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(54) Title: DRUG TARGET ISOGENES: POLYMORPHISMS IN THE CHOLINERGIC RECEPTOR, MUSCARINIC 2 GENE

(57) Abstract: Polynucleotides comprising 1 novel single nucleotide polymorphism in the human cholinergic receptor, muscarinic 2 (CHRM2) gene are described. Compositions and methods for detecting this polymorphism are also disclosed. In addition, various genotypes and haplotypes for the CHRM2 gene that exist in the population are described.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/28212

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C07H 21/04; C12N 1/20, 5/00; G01N 33566
US CL :536/23.5, 24.31, 24.33; 435/252.3, 325; 436/501

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. : 536/23.5, 24.31, 24.33; 435/252.3, 325; 436/501

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)

STN: MEDLINE CAPLUS BIOSIS EMBASE BIOTECHDS
STIC SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database CAPLUS on STN, No. 123:331254, Multipoint genetic linkage analysis of the m2 human muscarinic receptor gene, abstract, Badner et al, 1995.	1-4, 6-8, 13-20
A	Database MEDLINE on STN, No. 200016844, Mapping of five subtype genes for muscarinic acetylcholine receptor to mouse chromosomes, abstract, Matsui et al, February 1999.	1-4, 6-8, 13-20
A	Database CAPLUS on STN, No. 134:158204, Suspension arrays for high throughput, multiplexed single nucleotide polymorphism genotyping, .abstract, Armstrong et al , 2000.	17-20

[X] 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

"E" earlier document 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

19 APRIL 2001

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/28212

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BONNER et al Identification of a Family of Muscarinic Acetylcholine Receptor Genes, Science 30 July 1987, Vol. 237, pages 527-532, see entire document, especially abstract, Fig. 1 on page 528, and Fig 4 on page 531.	1-4, 6-8, 13, 14, and 16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/28212

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. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims 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. ☐ 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:

Please See Extra 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.:
1-4, 6-8, 13-20

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

Group 1, claim(s)1-4,6-8,and 13-20, drawn to a method of genotyping or hapotyping the cholinergic receptor, muscarinic 2 (CHRM2) gene with polymorphic site 1 (PS1), an isolated polynucleotide comprising a nucleotide sequencewith a polymorphic variance for CHRM2 or a fragment thereof, unicellular (non-animal) organisms comprising the polynucleotides, and a composition comprising a genotyping oligonucleotide comprising PS1. Claims 4 and 8 are encompass unicellular organisms and transgenic animals. If only group 1 is elected, claims 4 and 8 will in ly be considered to the extent that they are drawn to unicellular organisms.

Group 2, claim(s) 21, drawn to a method for predicting a haplotype pair for the CHMR2 gene by identifying a CHRM2 genotype for an individual at two or more polymorphic sites.

Group 3, claims 22-24, drawn to a method for identifying an association between a trait and a genotype or haplotype comprising PS1.

Group 4, claim(s) 4, 5, 8, and 9, drawn to transgenic animals carrying a transgene comprising PS1.

Group 5, claim(s) 10, drawn to a polypeptide comprising an amino acid sequence which is a polymorphic variant of a reference sequence for CHRM2, wherein the polymorphic variant is PS1.

Group 6, claim(s) 11, drawn to an antibody which binds to the polypeptide of claim 10.

Group 7 claim(s) 12, drawn to a method of screening for drugs targeting the CHRM2 variant polypeptide of claim 10.

Groups 8 and 9, claim(s) 25 and 26, drawn to a computer system and genome anthology (database) comprising the polymorphism data of the two haplotypes in Table 4. If group 7 is selected, the computer system will be examined to the extent that it applies to the first of the two haplotypes.

The inventions listed as Groups 1-9 do not relate to a single 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 broadest recitation of the first claimed product, namely a fragment of the nucleic acid of the CHRM2 gene is known and well characterized. For example, Bonner et al (Science 237 (4814), 527-532 (1987)) teach the nucelotide sequence of the CHRM2 gene. Thus the technical feature which links the claims is not a special technical feature according to PCT Rule 13.2.

The transgenic animals of group 4, the polypeptide of group 5, the antibody of group 6, and the computer systems of groups 8 and 9 cannot be used in the method of group 1, thus these inventions are distinct. The methods of group 2, and 3 employ different method steps and reagents than the method of group 1, and cannot provide the same results, thus these inventions are distinct.