(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 March 2015 (26.03.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/040142 A1

(51) International Patent Classification:
*C12N 5/077* (2010.01)

(21) International Application Number:
PCT/EP2014/069951

(22) International Filing Date:
19 September 2014 (19.09.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
13185344.2 20 September 2013 (20.09.2013) EP

(71) Applicant: **GEORG-AUGUST-UNIVERSITÄT GÖTTINGEN STIFTUNG ÖFFENTLICHEN RECHTS, UNIVERSITÄTSMEDIZIN** [DE/DE]; Robert-Koch-Str. 40, 37099 Göttingen (DE).

(72) Inventors: **ZIMMERMANN, Wolfram-Hubertus**; Bühlstr. 15, 37073 Göttingen (DE). **HUDSON, James**; 12/79 Cambridge St., 4152, Queensland Carina Heights (AU). **TIBURCY, Malte**; Riemannstr. 16, 37083 Göttingen (DE).

(74) Agent: **WICHMANN, Hendrik**; Wuesthoff & Wuesthoff, Patent- und Rechtsanwälte, Schweigerstraße 2, 81541 München (DE).

(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).

**Published**:

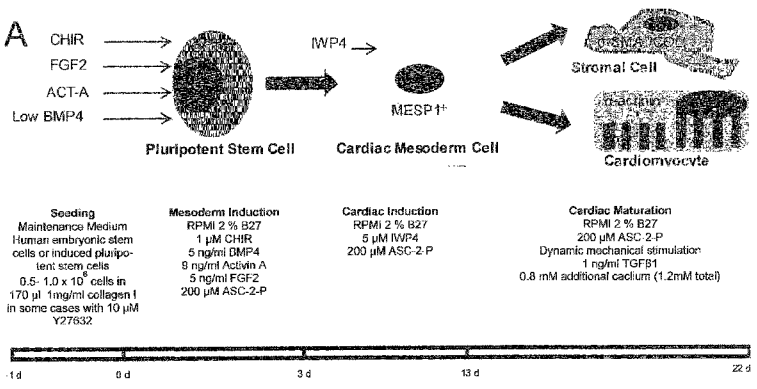
— *with international search report (Art. 21(3))*

— *with sequence listing part of description (Rule 5.2(a))*

WO 2015/040142 A1

(54) Title: A METHOD TO DIRECT DIFFERENTIATION OF PLURIPOTENT STEM CELLS INTO FUNCTIONAL HEART MUSCLE

Figure 1




(57) Abstract: The present invention is directed to a method for producing bioengineered heart muscle (BHM) from pluripotent stem cells, generally comprising the steps of inducing mesoderm differentiation, cardiac differentiation, and cardiac maturation by directed tissue formation. The method is a robust, serum-free and reproducible way to produce BHM for multiple applications, and is applicable to multiple pluripotent stem cell lines. The present invention is also directed to the BHM produced by the method disclosed herein, as well as to uses of said BHM in pharmacologic and toxicity screenings, and its use in medicine.