

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
5 February 2004 (05.02.2004)

PCT

(10) International Publication Number
WO 2004/011902 A3

(51) International Patent Classification⁷: A61K 38/00, 38/46, C07K 7/02, C12N 1/20, C12P 21/06, C12Q 1/68

(21) International Application Number:
PCT/US2003/023171

(22) International Filing Date: 25 July 2003 (25.07.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/398,682 25 July 2002 (25.07.2002) 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, 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 (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).

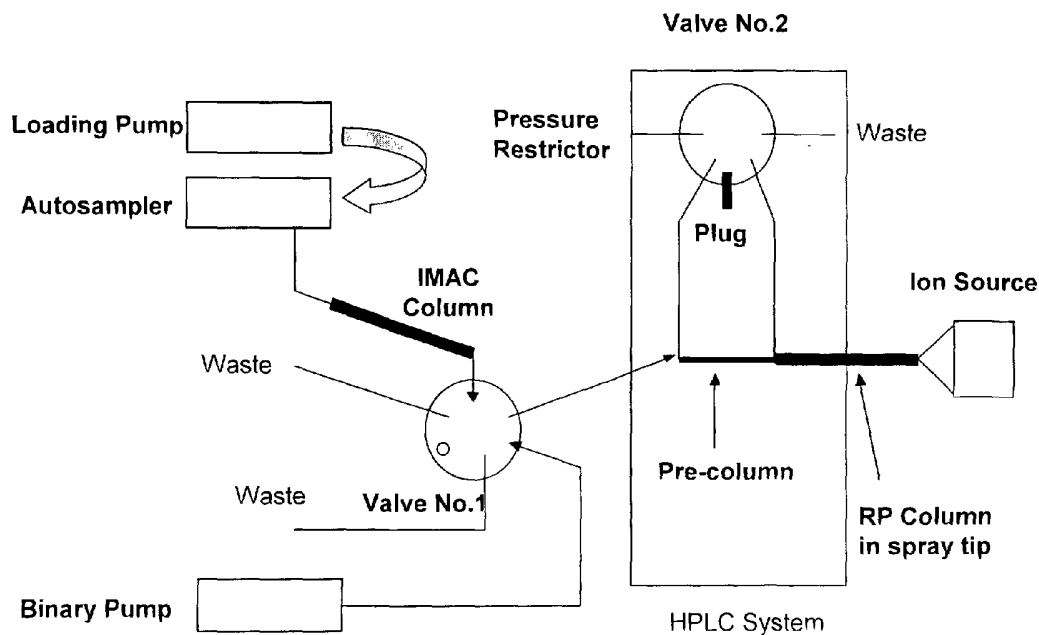
Published:

- 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:
18 November 2004

[Continued on next page]

(54) Title: IMPROVED SYSTEMS AND METHODS FOR ANALYSIS OF PROTEIN POST-TRANSLATIONAL MODIFICATION



(57) Abstract: The invention relates to a method for the detection and identification of amino acid modifications, such as phosphorylation, using a combination of affinity capture and mass-spectroscopy.

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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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/23171

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/00, 38/46; C07K 7/02; C12N 1/20; C12P 21/06; C12Q 1/68
 US CL : 424/94.6; 435/6, 69.1, 252.3; 530/332, 345; 514/2, 15-19

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. : 424/94.6; 435/6, 69.1, 252.3; 530/332, 345; 514/2, 15-19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
 REGISTRY, IUBMB DATA BASE

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.
Y	US 6,375,947 B1 (BOLEN et al.) 23 April 2002 (23.04.2002), Abstarct, Lines 1-13; Column 4, Line 60 to Column 5, Line 20	1-22, 28-31
Y	US 6,075,121 A (Simon et al.) 13 June 2000 (13.06.2000), Abstract, Lines 1-25; Examples 9 and 11; Column 32, Line 29 to Column 34, Line 45.	23-27
Y, P	US 2003/0083575 A1 (SCHULZ et al.) 1 May 2003 (01.05.2003), Abstrct, Lines 1-4; Claims 1-140; Page 28, Paragraph 0246 to Page 30, Paragraph 0263.	1-31
X	BUDISA, N. et al. Residue-specific Bioincorporation of Non-natural, Biologically Active Amino Acids into Proteins as Possible Drug Carriers: Structure and Stability of the per-	1-27
---	Thiaproline Mutant of Annexin V. Proc. Natl. Acad. Sci., U.S.A. 1998. Volume 95, Pages 455-459, Especially Abstract, Lines 1-19-20.	-----
Y		28-31

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 05 August 2004 (05.08.2004)	Date of mailing of the international search report 15 SEP 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) 872-9306	Authorized officer <i>Lalere Bell-Harris</i> Dr. Kalash C. Srivastava Telephone No. (571)-272-1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/23171

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.:
- 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

PCT/US03/23171

Continuation of Item 4 of the first sheet:

This International Search Authority has established the following title for this application. This title, in this International Search Authority's opinion is preciser than the one that applicant has given.

SYSTEMS AND METHODS TO ANALYSE PROTEIN POST-TRANSLATIONAL MODIFICATIONS

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This International Authority has found 5 inventions claimed in this International application covered by the claims indicated below:

This application contains the following inventions or groups of inventions that 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) 1-22, drawn to a method of identifying modified amino acids in proteins within the proteome.

Group II, Claim (s) 23-27, Drawn to an assay for compounds that modulate post-translational modification.

Group III, Claim (s) 28-29, drawn to a first drug discovery business for agents that meet a specific pattern of post-translational patterns.

Group IV, Claim 30, drawn to a second drug discovery business for identifying post-translational modifying enzymes.

Group V, Claim 31, drawn to a second drug discovery business for the proteins in the proteome that are post-translationally modified.

This International Authority considers that this International application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I-V 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 alleged special Technical feature, proteins that have a post-translational modification that are further modified at the side chains, N-terminus, or C-terminus is not a contribution over the art as evidenced for example, by Bolen et al. (U.S. Patent 6,375, 947) (See Column 4, Line 60 to Column 5, Line 20).

Continuation of B. FIELDS SEARCHED Item 3:

USPT, PGPB, USOC, EPAB, JPAB, ADISNEWS, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CONFSCI, DRUGB, EMBASE, ESBIODBASE, FROSTI, IFIPAT, JICST-EPLUS, LEFESCI, MEDICONF, MEDLINE, NIOSHTIC, RDISCLOSURE, SCISEARCH, USPATFUL, WPIDS.

Search Strategy:

acetyl\$5, carboxyl\$5, phosphoryl\$5, glycisyl\$4, ubiquitin\$5, farnesyl\$5, meristoyl\$5, posttranslat\$4, alkyl\$4, (peptide, polypeptide, protein)modif\$6, modul\$7, enzyme\$6, drug\$9, pharmaceutical\$, therapeutic\$3, discovery.