 1, wherein the pluripotent cells are:

a) Embryonic stem cells; or

b) Cells expressing pluripotency markers, derived from embryonic stem cells, wherein preferably, the cells expressing pluripotency markers express at least one of the following pluripotency markers selected from the group consisting of: ABCG2, cripto, FoxD3, Connexin43, Connexin45, Oct4, SOX-2, Nanog, hTERT, UTF-1, ZFP42, SSEA-3, SSEA-4, Tra1-60, and Tra1-81; or

c) Differentiated into cells expressing markers characteristic of the definitive endoderm lineage; or

d) Treated with the inhibitor of GSK-3B enzyme activity for one to 72 hours; or

e) Treated with the inhibitor of GSK-3B enzyme activity for 12 to 48 hours; or

f) Treated with the inhibitor of GSK-3B enzyme activity for 48 hours.

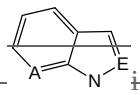
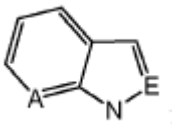
3. The method of claim 1, wherein the inhibitor of GSK-3B enzyme activity is:

a) Used at a concentration of 100nM to 100µM; or

b) Used at a concentration of 1µM to 10µM; or

used at a concentration of 10µM.

4. The method of any one of claims 1 to 3, wherein using a compound of the Formula (III), wherein A and E are ~~each~~ independently selected from the group consisting of a hydrogen substituted carbon atom and a nitrogen atom; wherein

~~wherein~~  ~~is 1*H*~~ 

is independently selected from the group consisting of 1 *H*-indole, ~~1*H*-~~1 *H*-pyrrolo[2,3-*b*]pyridine, ~~1*H*-~~1 *H*-pyrazolo[3,4-*b*]pyridine ~~or 1*H*-~~and 1 *H*-indazole~~;~~.

~~Z is O or dihydro;~~

5. The method of any one of claims 1 to 4, wherein Z is selected from O; alternatively, Z is selected from dihydro; wherein each hydrogen atom is attached by a single bond~~;~~.

6. The method of any one of claims 1 to 5, wherein R_4 and R_5 are independently selected from C_{1-8}alkyl, C_{2-8}alkenyl and C_{2-8}alkynyl optionally substituted with oxo~~;~~.

~~R_2 is C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, O(C_{1-8})alkyl-O, O(C_{2-8})alkenyl-O,~~

~~O(C_{2-8})alkynyl-O, C(O)(C_{1-8})alkyl-C(O), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy, hydroxy, hydroxy(C_{1-8})alkyl, oxo, cycloalkyl, heterocyclyl, aryl, heteroaryl; and~~

~~R_1 and R_3 are independently selected from hydrogen, C_{1-8}alkyl, C_{2-8}alkenyl, and C_{2-8}alkynyl, amino(C_{1-8})alkyl;~~

~~wherein each alkyl, alkenyl and alkynyl linking group is optionally substituted with one to four substituents independently selected from heterocyclyl, aryl, heteroaryl, spirocycloalkyl, spiroheterocyclyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl, heteroaryl(C_{1-8})alkyl, C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, C(O)O(C_{1-8})alkyl, C_{1-8}alkyl-C(O)O(C_{1-8})alkyl, amino, amino(C_{1-8})alkyl, cyano, halogen, hydroxy and nitro;~~

~~wherein each amino group is optionally substituted with hydrogen and C_{1-4}alkyl~~

~~wherein each cycloalkyl, heterocyclyl, aryl and heteroaryl group is optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino, and amino(C_{1-8})alkyl, cyano, halogen, hydroxy and nitro;~~

