

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
27 May 2004 (27.05.2004)

PCT

(10) International Publication Number
WO 2004/043886 A3

- (51) International Patent Classification⁷: C12N 15/82, A01G 9/00
- (21) International Application Number: PCT/US2003/036056
- (22) International Filing Date: 12 November 2003 (12.11.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 10/294,314 12 November 2002 (12.11.2002) US
- (71) Applicant (for all designated States except US): NUCY-CLE THERAPY, INC. [US/US]; 255 Long Avenue, Hillside, NJ 07205 (US).
- (72) Inventor; and
- (75) Inventor/Applicant (for US only): ENSLEY, Burt [US/US]; PMB 1319, 2675 West Highway 89A, Sedona, AZ 86336 (US).
- (74) Agent: GERBER, Monica, R.; Choate, Hall & Stewart, Exchange Place, 53 State Street, Boston, MA 02109 (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 (BW, 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: 29 December 2004
- 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.*

(54) Title: PRODUCTION OF PHARMACEUTICALLY ACTIVE PROTEINS IN SPROUTED SEEDLINGS

(57) Abstract: The present invention provides systems and methods for producing pharmaceutically active proteins in transgenic sprouted seedlings. The transgenic sprouted seedlings of the invention are grown in a contained, regulatable environment, wherein expression of a pharmaceutically active protein is controlled by an exogenously inducible promoter. The transgenic sprouted seedlings may be eaten live or preferably harvested live to preserve the maximal biological activity of the pharmaceutically active protein.

WO 2004/043886 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/36056

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.: 1-32, 98-118
- Remark on Protest The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/36056

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/82; A01G 9/00
 US CL : 800/288; 47/17

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. : 800/288; 47/17

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 6,127,145 A (SUTLIFF et al.) 3 October 2000 (03.10.2000), column 1 line 66 to column 2 line 3, column 3 lines 40-58, column 10 line 33 to column 11 line 52, column 28 lines 27-34.	1-6, 10-12, 16-18, 21, 26-32, 98-99, 112-118 ----- 7-9, 13-15, 19-20, 22-25, 100-111
Y	US 4,028,847 (DAVIS et al.) 14 June 1977 (14.06.1977), column 1 line 1 to column 2 line 42, column 3 line 62 to column 4 line 25, column 7 lines 31-37, column 16 lines 14-52, column 17 lines 7-21, column 19 lines 10-20.	1-32, 98-118

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

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"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 16 April 2004 (16.04.2004)	Date of mailing of the international search report 22 OCT 2004
---	--

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 Cynthia Collins <i>J. Whitefield</i> Telephone No. (703) 308-0196 <i>for</i>
---	---

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 examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-32 and 98-118, drawn to a method for producing pharmaceutically active proteins in sprouted seedlings, said method comprising growing a seed and inducing protein expression, and to a system for producing pharmaceutically active proteins in sprouted seedlings.

Group II, claim(s) 33-65, drawn to a method for producing pharmaceutically active proteins in sprouted seedlings, said method comprising infecting seedlings with a viral expression cassette and growing seedlings.

Group III, claim(s) 66-97, drawn to a method for producing pharmaceutically active proteins in sprouted seedlings, said method comprising transforming plants with an expression cassette using an *Agrobacterium* transformation system, and obtaining and growing transgenic seeds.

Group IV, claim(s) 119-150, drawn to a method of treating a mammal with a pharmaceutically active protein expressed in a sprouted seedling.

The inventions listed as Groups I-IV 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 technical feature linking inventions I-IV is a pharmaceutically active protein produced in sprouted seedlings. However, a pharmaceutically active protein produced in sprouted seedlings is obvious or anticipated over RODRIGUEZ (US Patent No. 5,994,628 issued 30 November 1999), and therefore does not constitute a special technical feature as defined by PCT Rule 13.2, because it does not define a contribution over the prior art. Furthermore, inventions I-IV have different technical requirements. Invention I requires growing a seed and inducing protein expression, which is not required of inventions II-IV. Invention II requires infecting seedlings with a viral expression cassette and growing seedlings, which is not required of inventions I and III-IV. Invention III requires transforming plants with an expression cassette using an *Agrobacterium* transformation system, and obtaining and growing transgenic seeds, which is not required of inventions I-II and IV. Invention IV requires treating a mammal with a pharmaceutically active protein expressed in a sprouted seedling, which is not required of inventions I-III.

Continuation of B. FIELDS SEARCHED Item 3:

INTERNATIONAL SEARCH REPORT

PCT/US03/36

WEST/STN (agricola, biosis, biotechno, caba, caplus, medline): inventor name, seed, seedling, sprout, transgenic, pharmaceutical, therapeutic, induce, greenhouse