04/04/03
20030178 52

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

(19) World Intellectual Property Organization
International Bureau

162162

(43) International Publication Date
11 April 2002 (11.04.2002)

PCT

(10) International Publication Number
WO 02/028997 A3

(51) International Patent Classification[7]: C12N 5/06, 5/08, 5/10, A61K 35/407

(21) International Application Number: PCT/US00/27429

(22) International Filing Date: 3 October 2000 (03.10.2000)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant: UNIVERSITY OF NORTH CAROLINA [US/US]; 308 Bynum Hall, CB 4105, Chapel Hill, NC 27599-4105 (US).

(72) Inventors: KUBOTA, Hiroshi; 273 Summerwalk Circle, Chapel Hill, NC 27514 (US). REID, Lola, M.; 3621 Sweeten Creek Road, Chapel Hill, NC 27516 (US).

(74) Agents: POULIQUEN, Corinne, M. et al.; Pepper Hamilton LLP, 600 Fourteenth Street, N.W., Washington, DC 20005-2004 (US).

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

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

Published:
— *with international search report*

(88) Date of publication of the international search report:
12 September 2002

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.

ACTION

(54) Title: METHODS OF ISOLATING BIPOTENT HEPATIC PROGENITOR CELLS

(57) Abstract: A method of obtaining a mixture of cells enriched in hepatic progenitors is developed which comprises methods yielding suspensions of a mixture of cell types, and selecting those cells that are classical MHC class I antigen(s) negative and ICAM-1 antigen positive. The weak or dull expression of nonclassical MHC class I antigen(s) can be used for further enrichment of hepatic progenitors. Furthermore, the progenitors can be selected to have a level of side scatter a measure of granularity or cytoplasmic droplets, that is higher than that in non-parenchymal cells, such as hemopoietic cells, and lower than that in mature parenchymal cells, such as hepatocytes. Furthermore, the progeny of the isolated progenitors can express alpha-fetoprotein and/or albumin and/or CK19. The hepatic progenitors, so isolated, can grow clonally, that is an entire population of progeny can be derived from one cell. The clones of progenitors have a growth pattern in culture of piled-up aggregates or clusters. These methods of isolating the hepatic progenitors are applicable to any vertebrates including human. The hepatic progenitor cell population is expected to be useful for cell therapies, for bioartificial livers, for gene therapies, for vaccine development, and for myriad toxicological, pharmacological, and pharmaceutical programs and investigations.

WO 02/028997 A3