~~wherein each heterocyclyl is optionally substituted with halogen, cyano, hydroxyl, nitro (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy, hydroxy, hydroxy(C_{1-8})alkyl), oxo, -(O-(CH_2)$_{1-6}$)$_{0-5}$-O-, -O-(CH_2)$_{1-6}$-O-(CH_2)$_{1-6}$-O-, -O-(CH_2)$_{1-6}$-O-(CH_2)$_{1-6}$-O-(CH_2)$_{1-6}$-O-, -(O-(CH_2)$_{1-6}$)$_{0-5}$-NR_6-, -O-(CH_2)$_{1-6}$-NR_6-(CH_2)$_{1-6}$-O-, -O-(CH_2)$_{1-6}$-O-(CH_2)$_{1-6}$-NR_6-, -(O-(CH_2)$_{1-6}$)$_{0-5}$-S-, -O-(CH_2)$_{1-6}$-S-(CH_2)$_{1-6}$-O-, -O-(CH_2)$_{1-6}$-O-(CH_2)$_{1-6}$-S-, -NR_6-, -NR_6-NR_7-, -NR_6-(CH_2)$_{1-6}$-NR_7-, -NR_6-(CH_2)$_{1-6}$-NR_7-(CH_2)$_{1-6}$-NR_8-, -NR_6-C(O)-, -C(O)-NR_6-, -C(O)-(CH_2)$_{0-6}$-NR_6-(CH_2)$_{0-6}$-C(O)-, -NR_6-(CH_2)$_{0-6}$-C(O)-(CH_2)$_{1-6}$-C(O)-(CH_2)$_{0-6}$-NR_7-, -NR_6-C(O)-NR_7-, -NR_6-C(NR_7)-NR_8-, -O-(CH_2)$_{1-6}$-NR_6-(CH_2)$_{1-6}$-S-, -S-(CH_2)$_{1-6}$-NR_6-(CH_2)$_{1-6}$-O-, -NR_9-C(O)-, -C(O)-NR_9-, -S-(CH_2)$_{1-6}$-NR_6-(CH_2)$_{1-6}$-S-, -NR_6-(CH_2)$_{1-6}$-S-(CH_2)$_{1-6}$-NR_7- and -SO_2-, wherein R_6, R_7 and R_8 are each independently selected from hydrogen, C_{1-8}alkyl, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl, hydroxy(C_{1-8})alkyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl and heteroaryl(C_{1-8})alkyl; and wherein R_9 is selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl;~~

~~with the proviso that, if A and E are a hydrogen substituted carbon atom, then R_2 is -C_{2-8}alkynyl-, -O-(C_{1-8})alkyl-O-, -O-(C_{2-8})alkenyl-O-, -O-(C_{2-8})alkynyl-O-, or -C(O)-(C_{1-8})alkyl-C(O)-.~~

7. The method of any one claims 1 to 6, wherein R_2 is selected from the group consisting of -C_{1-8}alkyl-, -C_{2-8}alkenyl-, -C_{2-8}alkynyl-, -O-(C_{1-8})alkyl-O-, -O-(C_{2-8})alkenyl-O-, -O-(C_{2-8})alkynyl-O-, -C(O)-(C_{1-8})alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, -C(O)O-($_{1-8}$)alkyl, -C_{1-8}alkyl-C(O)O-(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$ (C_{1-8})alkyl, (halo)$_{1-3}$ (C_{1-8})alkoxy, hydroxy, hydroxy(C_{1-8})alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl, heteroaryl(C_{1-8})alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy and hydroxy(C_{1-8})alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with

oxo)), cycloalkyl, heterocyclyl, aryl, heteroaryl (wherein cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo), -(O-$(CH_2)_{1-6}$)$_{0-5}$-O-, -O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-O-, -O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-O-, -(O-$(CH_2)_{1-6}$)$_{0-5}$-NR_6-, -O-$(CH_2)_{1-6}$-NR_6-$(CH_2)_{1-6}$-O-, -O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-NR_6-, -(O-$(CH_2)_{1-6}$)$_{0-5}$-S-, -O-$(CH_2)_{1-6}$-S-$(CH_2)_{1-6}$-O-, -O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-S-, -NR_6-, -NR_6-NR_7-, -NR_6-$(CH_2)_{1-6}$-NR_7-, -NR_6-$(CH_2)_{1-6}$-NR_7-$(CH_2)_{1-6}$-NR_8-, -NR_6-C(O)-, -C(O)-NR_6-, -C(O)-$(CH_2)_{0-6}$-NR_6-$(CH_2)_{0-6}$-C(O)-, -NR_6-$(CH_2)_{0-6}$-C(O)-$(CH_2)_{1-6}$-C(O)-$(CH_2)_{0-6}$-NR_7-,-NR_6-C(O)-NR_7-, -NR_6-C(NR_7)-NR_8-, -O-$(CH_2)_{1-6}$-NR_6-$(CH_2)_{1-6}$-S-, -S-$(CH_2)_{1-6}$-NR_6-$(CH_2)_{1-6}$-O-, -S-$(CH_2)_{1-6}$-NR_6-$(CH_2)_{1-6}$-S-, -NR_6-$(CH_2)_{1-6}$-S-$(CH_2)_{1-6}$-NR_7- and -SO_2- (wherein R_6, R_7 and R_8 are independently selected from the group consisting of hydrogen, C_{1-8}alkyl, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), hydroxy(C_{1-8})alkyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl and heteroaryl(C_{1-8})alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo)); with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R_2 is selected from the group consisting of -C_{2-8}alkynyl-, -O-(C_{1-8})alkyl-O-, -O-(C_{2-8})alkenyl-O-, -O-(C_{2-8})alkynyl-O-, -C(O)-(C_{1-8})alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, -C(O)O-(C_{1-8})alkyl, -C_{1-8}alkyl-C(O)O-(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy, hydroxy(C_{1-8})alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl, heteroaryl(C_{1-8})alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy and hydroxy(C_{1-8})alkyl; and, wherein any of the

foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl (wherein cycloalkyl is optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy and hydroxy(C_{1-8})alkyl), -(O-$(CH_2)_{1-6})_{1-5}$-O-, -O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-O-, -O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-O-, -(O-$(CH_2)_{1-6})_{1-5}$-NR_6-, -O-$(CH_2)_{1-6}$-NR-$(CH_2)_{1-6}$-O-, -O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-NR_6-, -(O-$(CH_2)_{1-6})_{0-5}$-S-, -O-$(CH_2)_{1-6}$-S-$(CH_2)_{1-6}$-O-, -O-$(CH_2)_{1-6}$-O-$(CH_2)_{1-6}$-S-, -NR_6-NR_7-, -NR_6-$(CH_2)_{1-6}$-NR_7-, -NR_6-$(CH_2)_{1-6}$-NR_7-$(CH_2)_{1-6}$-NR_8-, -NR 9 -C(O)-, -C(O)-NR 9 -, -C(O)-$(CH_2)_{0-6}$-NR_6-$(CH_2)_{0-6}$-C(O)-, -NR_6-$(CH_2)_{0-6}$-C(O)-$(CH_2)_{1-6}$-C(O)-$(CH_2)_{0-6}$-NR_7-,-NR_6-C(O)-NR_7-, -NR_6-C(NR_7)-NR_8-, -O-$(CH_2)_{1-6}$-NR_6-$(CH_2)_{1-6}$-S-, -S-$(CH_2)_{1-6}$-NR_6-$(CH_2)_{1-6}$-O-, -S-$(CH_2)_{1-6}$-NR_6-$(CH_2)_{1-6}$-S- and -NR_6-$(CH_2)_{1-6}$-S-$(CH_2)_{1-6}$-NR_7- (wherein R_6, $R_7$and $R_8$are independently selected from the group consisting of hydrogen, C_{1-8}alkyl, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), hydroxy(C_{1-8})alkyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl and heteroaryl(C_{1-8})alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo); and, wherein R_9 is selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), hydroxy(C_{1-8})alkyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl and heteroaryl(C_{1-8})alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, C_{1-8}alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo)).

8. The method of any one claims 1 to 7, wherein R_1 and R_3 are independently selected from the group consisting of hydrogen, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl (wherein alkyl, alkenyl and alkynyl are optionally substituted with a substituent selected from the group consisting of C_{1-8}alkoxy, alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), (halo)$_{1-3}$, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy, hydroxy(C_{1-8})alkyl and oxo), C_{1-8}alkoxy, C_{1-8}alkoxycarbonyl, (halo)$_{1-3}$(C_{1-8})alkoxy,C_{1-8}alkylthio, aryl, heteroaryl (wherein aryl and heteroaryl are

optionally substituted with a substituent selected from the group consisting of C_{1-8}alkyl, C_{1-8}alkoxy, alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), halogen, (halo)$_{1-3}$(C_{1-8})alkyl, (halo)$_{1-3}$(C_{1-8})alkoxy,hydroxy and hydroxy(C_{1-8})alkyl), amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4}alkyl), cyano, halogen, hydroxy and nitro; and pharmaceutically acceptable salts thereof.

