

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 356022D27145	<b>FOR FURTHER ACTION</b>		see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/EP2010/050723	International filing date (day/month/year) 22/01/2010	(Earliest) Priority Date (day/month/year) 22/01/2009	
Applicant  CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE...			

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- the international application in the language in which it was filed  
 a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b.  This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c.  With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2.  **Certain claims were found unsearchable** (See Box No. II)

3.  **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- the text is approved as submitted by the applicant  
 the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant  
 the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 1  
 as suggested by the applicant  
 as selected by this Authority, because the applicant failed to suggest a figure  
 as selected by this Authority, because this figure better characterizes the invention
- b.  none of the figures is to be published with the abstract

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2010/050723

## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. (means)
    - on paper
    - in electronic form
  - b. (time)
    - in the international application as filed
    - together with the international application in electronic form
    - subsequently to this Authority for the purpose of search
2.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

**INTERNATIONAL SEARCH REPORT**

International application No  
PCT/EP2010/050723

**A. CLASSIFICATION OF SUBJECT MATTER**  
 INV. C07K14/72 C12N9/00 C12N15/90 C12N9/90  
 ADD.

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)  
 C07K C12N

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, BIOSIS, Sequence Search, EMBASE, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2006/199250 A1 (ZHAO HUIMIN [US] ET AL) 7 September 2006 (2006-09-07) cited in the application figures 3-5; examples	1-26
Y	CHOCKALINGAM KARUPPIAH ET AL: "Directed evolution of specific receptor-ligand pairs for use in the creation of gene switches" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA. (PNAS), NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 102, no. 16, 19 April 2005 (2005-04-19), pages 5691-5696, XP002508545 ISSN: 0027-8424 cited in the application the whole document	1-26

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 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  <b>31 March 2010</b>	Date of mailing of the international search report  <b>12/04/2010</b>
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  <b>Madruga, Jaime</b>
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## INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2010/050723

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	EP 1 692 936 A1 (GIE CERBM CT EUROP DE RECH EN [FR]) 23 August 2006 (2006-08-23) cited in the application the whole document	16-18, 20-26 1-26
Y	----- FEIL ROBERT ET AL: "Regulation of Cre recombinase activity by mutated estrogen receptor ligand-binding domains" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 237, no. 3, 1 January 1997 (1997-01-01), pages 752-757, XP002144708 ISSN: 0006-291X cited in the application the whole document	1-26
A	----- WO 02/097050 A2 (NOVARTIS AG [CH]; BRACKEN KATHRYN RENE [US]; DE LOS ANGELES JOSEPH E []) 5 December 2002 (2002-12-05) the whole document	1-26
A	----- EKENA K ET AL: "Identification of amino acids in the hormone binding domain of the human estrogen receptor important in estrogen binding" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, INC, US, vol. 33, no. 271, 16 August 1996 (1996-08-16), pages 20053-20059, XP002075903 ISSN: 0021-9258 the whole document	1-26
A	----- ISLAM KAZI MOHAMMED DIDARUL ET AL: "Directed evolution of estrogen receptor proteins with altered ligand-binding specificities" PROTEIN ENGINEERING DESIGN & SELECTION, vol. 22, no. 1, 1 January 2009 (2009-01-01), pages 45-52, XP002575645 ISSN: 1741-0126 the whole document	1-26
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2010/050723

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>EKENA KIRK ET AL: "Different residues of the human estrogen receptor are involved in the recognition of structurally diverse estrogens and antiestrogens" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 8, 1997, pages 5069-5075, XP002575646 ISSN: 0021-9258 the whole document</p> <p>-----</p>	1-26
A	<p>BUSH S M ET AL: "Use of the yeast one-hybrid system to screen for mutations in the ligand-binding domain of the estrogen receptor" STEROIDS, ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, US, vol. 61, no. 3, 1 March 1996 (1996-03-01), pages 102-109, XP004026431 ISSN: 0039-128X the whole document</p> <p>-----</p>	1-26
A	<p>ANSTEAD G M ET AL: "The estradiol pharmacophore: Ligand structure-estrogen receptor binding affinity relationships and a model for the receptor binding site" STEROIDS, ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, US, vol. 62, no. 3, 1 March 1997 (1997-03-01), pages 268-303, XP004057108 ISSN: 0039-128X the whole document</p> <p>-----</p>	1-26
A	<p>EKENA KIRK ET AL: "Determinants of ligand specificity of estrogen receptor-alpha: Estrogen versus androgen discrimination" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 2, 9 January 1998 (1998-01-09), pages 693-699, XP002575647 ISSN: 0021-9258 the whole document</p> <p>-----</p>	1-26

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/EP2010/050723
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Patent document cited in search report	Publication date	Publication date	Patent family member(s)	Publication date
US 2006199250	A1	07-09-2006	NONE	
EP 1692936	A1	23-08-2006	NONE	
WO 02097050	A2	05-12-2002	AT 403676 T	15-08-2008
			AU 2002303903 A1	09-12-2002
			EP 1397382 A2	17-03-2004
			EP 2060582 A1	20-05-2009
			JP 2004537293 T	16-12-2004