



(51) International Patent Classification:

C12N 5/0786 (2010.01) A61K 35/15 (2015.01)
G01N 33/50 (2006.01) A61P 17/02 (2006.01)

(21) International Application Number:

PCT/SG2016/050018

(22) International Filing Date:

18 January 2016 (18.01.2016)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

10201500366V 16 January 2015 (16.01.2015) SG

(71) Applicant: AGENCY FOR SCIENCE, TECHNOLOGY
AND RESEARCH [SG/SG]; 1 Fusionopolis Way, #20-10
Connexis, Singapore 138632 (SG).

(72) Inventors: LIM, Hwei-In Shawn; c/o Genome institute of
Singapore, 60 Biopolis Street, Genome #02-01, Singapore
138672 (SG). HUBER, Tara; c/o Genome institute of
Singapore, 60 Biopolis Street, Genome #02-01, Singapore
138672 (SG). GINHOX, Florent; 8A Biomedical Grove,
IMMUNOS Building, Level 3, Singapore 138648 (SG).

(74) Agent: SPRUSON & FERGUSON (ASIA) PTE LTD;
P.O. Box 1531, Robinson Road Post Office, Singapore
903031 (SG).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ,
TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,
TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

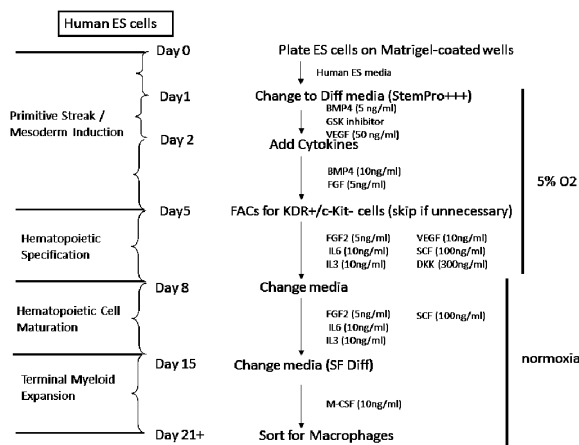
— of inventorship (Rule 4.17(iv))

Published:

— with international search report (Art. 21(3))

(54) Title: DIFFERENTIATION OF MACROPHAGES FROM PLURIPOTENT STEM CELLS

FIG. 1



(57) Abstract: The present invention relates to a method of culturing primitive-like macrophages from stem cells, a kit when used in the method thereof and uses of the primitive like macrophage for in-vitro disease models and for screening compounds for therapy. One embodied culture method comprises contacting and incubating embryonic stem cells or induced pluripotent stem cells with a serum-free culture media comprising a GSK3 inhibitor to differentiate stem cells into cells of the mesoderm lineage, followed by incubation with a culture media comprising Dickkopf-related protein 1 (DKK1) to differentiate the mesoderm into cells of hematopoietic lineage, maturing hematopoietic cells and incubating these cells with a culture media comprising M-CSF to drive differentiation into primitive-like macrophages. Another embodiment comprises incubating the stem cells with serum-free culture media comprising FGF2 and BMP4 to induce differentiation into cells of the mesoderm lineage, followed by incubating the cells with a culture media comprising FGF2, BMP4, Activin A and VEGF to differentiate the cells of the mesoderm lineage into cells of the hematopoietic cell lineage, maturing the cells of the hema-

topoietic cell lineage and lastly, incubating the matured hematopoietic cells with culture media comprising M-CSF to drive the differentiation of hematopoietic cells into primitive-like macrophages.