

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
29 November 2001 (29.11.2001)

PCT

(10) International Publication Number
WO 01/090148 A3

(51) International Patent Classification⁷: **C07K 14/705**,
C12N 15/12, C07K 16/18, C12Q 1/68, G01N 33/53,
33/68, A61K 38/17

(21) International Application Number: PCT/US01/16283

(22) International Filing Date: 17 May 2001 (17.05.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/205,518 19 May 2000 (19.05.2000) US
60/213,956 22 June 2000 (22.06.2000) US
60/215,105 28 June 2000 (28.06.2000) US
60/218,947 14 July 2000 (14.07.2000) US
60/221,488 27 July 2000 (27.07.2000) 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, 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, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, 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, TR), 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:
14 August 2003

(15) Information about Correction:

Previous Correction:

see PCT Gazette No. 27/2002 of 4 July 2002, Section II

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: NEUROTRANSMITTER TRANSPORTERS

(57) Abstract: The invention provides human neurotransmitter transporter (NTT) and polynucleotides which identify and encode NTT. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with aberrant expression of NTT.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/16283

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/705 C12N15/12 C07K16/18 C12Q1/68 G01N33/53
G01N33/68 A61K38/17

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)

IPC 7 C07K G01N A61K

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 practical, search terms used)

EPO-Internal, WPI Data, PAJ, EMBL, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 18143 A (SYNAPTIC PHARMA CORP) 16 September 1993 (1993-09-16) page 18, line 3 - line 12; claims 1-159; figure 1A	1-45,51
X	--- BORDEN L A ET AL: "MOLECULAR HETEROGENEITY OF THE GAMMA-AMINOBUTYRIC ACID (GABA) TRANSPORT SYSTEM" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 267, no. 29, 15 October 1992 (1992-10-15), pages 21098-21104, XP002916398 ISSN: 0021-9258 the whole document --- -/--	1-5,9, 11,12

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"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)

"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

"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

"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

"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.

"&" document member of the same patent family

Date of the actual completion of the international search

4 November 2002

Date of mailing of the international search report

29. 01. 2003

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/16283

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	RASOLA A ET AL: "MOLECULAR CLONING AND FUNCTIONAL CHARACTERIZATION OF A GABA/BETAINE TRANSPORTER FROM HUMAN KIDNEY" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 373, 1995, pages 229-233, XP002932543 ISSN: 0014-5793 the whole document ---	1-45,51
A	SCHULDINER S ET AL: "VESICULAR NEUROTRANSMITTER TRANSPORTERS: FROM BACTERIA TO HUMANS" PHYSIOLOGICAL REVIEWS, AMERICAN PHYSIOLOGICAL SOCIETY, US, vol. 75, no. 2, 1 April 1995 (1995-04-01), pages 369-392, XP000199557 ISSN: 0031-9333 the whole document ---	1-45,51
A	BARNWELL L F S ET AL: "Cloning and sequencing of a cDNA encoding a novel member of the human brain GABA/noradrenaline neurotransmitter transporter family" GENE, ELSEVIER BIOMEDICAL PRESS, AMSTERDAM, NL, vol. 159, no. 2, 4 July 1995 (1995-07-04), pages 287-288, XP004042226 ISSN: 0378-1119 the whole document ---	1-45,51
P,X	WO 00 77045 A (KIMURA HIROYUKI ; SAWADA HIDEKAZU (JP); SAKAMOTO JUNICHI (JP); TAKE) 21 December 2000 (2000-12-21) Sequence listing, Seq ID No 1 and 2 ---	1-45,51
E	WO 01 77321 A (MERCK PATENT GMBH ; BRANDT SILKE (DE)) 18 October 2001 (2001-10-18) claims 1-11; figure 1 -----	1-45,51

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/16283

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

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

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 20 and 23 partially
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:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims 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:

see additional 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.:
1-44 (partially); 45, 51 (complete)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim(s) 32 and 34 are interpreted as directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound.

Although claims 18, 21, 24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.

Continuation of Box I.2

Claims Nos.: 20 and 23 partially

Present claims 20, and 23, relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the polypeptide and antibodies of the invention.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-44, all partially, and claims 45 and 51, completely

Isolated peptide (Seq ID No 1), or a naturally occurring polypeptide comprising a sequence of at least 90% identity, biological active fragments, and immunogenic fragments thereof. A method for producing said polypeptides. Specific binding poly- and monoclonal antibodies to said polypeptide and methods of generating said antibodies. Pharmaceutical composition comprising said polypeptide. Methods for treating diseases, and methods for screening for agonists, antagonists and modulating compounds. Agonists and antagonists isolated by said methods. Diagnostic test and methods of diagnosis using specific antibodies. Compositions comprising said antibodies. Methods of detecting and purifying the polypeptide of the invention using said antibodies.

Polynucleotides encoding the polypeptide with Seq ID No 1, the biological active fragments, and immunogenic fragments. The polynucleotide with Seq ID No 7 and those with at least 90% identity, and fragments of said polynucleotides comprising at least 60 nucleotides. Recombinant polynucleotides comprising said polynucleotides. A cell transformed with said polynucleotide. A transgenic organism comprising said polynucleotide. Method of detecting said polynucleotides. Method for screening a compound, or assessing the toxicity of a compound using said polynucleotide.

2. Claims: 1-44, all partially, and claims 46 and 52, completely

Isolated peptide (Seq ID No 2), or a naturally occurring polypeptide comprising a sequence of at least 90% identity, biological active fragments, and immunogenic fragments thereof. A method for producing said polypeptides. Specific binding poly- and monoclonal antibodies to said polypeptide and methods of generating said antibodies. Pharmaceutical composition comprising said polypeptide. Methods for treating diseases, and methods for screening for agonists, antagonists and modulating compounds. Agonists and antagonists isolated by said methods. Diagnostic test and methods of diagnosis using specific antibodies. Compositions comprising said antibodies. Methods of detecting and purifying the polypeptide of the invention using said antibodies.

