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- (71) Applicant (for all designated States except US): GENE EXPRESSION TECHNOLOGIES LIMITED [GB/GB]; 90 Fetter Lane, London EC4A 1JP (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): BULUWELA, Lakjaya [GB/GB]; Imperial College School of Medicine,

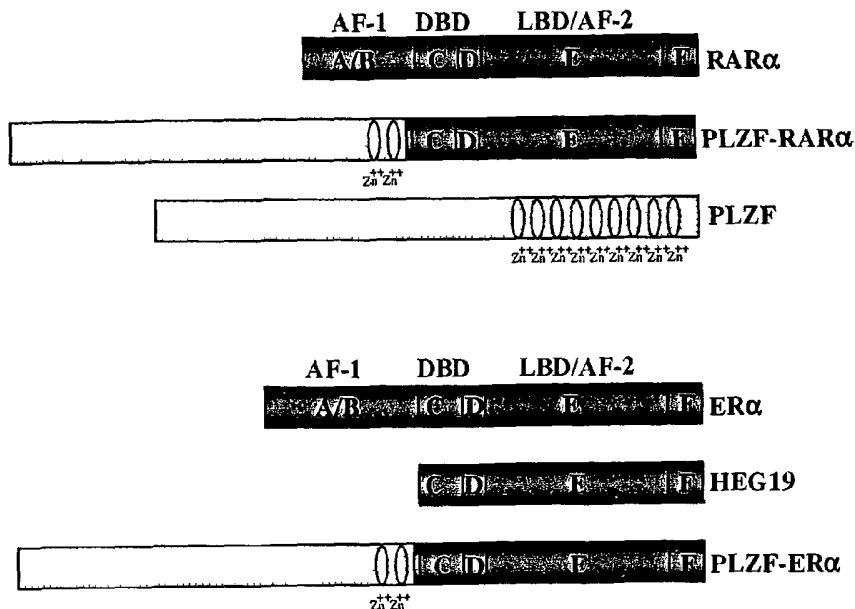
Dept. of Cancer Medicine, Du Cane Road, London W12 0NN (GB). **HOLMES, David** [GB/GB]; Imperial College School of Medicine, Dept. of Cancer Medicine, Du Cane Road, London W12 0NN (GB). **KAMALATI, Tahereh** [GB/GB]; Imperial College School of Medicine Dept. of Cancer Medicine, Du Cane Road, London W12 0NN (GB). **WAXMAN, Jonathan** [GB/GB]; Imperial College School of Medicine, Dept. of Cancer Medicine, Du Cane Road, London W12 0NN (GB). **ALI, Simak** [GB/GB]; Imperial College School of Medicine, Dept. of Cancer Medicine, Du Cane Road, London W12 0NN (GB).

(74) Agent: MILES, John, S.; Eric Potter Clarkson, Park View House, 58 The Ropewalk, Nottingham NG1 5DD (GB).

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[Continued on next page]

(54) Title: CONTROL OF GENE EXPRESSION



(57) Abstract: A method of suppressing the expression of a selected endogenous gene in a eukaryotic cell the method comprising introducing into the cell (a) a polypeptide comprising a nucleic acid binding portion which binds to a site at or associated with the selected gene and a modifying portion which comprises a polypeptide or peptidomimetic which is capable of modulating covalent modification of nucleic acid or chromatin, for example a chromatin inactivation portion, or (b) a polynucleotide encoding said polypeptide. The binding of the molecule to nucleic acid may be modulated by a ligand and the molecule may comprise a ligand binding portion. The nucleic acid binding portion may be a nucleic acid binding portion of a nuclear receptor DNA binding protein.



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**Published:**

— *with international search report*

*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.*

**INTERNATIONAL SEARCH REPORT**

International Application No  
PCT/GB 02/03336

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 C12N15/11 C07K14/47 C12N15/67 A61K38/16 A61K47/48  
 C12N5/10 A01K67/027 C12N15/82

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 C07K 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)  
 EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CH IEN P-Y ET AL: "A FUSION PROTEIN OF THE ESTROGEN RECEPTOR (ER) AND NUCLEAR RECEPTORCOREPRESSOR (NCOR) STRONGLY INHIBITS ESTROGEN-DEPENDENT RESPONSES IN BREAST CANCER CELLS" MOLECULAR ENDOCRINOLOGY, BALTIMORE, MD, US, vol. 13, no. 12, December 1999 (1999-12), pages 2122-2136, XP000978743 ISSN: 0888-8809 the whole document	1-57
X	WO 01 02019 A (IMP COLLEGE INNOVATIONS LTD ;ALI SIMAK (GB); BULUWELA LAKJAYA (GB)) 11 January 2001 (2001-01-11)  the whole document	1-16, 28-32, 35-39, 58-60

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.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search  12 March 2003	Date of mailing of the international search report  28/03/2003
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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, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  Seranski, P
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## INTERNATIONAL SEARCH REPORT

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PC 17 GB 02/03336

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>MANTEUFFEL-CYMBOROWSKA MALGORZATA:            "Nuclear receptors, their coactivators and modulation of transcription."            ACTA BIOCHIMICA POLONICA,            vol. 46, no. 1, 1999, pages 77-89,            XP009005858            ISSN: 0001-527X            page 83 -page 84</p> <p style="text-align: center;">---</p>	<p>17-27,            32-57</p>
A	<p>RAZIN AHARON: "CpG methylation, chromatin structure and gene silencing - a three-way connection."            EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL,            vol. 17, no. 17, pages 4905-4908,            XP002233552            ISSN: 0261-4189            the whole document</p> <p style="text-align: center;">-----</p>	<p>1-16,            28-32,            35-39,            58-60</p>

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 02/03336

## 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:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
2.  Claims Nos.: 58-60  
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.1

Although claims 1-21, 24-30, 32, 33, 35-39, 46-48, 53-55, 56 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.

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Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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Continuation of Box I.2

Claims Nos.: 58-60

Present claims 58-60 relate to an extremely large number of possible products and methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds and methods claimed. 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. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the products and methods methods of claims 1-57.

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/GB 02/03336

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0102019 A	11-01-2001	AU 5556600 A	22-01-2001
		EP 1190073 A2	27-03-2002
		WO 0102019 A2	11-01-2001
		GB 2367555 A	10-04-2002
		JP 2003503082 T	28-01-2003

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