~~2.~~ 9. The method of claim 1, wherein the compound of the Formula(III) is:

a) 6,7,9,10,12,13,15,16-octahydro-23H-5,26:17,22-dimetheno-5H-dipyrido[2,3-k:3',2'-q]pyrrolo[3,4-n][1,4,7,10,19]trioxadiazacyclohenicosine-23,25(24H)-dione; or

b) 10,11,13,14,16,17,19,20,22,23-decahydro-9,4:24,29-dimetheno-1H-dipyrido[2,3-n:3',2'-t]pyrrolo[3,4-q][1,4,7,10,13,22]tetraoxadiazacyclotetracosine-1,3(2H)-dione; or

c) 10,11,13,14,16,17,19,20,22,23,25,26-dodecahydro-9,4:27,32-dimetheno-1H-dipyrido[2,3-q:3',2'-w]pyrrolo[3,4-t][1,4,7,10,13,16,25]-pentaoxadiazacycloheptacosine-1,3(2H)-dione; or

d) 6,7,9,10,12,13-hexahydro-20H-5,23:14,19-dimetheno-5H-dibenzo[h,n]pyrrolo[3,4-k][1,4,7,16]dioxadiazacyclooctadecine-20,22(21H)-dione; or

e) 6,7,9,10,12,13,15,16-octahydro-23H-5,26:17,22-dimetheno-5H-dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]trioxadiazacycloheneicosine-23,25(24H)-dione; or

f) 10,11,13,14,16,17,19,20,22,23-decahydro-9,4:24,29-dimetheno-1H-dibenzo[n,t]pyrrolo[3,4-q][1,4,7,10,13,22]tetraoxadiazacyclotetracosine-1,3(2H)-dione; or

g) 3-[1-[3-[(2-hydroxyethyl)methylamino]propyl]-1H-indazol-3-yl]-4-[1-(3-pyridinyl)-1H-indol-3-yl]-1H-pyrrole-2,5-dione; or

h) 3,5-dichloro-N-[3-chloro-4-[(3,4,12,12a-tetrahydro-1H-[1,4]thiazino[3,4-c][1,4]benzodiazepin-11(6H)-yl)carbonyl]phenyl]-benzamide; or

~~3-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-4-(1-pyridin-3-yl-1H-indol-3-yl)-pyrrole-2,5-dione;~~

i) 3-(2-methoxy-phenyl)-4-(1-pyridin-3-yl-1H-indol-3-yl)-pyrrole-2,5-dione; or

j) 6-[[2-[[4-(2,4-dichlorophenyl)-5-(4-methyl-1H-imidazol-2-yl)-2-pyrimidinyl]amino]ethyl]amino]-3-pyridinecarbonitrile; or

k) 3-(5-chloro-1-methyl-1H-indol-3-yl)-4-[1-(3-imidazol-1-yl-propyl)-1H-indazol-3-yl]-pyrrole-2,5-dione; or

l) 3-(5-chloro-1-methyl-1H-indol-3-yl)-4-[1-(3-[1,2,3]triazol-1-yl-propyl)-1H-indazol-3-yl]-pyrrole-2,5-dione; or

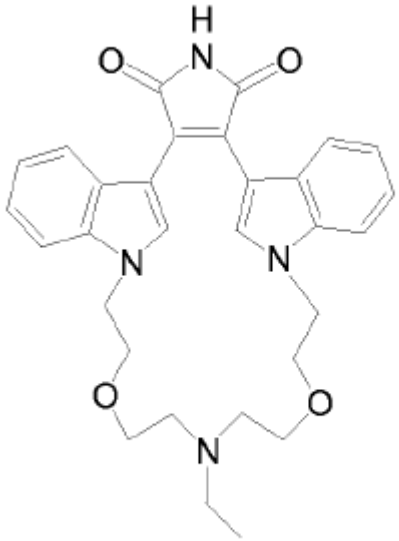
m) 3-[1-(3-hydroxy-propyl)-1H-pyrrolo[2,3-b]pyridin-3-yl]-4-(1-methyl-1H-pyrazol-3-yl)-pyrrole-2,5-dione; or

n) 3-[1-(3-hydroxy-3-methyl-butyl)-1H-indazol-3-yl]-4-(1-pyridin-3-yl-1H-indol-3-yl)-pyrrole-2,5-dione; or

