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(54) Title: COMPUTER SYSTEMS AND METHODS FOR SUBDIVIDING A COMPLEX DISEASE INTO COMPONENT DISEASES

(57) Abstract: A method for identifying a quantitative trait loci for a complex trait that is exhibited by a plurality of organisms in a population. The population is divided into a plurality of sub-populations using a classification scheme. Depending on what is known about the population, either a supervised or unsupervised classification is used. The classification scheme is derived from a plurality of cellular constituent measurements obtained from each organism in the population. For each sub-population in the plurality of sub-populations, a quantitative genetic analysis is performed on the sub-population in order to identify one or more quantitative trait loci for the complex trait.



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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/15768

A. CLASSIFICATION OF SUBJECT MATTER
 IPC(7) : G06F 19/00
 US CL : 702/19
 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. : 702/19

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.
A	JANSEN et al. Genetical genomics: the added value from segregation. Trends in Genetics. July 2001, Vol. 17, No. 7, pages 388-391, especially page 388.	1, 2, 8-101, 106-126, 132-218, 223-245, 251-333
A	DOERGE Mapping and Analysis of Quantitative Trait Loci in Experimental Populations. Nature Reviews Genetics. January 2002, Vol. 31, pages 43-52, especially page 43.	1, 2, 8-101, 106-126, 132-218, 223-245, 251-333

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	

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/15768

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.: Please See Continuation Sheet
- 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 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:

The species of constituents are 1) transcription products, 2) translation products, and 3) metabolites.

The species of disease traits are: asthma, ataxia telangiectasia, bipolar disorder, cancer, common late-onset Alzheimer's disease, diabetes, heart disease, hereditary early-onset Alzheimer's disease, hereditary nonpolyposis colon cancer, hypertension, infection, maturity-onset diabetes of the young, mellitus, migraine, nonalcoholic fatty liver, nonalcoholic steatohepatitis, non-insulin-dependent diabetes mellitus, obesity, polycystic kidney disease, psoriasis, schizophrenia, and xeroderma pigmentosum.

The claims are deemed to correspond to the species listed above in the following manner:

For the species of constituents:

transcription product claims 2, 8, 31-68, 70, 71, 101, 106, 126, 132, 155-188, 218, 223, 245, 251, 274-307

translation product claims 2, 3, 8, 101, 106, 126, 132, 218, 223, 245, 246, 251

metabolite claims 4-8, 102-106, 128-132, 219-223, 247-251

For the species of disease traits: Markush claims 15, 113, 139, 230, 258

The following claim(s) are generic:

For the species of constituents: claims 1, 9-30, 69, 72-100, 107-125, 133-154, 189-217, 224-244, 252-273, 308-333

For the species of disease traits: claims 1-14, 16-112, 114-138, 140-229, 231-257, 259-333

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: each species of constituent is structurally different and has a different biological function. Each disease trait is a distinct and unrelated disease.

The total number of inventions was calculated based on the number of combinations that exist between the species. The formula is recited below:

Total Number of Inventions = number of species of constituents x number of disease trait species.

Continuation of Box II Item 4:

1, 2, 8-101, 106-126, 132-218, 223-245, 251-333, and transcript constituents and asthma trait species

Continuation of B. FIELDS SEARCHED Item 3:

INTERNATIONAL SEARCH REPORT

PCT/US03/15768

Medline, Biosis, US Patent publications and issued, Derwent WPI
search terms: quantitative trait locus, subpopulation