

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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
24 April 2003 (24.04.2003)

PCT

(10) International Publication Number
WO 03/033678 A3

- (51) International Patent Classification⁷: C12N 5/00, A01N 61/00, A61K 31/00
- (21) International Application Number: PCT/US02/33570
- (22) International Filing Date: 17 October 2002 (17.10.2002)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/335,705 18 October 2001 (18.10.2001) US
60/343,854 25 October 2001 (25.10.2001) US
- (71) Applicants (for all designated States except US): **THE GOVERNMENT OF THE UNITED STATES OF AMERICA AS REPRESENTED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES** [US/US]; c/o National Institutes of Health, Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852-3804 (US). **THE SALK INSTITUTE FOR BIOLOGICAL STUDIES** [US/US]; Peptide Biology Laboratory, 10010 North Torrey Pines Road, La Jolla, CA 92037-1099 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **SARTORELLI, Vittorio** [US/US]; 6300 Hollins Drive, Bethesda, MD 20817 (US). **PURI, Pier, Lorenzo** [IT/US]; 4985 Ocean Boulevard, San Diego, CA 92109 (US).
- (74) Agent: **HARDING, Tanya, M.**; Klarquist Sparkman, LLP, One World Trade Center, Suite 1600, 121 SW Salmon Street, Portland, OR 97204 (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, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, 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, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- (88) Date of publication of the international search report:
16 October 2003
- 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.



WO 03/033678 A3

(54) Title: METHODS OF USING DEACETYLASE INHIBITORS TO PROMOTE CELL DIFFERENTIATION AND REGENERATION

(57) Abstract: A method of enhancing progenitor cell differentiation, including enhancing myogenesis, neurogenesis, and hematopoiesis, by contacting a progenitor cell with an effective amount of a deacetylase inhibitor (DI). The progenitor cell can be part of cell culture, such as a cell culture used for *in vitro* or *in vivo* analysis of progenitor cell differentiation, or can be part of an organism, such as a human or other mammal. Contacting the progenitor cell with a DI can lead to enhancement of expression of terminal cell-type specific genes in the progenitor cell, such as enhancing expression of muscle-specific genes in myoblasts. Administering a DI to a subject also can provide some prophylactic or therapeutic effect for inhibiting, preventing, or treating associated with a degeneration or loss of tissue. The DI can be administered to a subject as part of a pharmaceutical composition.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/33570

A. CLASSIFICATION OF SUBJECT MATTER
 IPC(7) : C12N 5/00; A01N 61/00; A61K 31/00
 US CL : 435/375, 377; 514/1, 12
 According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
 Minimum documentation searched (classification system followed by classification symbols)
 U.S. : 435/375, 377; 514/1, 12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 EAST CAPLUS BIOSIS EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DAVIS, T. et al. Histone Deacetylase Inhibitors Decrease Proliferation and Modulate Cell Cycle Gene Expression in Normal Mammary Epithelial Cells. Clinical Cancer Research. November 2000, Vol. 6, No. 11, pages 4334-4342.	1-45
A	STEINBACH, O. et al. Histone Deacetylase Activity is Required for the Induction of the MyoS Biological Chemistry Muscle Cell Lineage in Xenopus. Biological Chemistry. September/October 2000, Vol. 381, No. 9/10, pages 1013-1016.	1-45
A	GABBIANELLI, M. et al. Hemoglobin Switching in Unicellular Erythroid Culture of Sibling Erythroid Burst-Forming Units: Kit Ligand Induces a Dose-Dependent Fetal Hemoglobin Reactivation Potential by Sodium Butyrate. Blood. 01 June 2000, Vol. 95, No. 11, pages 3555-3561.	1-45
A	O'NEIL, L. P. et al. A Developmental Switch in H4 Acetylation Upstream of Xist Plays a Role in X Chromosome Inactivation. EMBO Journal. 1999, Vol. 18, No. 10, pages 2897-2907.	1-45

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search
02 February 2003 (02.02.2003)

Date of mailing of the international search report
03 JUL 2003

Name and mailing address of the ISA/US
 Commissioner of Patents and Trademarks
 Box PCT
 Washington, D.C. 20231
 Facsimile No. (703)305-3230

Authorized officer
 Deborah Crouch, Ph.D.
 Telephone No. 703-308-0196

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SCHULTZ, R. M. et al. Reprogramming of Gene Expression during Preimplantation Development. Journal of Experimental Zoology. 15 October 1999, Vol. 285, No. 3, pages 276-282.	1-45