

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
9 October 2003 (09.10.2003)

PCT

(10) International Publication Number  
WO 03/082187 A3

(51) International Patent Classification<sup>7</sup>: C12N 15/63,  
15/85, 15/87, A01N 43/04, A61K 31/70, C07H 21/0, 21/04

(21) International Application Number: PCT/US03/07563

(22) International Filing Date: 13 March 2003 (13.03.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/368,078 26 March 2002 (26.03.2002) US

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(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, SC, SD, SE, SG, 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, 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:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
4 December 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 03/082187 A3

(54) Title: PURIFICATION AND CLONING OF NMN ADENYLYLTRANSFERASE AND ITS THERAPEUTIC USE

(57) Abstract: There is provided a composition for modifying NAD production, the composition including an NMNAT modifying compound and a pharmaceutically acceptable carrier. Also provided is a cDNA sequence encoding NMNAT. A method of treating for example, diabetes, cancer, myocardial infarction, stroke, neurodegenerative disorders, shock, and aging by administering to the patient an effective amount of a composition for modifying NAD production is also provided. There is further provided a gene therapy including a sequence encoding NMNAT included therein and the method for incorporating the sequence effectively into a host genome.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/07563

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>			
IPC(7) : C12N15/63,85,87;A01N43/04;A61K31/70;C07H21/0,04 US CL : 435/455; 514/44; 536.23.1			
According to International Patent Classification (IPC) or to both national classification and IPC			
<b>B. FIELDS SEARCHED</b>			
Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/455; 514/44; 536.23.1			
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) Please See Continuation Sheet			
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>			
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
X	BALDUCCI et al. Assay methods for nicotinamide mononucleotide adenylytransferase of wide applicability Analytical Biochemistry. 1995, Vol 228, pages 64-68.	1-3	
X,P	RAFFAELLI et al. Identification of a novel human nicotinamide mononucleotide adenylytransferase Biochemical and Biophysical Research Communication. 2002, Vol 297, pages 835-840.	4-7	
X	WOOD et al. The genome of the natural genetic engineer agrobacterium tumefaciens C58 Science. December 2001, Vol 294, pages 2317-2323.	7	
A	ROSENBERG et al. Gene therapist, heal thyself Science. March 2000, Vol 287, page 1751.	8-15	
<input type="checkbox"/> Further documents are listed in the continuation of Box C.		<input type="checkbox"/> 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		Date of mailing of the international search report	
08 August 2003 (08.08.2003)		08 OCT 2003	
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230		Authorized officer Brian Whiteman Telephone No. (703) 308-0196	

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-15, drawn to a composition for modifying NAD comprising a NMNAT modifying compound and a pharmaceutically acceptable carrier.

Group II, claim(s) 16, drawn to a method of purifying a protein.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the NMNAT modifying compound in Group I is not required in the method of Group II.

The special technical feature of Group I is considered to be a composition comprising NMNAT modifying compound.

The special technical feature of Group II is considered to be a method of purifying a protein.

Accordingly, Groups I-II are not so linked by the same or a corresponding technical feature as to form a single general inventive concept.

**Continuation of B. FIELDS SEARCHED Item 3:**

WEST2.1, STN

search terms: NAD, NMNAT, NMNAT-2, nicotinamide mononucleotide adenytransferase, NMN adenytransferase

# INTERNATIONAL SEARCH REPORT

International application No.

PCT US03/07563

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
  4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-15
- Remark on Protest**  The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.