o) 3-[1-(2-hydroxy-ethyl)-1H-~~indazol~~indazo1-3-yl]-4-(1-pyrimidin-5-yl-1H-indol-3-yl)-pyrrole-2,5-dione; or

p) 3-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-4-(1-pyrimidin-5-yl-1H-indol-3-yl)-pyrrole-2,5-dione; or

q) Compound 1a

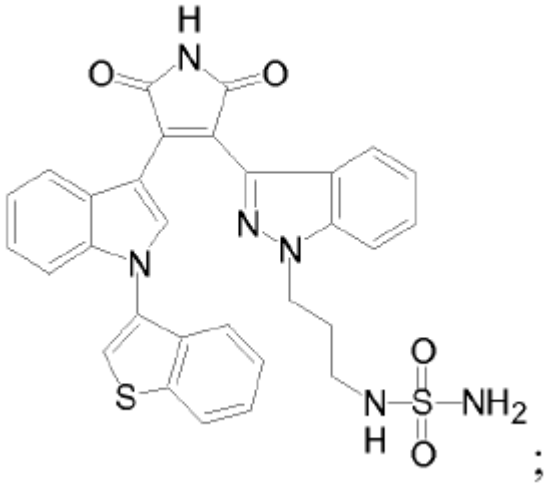


;

---

or

r) Compound 10a



or

s) (11Z)-8,9,10,13,14,15-hexahydro-2,6:17,21-di(metheno)pyrrolo[3,4-h][1,15,7]dioxazacyclotricosine-22,24(1H,23H)-dione;' or

t) 3-(5-chloro-1-pyridin-3-yl-1H-indol-3-yl)-4-[1-(3-hydroxy-propyl)-1H-indazol-3-yl]-pyrrole-2,5-dione; or

u) 3-(2-methoxy-phenyl)-4-[1-(3-methoxy-propyl)-1H-pyrrolo[3,2-c]pyridin-3-yl]-pyrrole-2,5-dione; or

v) 3-[1-(3-hydroxy-propyl)-1H-indazol-3-yl]-4-[1-(tetrahydro-pyran-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione; or

w) 2-{3-[4-(5-chloro-1-methyl-1H-indol-3-yl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl]-indazol-1-yl}-N-(2-hydroxy-ethyl)-acetamide; or

x) 4-(3-chloro-phenyl)-6-(3-dimethylamino-propyl)-5,6-dihydro-4H-2,4,6-triaza-cyclopenta[c]fluorine-1,3-dione; or

y) 14-ethyl-6,7,9,10,13,14,15,16-octahydro-12H,23H-5,26:17,22-dimethenodibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione; or

z) 14-benzyl-6,7,9,10,13,14,15,16-octahydro-12H,23H-5,26:17,22-di(metheno)dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]dioxatriazacyclohenicosine-23,25(24H)-dione; or

aa) 3-(1-{2-[2-(2-hydroxy-ethoxy)-ethoxy]-ethyl}-1H-indol-3-yl)-4-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-pyrrole-2,5-dione; or

bb) 6,7,8,9,10,11,12,13-octahydro-8,11-dimethyl-5,23:14,19-dimetheno-20H-dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10]tetraazacyclooctadecine-20,22(21H)-dione; or

cc) 7,8,9,10,12,13,16,17,18,19-decahydro-8,17-dimethyl-15H,26H-5,29:20,25-dimetheno-6H-dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19,22]dioxatetraazacyclotetracosine-26,28(27H)-dione; or

dd) 14-(2-furylmethyl)-6,7,9,10,13,14,15,16-octahydro-12H,23H-5,26:17,22-di(metheno)dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]dioxatriazacyclohenicosine-23,25(24H)-dione; or

ee) 14-(2-thienylmethyl)-6,7,9,10,13,14,15,16-octahydro-12H,23H-5,26:17,22-di(metheno)dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]dioxatriazacyclohenicosine-23,25(24H)-dione; or

ff) 14-(1-naphthylmethyl)-6,7,9,10,13,14,15,16-octahydro-12H,23H-5,26:17,22-di(metheno)dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]dioxatriazacyclohenicosine-23,25(24H)-dione; or

gg) 14-(pyridin-4-ylmethyl)-6,7,9,10,13,14,15,16-octahydro-12H,23H-5,26:17,22-di(metheno)dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]dioxatriazacyclohenicosine-23,25(24H)-dione; or

