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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ALTERNATIVELY SPLICED ISOFORMS OF HUMAN HMG CO-A REDUCTASE

(57) Abstract: The present invention features nucleic acids and polypeptides encoding novel splice variant isoforms of 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR). The polynucleotide sequences of HMGCRsv1, HMGCRsv2, HMGCRsv3, and HMGCRsv4 are provided by SEQ ID NO 1, SEQ ID NO 3, SEQ ID NO 5, and SEQ ID NO 7, respectively. The amino acid sequences for HMGCRsv1, HMGCRsv2, HMGCRsv3, and HMGCRsv4 are provided by SEQ ID NO 2, SEQ ID NO 4, SEQ ID NO 6, and SEQ ID NO 8, respectively. The present invention also provides methods for using HMGCRsv1, HMGCRsv2, HMGCRsv3, and HMGCRsv4 polynucleotides and proteins to screen for compounds that bind respectively to HMGCRsv1, HMGCRsv2, HMGCRsv3, and HMGCRsv4.

WO 2003/102209 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/16337

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12N 9/00, 9/02, 9/04; C07K 1/00
US CL : 435/183, 189, 190; 530/350
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. : 435/183, 189, 190; 530/350

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)
CAS STN, WEST, STIC protein and nucleotide databases

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	Database mRNA, Accession Number BC033692, Strausberg et al., Homo sapiens 3-hydroxy-3-methylglutaryl-Coenzyme A reductase. 06 October 2003.	1-3, 6-11, 13
A	LUSKEY et al. Human 3-hydroxy-3-methylglutaryl coenzyme A reductase. Conserved domains responsible for catalytic activity and sterol-regulated degradation. J. Biol Chem. 25 Augsust 1985, Vol. 260, No. 18, pages 10271-10277.	1-3, 6-11, 13
A	BASSON et al. Structural and functional conservation between yeast and human 3-hydroxy-3-methylglutaryl coenzyme A reductases, the rate-limiting enzyme of sterol biosynthesis. Mol. Cell. Biol. September 1988 Vol. 8, No. 9, pages 3797-808.	1-3, 6-11, 13

☐ 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 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
25 August 2004 (25.08.2004)

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/16337

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.: 1-3, 6-11, 13, SEQ ID NO: 1 and SEQ ID NO: 2

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

PCT/US03/16337

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.

Invention 1 Claim(s) 1-3, 6-11, 13, 31-33, 36-41, 43, 61-63, 66-71, 73, 91-93, 96-101, 103, drawn to a nucleic acid, an expression vector, recombinant host cell comprising said expression vector, and a method for preparing a polypeptide.

Invention 2 Claim(s) 4, 5, 34, 35, 64, 65, 94, 95, drawn to a purified polypeptide.

Invention 3 Claim(s) 12, 42, 72, 102 , drawn to a purified antibody.

Invention 4 Claim(s) 14-18, 44-48, 74-78, 104-108, drawn to a method for screening for compound able to bind to a polypeptide.

Invention 5 Claim(s) 19-21, 49-51, 79-81, 109-111, drawn to a method for screening for a compound able to bind selectively to a polypeptide.

Invention 6 Claim(s) 22-29, 52-59, 82-89, 112-119, drawn to a method of screening for a compound able to bind to or interact with a polypeptide.

Invention 7 Claim(s) 30, 60, 90, 120, drawn to a method for screening for HMG CoA reductase activity.

The inventions listed as Inventions 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 technical feature shared by Inventions 1-7 is a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. However, the this feature has already been taught in the prior art by US 5,460,949.

US 5,460,949 teach a hamster HGM-CoA reductase (Accession ABP60398) that shares significant structural homology with SEQ ID NO: 2, where the amino acid sequence of the said hamster HGM-CoA reductase has 92.3% identity to SEQ ID NO: 2 (see attached alignment).

Since this technical feature was known in the prior art, it is not special and therefore cannot form the contribution that the group of inventions as a whole makes over the prior art.

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.

Species 1 SEQ ID Nos: 1 and 2
Species 2 SEQ ID Nos: 3 and 4
Species 3 SEQ ID Nos: 5 and 6
Species 4 SEQ ID Nos: 7 and 8

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 common technical feature between each of SEQ ID Nos: 1-8 (even-numbers) is a that they are functionally HMG-CoA reductases with structurally similar amino acid sequences. However, this feature has already been taught in the prior art by US 5,460,949.

US 5,460,949 teach a hamster HGM-CoA reductase (Accession ABP60398) that shares significant structural homology with SEQ ID NO: 2, where the amino acid sequence of the said hamster HGM-CoA reductase has 92.3% identity to SEQ ID NO: 2 (see attached alignment).

Since this technical feature was known in the prior art, it is not special and therefore the shared functional and structural similarity between SEQ ID Nos: 1-8 (even numbers) cannot form the contribution that the group of inventions as a whole makes over the prior art.