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(54) Title: BRAIN PROTEIN MARKERS

(57) Abstract: Protein markers for various psychiatric and neurological disorders were discovered. Diagnostic assays for these conditions were based on the levels of individual or combinations. The markers are targets or drug discovery for therapeutic and prophylactic uses.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/33903

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 21/04; C07K 1/00, 2/00; C12Q 1/00, 1/68; G01N 33/53
 US CL : 435/4, 6, 7.1; 530/300, 350; 536/23.1, 23.5

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. : 435/4, 6, 7.1; 530/300, 350; 536/23.1, 23.5

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	US 5,262,332 A (SELKOE) 16 November 1993 (16.11.1993), see entire document.	1
X	US 5,387,742 A (CORDELL) 07 February 1995 (07.02.1995), columns 34-36.	4
X	US 5,753,624 A (MCMICHAEL et al) 19 May 1998 (19.05.1998), columns 9-14.	7, 9
X	US 5,220,013 A (PONTE et al) 15 June 1993 (15.06.1993), columns 17-28.	8-9
X, P	JOHNSTON-WILSON et al. Disease-specific alterations in frontal cortex brain proteins in schizophrenia, bipolar disorder, and major depressive disorder. Mol. Psychiatry 2000, Vol 5, pages 142-149, see entire document.	1
A	LUBEC et al. Expression of the dihydropyrimidase related protein 2 (DRP-2) in Down Syndrome and Alzheimer's disease brain is downregulated at the mRNA and dysregulated at the protein level. J. Neural Trans. 1999, Vol 57 Supplement, pages 161-177, see entire document.	1

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	

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/33903

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.: 2,3,5 and 6
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:
A meaningful search cannot be carried out on all claims that read upon a protein selected from a group of proteins listed in Tables 2 and 4 (claims 2,3,5,6). A written form and a computer readable form of the sequence listing have not been provided.

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

International Application No.

PCT/US00/33903

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING^A

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, drawn to a method for diagnosing a brain disorder comprising obtaining a sample from a patient, measuring an amount of a protein, and comparing the result to a standard.

Group II, claim(s) 4, drawn to a method for determining whether a candidate drug is effective in treating a brain disorder.

Group III, claim(s) 7 and 9, in part, drawn to a composition comprising an effective amount of a protein having abnormal levels in an individual with a brain disorder.

Group IV, claim(s) 8-9, in part, drawn to a composition comprising an effective amount of a nucleic acid encoding a protein having abnormal levels in an individual with a brain disorder.

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:

Claims 1 broadly encompass the method of diagnosing any brain disorder and measuring any protein. Roses et al. (US patent 5,508,167) teaches the method diagnosing Alzheimer's disease comprising detecting the presence or absence of an apolipoprotein E type 4 (ApoE4) isoform in a subject. Further, observing whether or not the ApoE4 isoform is present or absent in a subject enables one to determine whether or not a subject is afflicted with or at increased risk of developing Alzheimer's disease. A subject with ApoE4 is at increased risk of developing Alzheimer's disease over subjects in which ApoE4 is absent (col 3 and 9-14). Thus, the technical feature of claims 1-3 is not a contribution over the prior art and is not considered a special technical feature.

Further, Group II recites the technical feature of contacting brain cells with a drug which is not required for the method of Group I. Groups III and IV claim different products which are structurally and functionally unrelated, each to each other. Group III recites the technical feature of a composition comprising a protein which is not required for the product of Group IV. Group IV recites the technical feature of a composition comprising a nucleic acid molecule which is not required for the product of Group III.

Continuation of B. FIELDS SEARCHED Item 3:

EAST, DIALOG, MEDLINE

search terms: inventors' names, carbonic anhydrase, dihydropyrimidinase related protein 2, fructose-biphosphate aldolase C, aspartate aminotransferase, depression, schizophrenia, bipolar, Alzheimer's disease, beta amyloid