hh) 3-[1-(2-{2-[2-(1,2,3,4-tetrahydro-naphthalen-1-ylamino)-ethoxy]-ethoxy}-ethyl)-1H-indol-3-yl]-4-{1-[2-(1,2,3,4-tetrahydro-naphthalen-1-ylamino)-ethyl]-1H-indol-3-yl}-pyrrole-2,5-dione; or

ii) 3-[1-(3-dimethylamino-phenyl)-1H-indol-3-yl]-4-[1-(2-hydroxy-ethyl)-1H-indazol-3-yl]-pyrrole-2,5-dione; or

jj) 3-[5-chloro-1-(6-dimethylamino-pyridin-3-yl)-1H-indol-3-yl]-4-[1-(2-hydroxy-ethyl)-1H-indazol-3-yl]-pyrrole-2,5-dione; or

kk)5-(5-chloro-3-{4-[1-(2-hydroxy-ethyl)-1H-indazol-3-yl]-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl}-indol-1-yl)-nicotinic acid methyl ester.

~~3. The method of claim 2, wherein the compound of the Formula(III) is:~~

~~3-[1-(3-hydroxy-3-methylbutyl)-1H-indazol-3-yl]-4-(1-pyridin-3-yl-1H-indol-3-yl)-1H-pyrrole-2,5-dione;~~

~~3-[1-(2-hydroxy-ethyl)-1H-indol-3-yl]-4-(1-pyridin-3-yl-1H-indol-3-yl)-pyrrole-2,5-dione;~~

~~6-[(2-{[4-(2,4-dichlorophenyl)-5-(4-methyl-1H-imidazol-2-yl)-2-yl]amino}ethyl)amino]-pyridine-3-carbonitrile;~~

~~3-[1-{3-[(2-hydroxyethyl)methyl)amino]propyl}-1H-indazol-3-yl)-4-(1-pyridin-3-yl-1H-indol-3-yl)-1H-pyrrole-2,5-dione;~~

~~14-ethyl-6,7,9,10,13,14,15,16-octahydro-12H,23H-5,26:17,22-di(metheno-dizenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19]dioxatriazacycloheneicosine-23,25(24H)-dione;~~

14-(thiophen-2-ylmethyl)-6,7,9,10,13,14,15,16-octahydro-12H,23H-5,26:17,22-di(metheno)dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19] dioxatriazacyclohenicosine-23,25(24H)-dione; and

14-(napthalen-1-ylmethyl)-6,7,9,10,13,14,15,16-octahydro-12H,23H-5,26:17,22-di(metheno)dibenzo[k,q]pyrrolo[3,4-n][1,4,7,10,19] dioxatriazacyclohenicosine-23,25(24H)-dione.

4. The method of any one of claims 1-3, wherein the pluripotent cells are embryonic stem cells.

5. The method of any one of claims 1-3, wherein the pluripotent cells are cells expressing pluripotency markers derived from embryonic stem cells.

6. The method of claim 5, wherein the cells expressing pluripotency markers express at least one of the following pluripotency markers selected from the group consisting of: ABCG2, cripto, FoxD3, Connexin43, Connexin45, Oct4, SOX-2, Nanog, hTERT, UTF-1, ZFP42, SSEA-3, SSEA-4, Tra1-60, and Tra1-81.

7. The method of any one of claims 1-3, wherein the pluripotent cells are differentiated into cells expressing markers characteristic of the definitive endoderm lineage.

8. The method of any one of claims 1-3, wherein the pluripotent cells are treated with the inhibitor of GSK-3B enzyme activity for about one to about 72 hours.

9. The method of any one of claims 1-3, wherein the pluripotent cells are treated with the inhibitor of GSK-3B enzyme activity for about 12 to about 48 hours.

10. The method of any one of claims 1-3, wherein the pluripotent cells are treated with the inhibitor of GSK-3B enzyme activity for about 48 hours.

11. The method of any one of claims 1-3, wherein the inhibitor of GSK-3B enzyme activity is used at a concentration of about 100 nM to about 100 μM.

12. The method of any one of claims 1-3, wherein the inhibitor of GSK-3B enzyme activity is used at a concentration of about 1 μM to about 10 μM.

13. The method of any one of claims 1-3, wherein the inhibitor of GSK-3B enzyme activity is used at a concentration of about 10 μM.