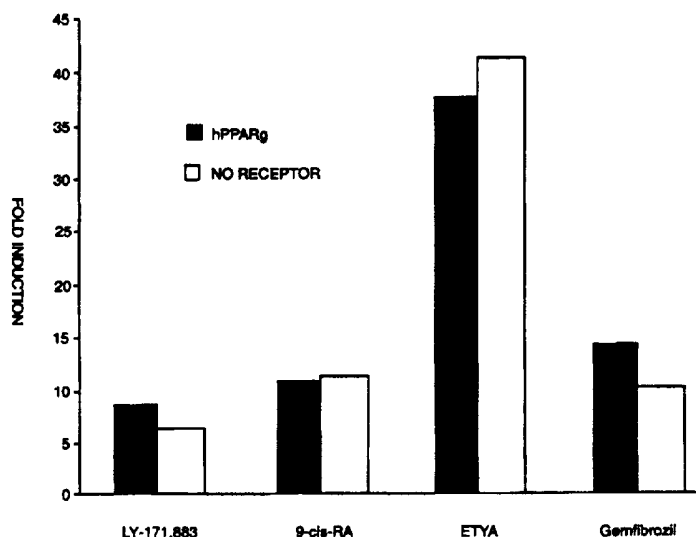




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification⁶ : C12N 15/12, C07K 14/705, C12Q 1/68, C07K 16/28, A61K 38/16, A01K 67/027, A61K 48/00</p>	<p>A3</p>	<p>(11) International Publication Number: WO 96/23884 (43) International Publication Date: 8 August 1996 (08.08.96)</p>
<p>(21) International Application Number: PCT/US96/01469 (22) International Filing Date: 29 January 1996 (29.01.96) (30) Priority Data: 08/380,051 30 January 1995 (30.01.95) US 08/484,487 7 June 1995 (07.06.95) US 60/005,809 23 October 1995 (23.10.95) US (71) Applicant: LIGAND PHARMACEUTICALS INCORPORATED [US/US]; 9393 Towne Centre Drive, San Diego, CA 92121 (US). (72) Inventor: MUKHERJEE, Ranjan; 11341 Avenida de Los Lobos, San Diego, CA 92127 (US). (74) Agents: CHEN, Anthony, C. et al.; Lyon & Lyon, First Interstate World Center, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-2066 (US).</p>	<p>(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AZ, BY, KG, KZ, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 3 October 1996 (03.10.96)</p>	

(54) Title: HUMAN PEROXISOME PROLIFERATOR ACTIVATED RECEPTORS



(57) Abstract

The present invention relates to two novel peroxisome proliferator activated receptor subtypes, hPPAR γ and hPPAR γ 2. hPPAR γ and hPPAR γ 2 differ from mouse peroxisome proliferator activated receptor γ in nucleotide sequence and amino acid sequence. The invention provides isolated, purified, or enriched nucleic acid encoding hPPAR γ or hPPAR γ 2 polypeptides and vectors containing thereof, cells transformed with such vectors, and method of screening for compounds capable of binding hPPAR γ or hPPAR γ 2 polypeptides. The invention also provides isolated, purified, enriched, or recombinant hPPAR γ or hPPAR γ 2 polypeptides, antibodies having specific binding affinity to hPPAR γ or hPPAR γ 2 polypeptides, and hybridomas producing such antibodies.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/01469

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/705 C12Q1/68 C07K16/28 A61K38/16
A01K67/027 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 6 C12N C07K C12Q A61K A01K

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CELL, vol. 79, 30 December 1994, pages 1147-1156, XP000577080 P. TONTOZ ET AL.: "Stimulation of adipogenesis in fibroblasts by PPARGamma2, a lipid activated transcription factor" cited in the application see the whole document ---	1-64
Y	GENES & DEVELOPMENT, vol. 8, 15 May 1994, pages 1224-1234, XP000577698 P. TONTOZ ET AL.: "mPPARGamma2: tissue-specific regulator of an adipocyte enhancer" cited in the application see the whole document ---	1-64
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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents:

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Date of the actual completion of the international search

9 August 1996

Date of mailing of the international search report

19. 08. 96

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Hix, R

INTERNATIONAL SEARCH REPORT

International Application No.

PL./US 96/01469

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BIOCHEM. AND BIOPHY. RES. COM., vol. 196, no. 2, 29 October 1993, pages 671-677, XP000577084 F. CHEN ET AL.: "Identification of two mPPAR related recetpros and evidence for the existence of five subfamily members." cited in the application see the whole document ---	1-64
Y	JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 268, no. 36, 25 December 1993, pages 26817-26820, XP000577081 Y. ZHU ET AL.: "Cloning of a new member of the peroxisome proliferator-activated receptor gene family from mouse liver." cited in the application see the whole document ---	1-64
Y	PROC. NATL. ACAD. SCI. USA., vol. 91, 19 July 1994, pages 7355-7359, XP000577088 S.A. KLIEWER ET AL.: "Differential expression and activation of a family of murine peroxisome proliferator-activated receptors." cited in the application see the whole document ---	1-64
Y	BIOCHEMISTRY, vol. 32, 1 June 1993, pages 5598-5604, XP000577090 T. SHER ET AL.: "cDNA cloning, chromosomal mapping, and functional characterization of the Human Peroxisome Proliferator Activated Receptor" cited in the application see the whole document ---	1-64
P,X	GENE EXPRESSION, vol. 4, 1995, pages 281-299, XP002010541 M.E. GREENE ET AL.: "Isolation of the Human Peroxisome Proliferator Activated Receptor Gamma cDNA: expression in Hematopoietic cells and chromosomal mapping" see the whole document ---	1-64
P,Y	WO,A,96 01317 (SALK INST FOR BIOLOGICAL STUDI) 18 January 1996 see the whole document ---	1-64
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INTERNATIONAL SEARCH REPORT

International Application No

Pct/US 96/01469

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GENE, vol. 162, 1995, pages 297-302, XP000577149 C. APERLO ET AL.: "cDNA cloning and characterization of the transcriptional activities of the hamster peroxisome proliferator-activated receptor haPPARgamma" see the whole document ---	1-64
P,X	WO,A,95 11974 (LIGAND PHARM INC) 4 May 1995 see the whole document ---	1-64
P,Y	EIGHTY-SIXTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, TORONTO, ONTARIO, CANADA, MARCH 18-22, 1995. PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING 36 (0). 1995. 520. ISSN: 0197-016X, XP002010542 ZHU Y ET AL: "Mouse PPAR- gamma gene: Genomic organization and promoter analysis." see the whole document ---	1-64
Y	ANNU. REV. BIOCHEM. , vol. 64, 1995, pages 345-73, XP000577985 O.A. MACDOUGALD ET AL.: "Transcriptional regulation of gene expression during adipocyte differentiation" see page 365 - page 366 ---	1-64
T	MUTATION RESEARCH, vol. 333, no. 1-2, 1995, pages 101-109, XP000577705 S. GREEN: "PPAR: a mediator of peroxisome proliferator action" see page 104, column 1, paragraph 2 -----	1-64

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/01469

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.: 40 and 41
because they relate to subject matter not required to be searched by this Authority, namely:
Although these claims are directed to a method of treatment of (diagnostic method practised on) 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:
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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 96/01469

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9601317	18-01-96	AU-B- 2952695	25-01-96
WO-A-9511974	04-05-95	AU-B- 8083194	22-05-95
		EP-A- 0724636	07-08-96