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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 January 2007 (04.01.2007)

PCT

(10) International Publication Number
WO 2007/002568 A1

(51) International Patent Classification:
C12N 5/10 (2006.01) *C12N 15/63* (2006.01)

(21) International Application Number:
PCT/US2006/024763

(22) International Filing Date: 22 June 2006 (22.06.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/693,319 22 June 2005 (22.06.2005) US
60/719,843 22 September 2005 (22.09.2005) US

(71) Applicant *(for all designated States except US)*: **GERON CORPORATION** [US/US]; 230 Constitution Drive, Menlo Park, CA 94025 (US).

(71) Applicant *(for US only)*: **Clark, Helen** (executrix for the deceased inventor) [GB/GB]; Roslin, Milothian, Scotland EH25 9PS (GB).

(72) Inventor: **CLARK, A., John** (deceased).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **WOLF, C., Roland** [GB/GB]; CXR Biosciences Limited, James Lindsay Place, Dundee Technopole, Dundee, Scotland DD1 5JJ (GB).

(74) Agent: **SCHIFF, J., Michael**; GERON CORPORATION, 230 Constitution Drive, Menlo Park, CA 94025 (US).

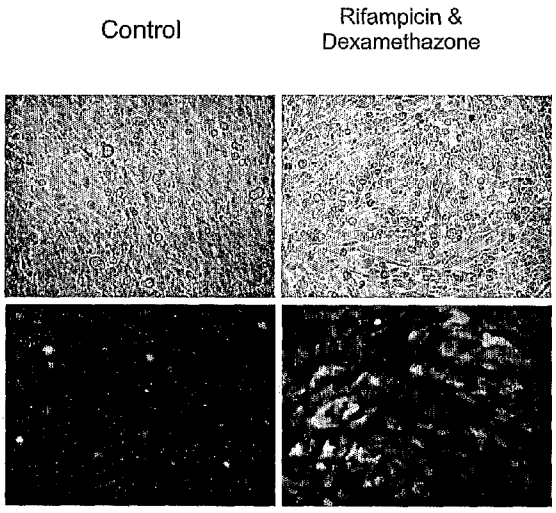
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, 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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

[Continued on next page]

(54) Title: REPORTER HEPATOCYTES AND OTHER CELLS FOR DRUG SCREENING AND TOXICITY TESTING



(57) Abstract: This invention provides a system for rapid determination of pharmacologic effects on target tissue types in cell populations cultured in vitro. The cells contain a promoter-reporter construct that reflects a toxicologic or metabolic change caused by the agent being screened. The promoter is taken from a gene known to be up- or down-regulated according to the metabolic state of the cell, and linked to a reporter gene that provides an external signal for monitoring promoter activity. The promoter-reporter cells may be produced by placing these genetic alterations into a line of human embryonic stem cells, bulking up the cells to any extent desired, and then differentiating the cells into the desired tissue type. This disclosure explains some of the powerful features of the promoter-reporter cells of this invention, and shows various ways the skilled reader can use the invention for pharmaceutical development and testing, or to monitor graft survival.

WO 2007/002568 A1

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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.