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(54) Title: HAPLOTYPE STRUCTURES OF CHROMOSOME 21

(57) Abstract: The present invention includes the use of any of the polymorphisms, SNP haplotype blocks or SNP haplotype patterns. In one embodiment, susceptibility to a phenotype resulting from an allele or marker in linkage disequilibrium with such polymorphic forms is evaluated. Novel therapeutic and diagnostic compounds and methods are also disclosed.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/26469

A. CLASSIFICATION OF SUBJECT MATTER				
IPC(7) : C07H 21/04				
US CL : 536/24.3, 24.31, 23.1				
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. : 536/24.3, 24.31, 23.1				
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)				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	NCBI Entrez database nucleotide sequences, National Center for Biotechnology Information, National Library of Medicine, NIH (Bethesda, MD, USA) Accession number NT_002836, GI: 8134249, 20 July 2000, see especially comments concerning nucleotides 21302875 (p. 6 of print out) and 21395712 (p. 7 of print out)..	1, 2, 3, 4, 5, 6		
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.				
* Special categories of cited documents: <table border="0" style="width: 100%;"> <tr> <td style="width: 50%;"> "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent 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 </td> <td style="width: 50%;"> "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 </td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent 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
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent 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		Date of mailing of the international search report		
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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 <i>Mary J. Water</i> Juliet Switzer Telephone No. 703 308 0196		

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International application No.

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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.: 1-5, with respect to species polymorphism at position 21302875
- 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 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 1, claims 1-5, drawn to isolated nucleic acids comprising SEQ ID NO: 1 and isolated nucleic acids comprising ten or more nucleotides of SEQ ID NO: 1, wherein the ten or more nucleotides overlap with a single position.

Group 2, claims 6-21, drawn to isolated nucleic acids comprising particular segments of SEQ ID NO: 1.

Group 3, claims 22-27, drawn to a database.

Group 4, claims 28-34 drawn to a method for identifying a genetic locus involved in the biological basis of a phenotypic trait.

Group 5, claims 35-38, drawn to a method for screening an individual for a predisposition.

Group 6, claims 39-41, a method for selecting a therapeutic.

Group 7, claims 42-43, drawn to kits for diagnosing disease.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Group 1, species are each of the polymorphisms listed in Figures 1 and 2. The first named invention that will be searched in this application is the first polymorphism listed in the first figure with the claims of Group 1, that is the polymorphism at position 21302875 as listed in Figure 1. There are 67 total polymorphisms listed.

Group 2, species are each of the particular nucleic acids that are recited in claims 7-21. There are 15 total specific nucleic acid sequences recited in these claims. If applicant elects to pay for the search of any or all of these please clearly identify the combinations of polymorphism desired for search by identifying the claim number.

Group 3, species are each of the polymorphisms listed in Figures 1 and 2. There are 67 total polymorphisms listed.

Group 4, species are each of the polymorphisms listed in Figures 1 and 2. There are 67 total polymorphisms listed.

Group 5, species are each of the polymorphisms listed in Figures 1 and 2. There are 67 total polymorphisms listed.

Group 6, species are each of the polymorphisms listed in Figures 1 and 2. There are 67 total polymorphisms listed.

Group 7, species are each of the polymorphisms listed in Figures 1 and 2. There are 67 total polymorphisms listed.

The inventions listed as Groups 1-7 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 invention of claim 1 (i.e. the first named invention) does not provide a special technical feature in view of the prior art. Claim 1 includes a claim to an isolated nucleic acid comprising at least 10 nucleotides of SEQ ID NO: 1, wherein said nucleic acid molecule includes at least one alternative base as listed in Figure 1 or Figure 2. Such a nucleic acid does not provide a special technical feature. The specification teaches that SEQ ID NO: 1 is a portion of a publicly available GenBank record, namely NT_002836. The first named polymorphism in Figure 1 is a polymorphism at position 21302875 of this sequence. The GenBank record teaches a polymorphism at this sequence. See the comments on p. of the printed record. Thus, the GenBank record teaches isolated nucleic acids that comprise

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either allele of the polymorphism at this position, and therefore teach an isolated nucleic acid comprising at least 10 nucleotides of SEQ ID NO: 1, wherein said nucleic acid comprises at least one alternative base as listed in Figure 1. Thus, the product of the main invention does not provide a special technical feature which joins all of the inventions of the instant application.

The special technical feature of the polynucleotides of group 2 is that each polynucleotide of group 2 is comprised of a particular combination of specific nucleotides, each of which are different from one another. There is no feature that joins each of these together.

The database of invention 3 has a technical feature in that it is itself a database. It is not joined to group 1 which is comprised of nucleic acids.

The methods of groups 4, 5, and 6 are each methods directed towards distinct goals and each have technical features of method steps that differentiate them from one another.

The products of group 7 encompass any number of reagents including restriction enzymes, nucleic acid arrays, etc.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The species are related to polymorphism and haplotypes within SEQ ID NO: 1. These are not joined by a special technical feature in view of the prior art because polymorphisms and haplotypes within SEQ ID NO: 1 were known at the time the invention was made, see above, for example.