Polynucleotides encoding the polypeptide with Seq ID No 2,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

the biological active fragments, and immunogenic fragments. The polynucleotide with Seq ID No 8 and those with at least 90% identity, and fragments of said polynucleotides comprising at least 60 nucleotides. Recombinant polynucleotides comprising said polynucleotides. A cell transformed with said polynucleotide. A transgenic organism comprising said polynucleotide. Method of detecting said polynucleotides. Method for screening a compound, or assessing the toxicity of a compound using said polynucleotide.

3. Claims: 1-44, all partially, and claims 47 and 53, completely

Isolated peptide (Seq ID No 3), or a naturally occurring polypeptide comprising a sequence of at least 90% identity, biological active fragments, and immunogenic fragments thereof. A method for producing said polypeptides. Specific binding poly- and monoclonal antibodies to said polypeptide and methods of generating said antibodies. Pharmaceutical composition comprising said polypeptide. Methods for treating diseases, and methods for screening for agonists, antagonists and modulating compounds. Agonists and antagonists isolated by said methods. Diagnostic test and methods of diagnosis using specific antibodies. Compositions comprising said antibodies. Methods of detecting and purifying the polypeptide of the invention using said antibodies.

Polynucleotides encoding the polypeptide with Seq ID No 3, the biological active fragments, and immunogenic fragments. The polynucleotide with Seq ID No 9 and those with at least 90% identity, and fragments of said polynucleotides comprising at least 60 nucleotides. Recombinant polynucleotides comprising said polynucleotides. A cell transformed with said polynucleotide. A transgenic organism comprising said polynucleotide. Method of detecting said polynucleotides. Method for screening a compound, or assessing the toxicity of a compound using said polynucleotide.

4. Claims: 1-44, all partially, and claims 48 and 54, completely

Isolated peptide (Seq ID No 4), or a naturally occurring polypeptide comprising a sequence of at least 90% identity, biological active fragments, and immunogenic fragments thereof. A method for producing said polypeptides. Specific binding poly- and monoclonal antibodies to said polypeptide and methods of generating said antibodies. Pharmaceutical composition comprising said polypeptide. Methods for

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

treating diseases, and methods for screening for agonists, antagonists and modulating compounds. Agonists and antagonists isolated by said methods. Diagnostic test and methods of diagnosis using specific antibodies. Compositions comprising said antibodies. Methods of detecting and purifying the polypeptide of the invention using said antibodies.

Polynucleotides encoding the polypeptide with Seq ID No 4, the biological active fragments, and immunogenic fragments. The polynucleotide with Seq ID No 10 and those with at least 90% identity, and fragments of said polynucleotides comprising at least 60 nucleotides. Recombinant polynucleotides comprising said polynucleotides. A cell transformed with said polynucleotide. A transgenic organism comprising said polynucleotide. Method of detecting said polynucleotides. Method for screening a compound, or assessing the toxicity of a compound using said polynucleotide.

5. Claims: 1-44, all partially, and claims 49 and 55, completely

Isolated peptide (Seq ID No 5), or a naturally occurring polypeptide comprising a sequence of at least 90% identity, biological active fragments, and immunogenic fragments thereof. A method for producing said polypeptides. Specific binding poly- and monoclonal antibodies to said polypeptide and methods of generating said antibodies. Pharmaceutical composition comprising said polypeptide. Methods for treating diseases, and methods for screening for agonists, antagonists and modulating compounds. Agonists and antagonists isolated by said methods. Diagnostic test and methods of diagnosis using specific antibodies. Compositions comprising said antibodies. Methods of detecting and purifying the polypeptide of the invention using said antibodies.

Polynucleotides encoding the polypeptide with Seq ID No 5, the biological active fragments, and immunogenic fragments. The polynucleotide with Seq ID No 11 and those with at least 90% identity, and fragments of said polynucleotides comprising at least 60 nucleotides. Recombinant polynucleotides comprising said polynucleotides. A cell transformed with said polynucleotide. A transgenic organism comprising said polynucleotide. Method of detecting said polynucleotides. Method for screening a compound, or assessing the toxicity of a compound using said polynucleotide.

6. Claims: 1-44, all partially, and claims 50 and 56, completely

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Isolated peptide (Seq ID No 6), or a naturally occurring polypeptide comprising a sequence of at least 90% identity, biological active fragments, and immunogenic fragments thereof. A method for producing said polypeptides. Specific binding poly- and monoclonal antibodies to said polypeptide and methods of generating said antibodies. Pharmaceutical composition comprising said polypeptide. Methods for treating diseases, and methods for screening for agonists, antagonists and modulating compounds. Agonists and antagonists isolated by said methods. Diagnostic test and methods of diagnosis using specific antibodies. Compositions comprising said antibodies. Methods of detecting and purifying the polypeptide of the invention using said antibodies.

Polynucleotides encoding the polypeptide with Seq ID No 6, the biological active fragments, and immunogenic fragments. The polynucleotide with Seq ID No 12 and those with at least 90% identity, and fragments of said polynucleotides comprising at least 60 nucleotides. Recombinant polynucleotides comprising said polynucleotides. A cell transformed with said polynucleotide. A transgenic organism comprising said polynucleotide. Method of detecting said polynucleotides. Method for screening a compound, or assessing the toxicity of a compound using said polynucleotide.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/16283

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WO 9318143	A	16-09-1993	AU 691469 B2	21-05-1998
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			EP 1276868 A2	22-01-2003
