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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 February 2004 (05.02.2004)

PCT

(10) International Publication Number
WO 2004/011621 A2

(51) International Patent Classification[7]: C12N

(21) International Application Number:
PCT/US2003/023852

(22) International Filing Date: 29 July 2003 (29.07.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/399,476	29 July 2002 (29.07.2002)	US
60/409,847	11 September 2002 (11.09.2002)	US
60/452,732	7 March 2003 (07.03.2003)	US

(71) Applicant *(for all designated States except US)*: **ES CELL INTERNATIONAL PTE LTD.** [SG/SG]; 41 Science Park Road, #04-14/15 The Gemini, Singapore Science Park II, Singapore 117610 (SG).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CLARKE, Diana** [US/US]; 89 Hancock Street, Apt. 6, Cambridge, MA 02139 (US). **D'ALESSANDRO, Josephine, S.** [US/US]; 16 Seaview Avenue, Marblehead, MA 01945 (US). **LU, Kuanghui** [US/US]; 65 Glen Road, Unit 8-5, Brookline, MA 02445 (US). **WANG, Anlai** [US/US]; 19 Lill Avenue, Newton, MA 02465 (US).

(74) Agents: **VINCENT, Matthew, P.** et al.; Ropes & Gray LLP, One International Place, Boston, MA 02110-2624 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

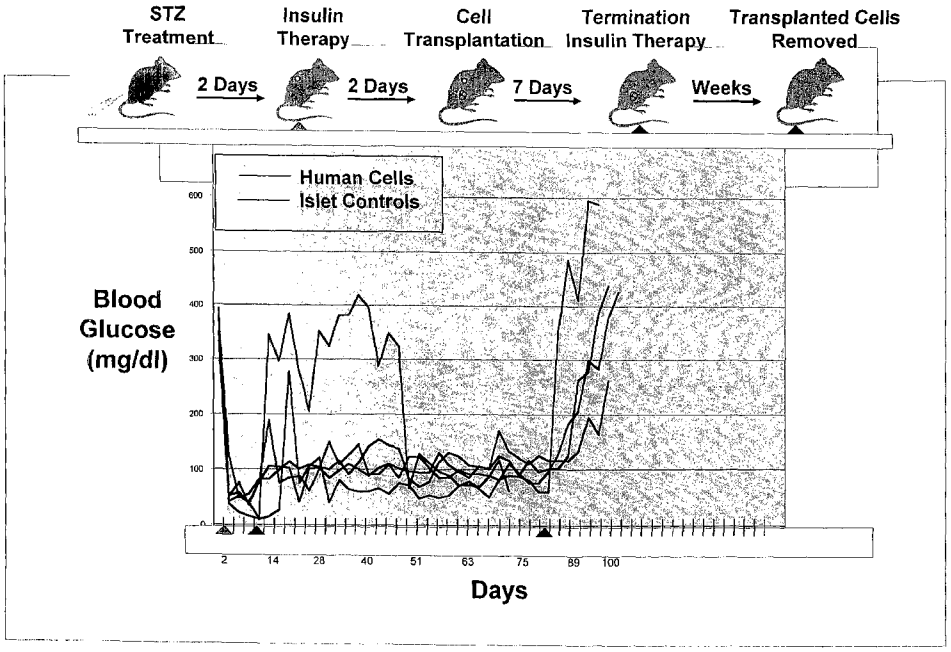
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

[Continued on next page]

(54) Title: MULTI-STEP METHOD FOR THE DIFFERENTIATION OF INSULIN POSITIVE, GLUCOSE



(57) Abstract: The present invention provides improved methods of differentiating insulin+, glucose responsive islet-like structures from insulin- cells. The invention further provides methods for using insulin+, glucose responsive islet-like structures, as well as the insulin+, glucose responsive cells which comprise said islet-like clusters.

WO 2004/011621 A2

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.