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(54) Title: CLONING AND CHARACTERIZATION OF A HUMAN CYTOCHROME P450, CYP 27C1, AND A HYBRID HOMOLOG FROM XENOPUS LAEVIS



(57) Abstract: The present invention relates to a novel cytochrome P450 protein, human CYP 27C1, and to the nucleic acid molecule comprising a nucleotide sequence encoding same. The invention also relates to species homologs thereto. A human/Xenopus laevis CYP 27C1 hybrid protein and nucleic acid molecule encoding same is also provided by the invention. In addition, the invention relates to vectors comprising the nucleic acid molecules of the invention, host cells and antibodies directed to CYP 27C1 protein and to recombinant methods directed to produce same. Furthermore, the invention relates to diagnostic and therapeutic methods for detecting and treating CYP 27C1-related disorders and to screening methods for identifying modulators, agonists and antagonists of CYP 27C1 expression and activity.



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INTERNATIONAL SEARCH REPORT

International Application No  
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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N9/02 C07K16/40 C12N15/63 C12Q1/68 G01N33/53  
A61K38/00 A61K39/00 A61K48/00

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 C12N C12Q C07K 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, BIOSIS, EMBASE, 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	OKUYAMA E. ET AL.: "A novel mutation in the cytochrome P450-27 (CYP27) gene caused cerebrotendinous xanthomatosis in a Japanese family" JOURNAL OF LIPID RESEARCH, vol. 37, no. 3, 1996, pages 631-639, XP008013912 page 635, column 1, paragraph 2 -page 636, column 2, paragraph 1; figure 3 --- -/--	34-36, 39,40

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

19 February 2003

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04/03/2003

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## INTERNATIONAL SEARCH REPORT

 In International Application No  
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EM_HUM 'Online! 29 March 2000 (2000-03-29) BIRREN B. ET AL.: "Homo sapiens clone RP11-30F3, WORKING DRAFT SEQUENCE, 40 unordered pieces" Database accession no. AC027142 XP002231763 cited in the application from bp 102501-103571 abstract ---	1,6,7
X	DATABASE EM_EST 'Online! 13 September 2000 (2000-09-13) NCI-CGAP: "dc59c04.y1 NICHD XGC Emb1 Xenopus laevis cDNA clone IMAGE:3401382 5' similar to SW:CP2B_MOUSE 035084 25-HYDROXYVITAMIN D-1 ALPHA HYDROXYLASE MITOCHONDRIAL PRECURSOR; mRNA sequence" Database accession no. BE669236 XP002231764 cited in the application abstract ---	1,6,7
E	WO 02 18558 A (MILLENNIUM PHARMACEUTICALS, INC.) 7 March 2002 (2002-03-07)  SEQ ID NO:1; SEQ ID NO:2 ---	1-3, 6-39, 41-48, 50-53, 55-57
A	WIKVALL K. : "Cytochrome P450 enzymes in the bioactivation of vitamin D to its hormonal form" INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, vol. 7, no. 2, February 2001 (2001-02), pages 201-209, XP008013916 page 205, column 2, paragraph 3 -page 206, column 2, paragraph 3; tables 1,2 -----	1-57

# INTERNATIONAL SEARCH REPORT

national application No.  
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## 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:  
  
Although claims 28,37,38 and 41 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/composition.
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:  
  
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:

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.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box I.2

Claims Nos.: 29,30,42,45,49,54-57 no search;  
26-28,34,37,41,43,44,46,48,52,53 incomplete search

Claims 26-28,37,41,44,46,52 and 53 refer in part to "modulators of CYP27C1" or generally to "substances or compounds identified using a method as claimed" without giving a true technical characterization of said modulators, substances or compounds. Moreover, no such modulators, substances or compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for those parts of the claims which are purely speculative and whose wording is, in fact, a mere recitation of the results to be achieved ( i.e. all part of claims 26-28,37,41,45,46,52 and 53 referring to such modulators, substances or compounds were not searched).

Further, present claim 30 is unclear (it contains a backreference to itself), so that no search could be carried out for said claim.

Present claim 34, which refers to a diagnostic kit, but does not name any components for a kit, was understood as "a diagnostic method for identification..." in view of the wording of claim 35.

Further, present claims 29,42 and partly claim 43 relate to methods for identifying CYP 27C1 biological activity or to methods for identifying modulators of CYP 27C1 biological activity. In the present case, the application is silent about the concrete biological activity of CYP 27C1, i.e. no substrate for CYP 27C1 is named, no reaction product for CYP 27C1 is indicated and no biological activity of the claimed CYP 27C1 has been demonstrated. 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. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the methods by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, no search was carried out for claims 29 and 42 and claim 43 has only been searched insofar as it relates to "a method of identifying a modulator of CYP 27C1 expression".

Furthermore, the search for claim 48 (which reads "a method for evaluating a compound for its ability to modulate the biological activity of 'CYP 27C1'...", but which refers in the following steps to the identification of substances that "associate" with CYP 27C1, instead of "modulate CYP 27C1 biological activity") was directed to "a method for evaluating a compound for its ability to "associate" with 'CYP 27C1'...".

Claims 49 and 54 refer to "CYP27C1 related proteins" without giving a technical characterization of said "CYP27C1 related proteins". Moreover, no such "CYP27C1 related proteins" are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

Furthermore, claim 54 is formulated as a method for doing business, which is excluded from patentability according to Rule 39.1(iii) PCT.

Present claims 55-57 relate to a product and methods defined by reference to a desirable characteristic or property, namely to a product with the property of being able to stimulate or enhance in a subject the production of antibodies against 'CYP 27C1' and to methods for stimulating or enhancing the production of antibodies against 'CYP 27C1'. The application does not specify the components of such a vaccine (except a statement that the undefined "CYP 27C1 related proteins" (see above objection) can be used to derive a vaccine therefrom; p. 80, 1.3-5). Further, claim 56 does not mention any step for carrying out the claimed method. 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. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the products and methods by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, no search has been carried out for said claims.

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/CA 02/00163

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0218558	A	AU 8699901 A	13-03-2002
		WO 0218558 A2	07-03-2002
		US 2002090699 A1	11-07-2002
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