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Bidea-Edificio 801A 2a Planta, Parque Tecnológico de Zamudio, E-48160 Derio (ES).

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(54) Title: METHOD FOR PROGNOSING OSTEOPOROSIS PHENOTYPES

(57) Abstract: A method for prognosing osteoporosis phenotypes or estimating osteoporosis quantitative traits comprising determining outcomes for selected SNP variables and clinical variables. Products and methods for genotyping multiple osteoporosis associated genetic variations.



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# INTERNATIONAL SEARCH REPORT

International application No  
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<b>A. CLASSIFICATION OF SUBJECT MATTER</b> INV. C12Q1/68		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) C12Q		
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, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/15836 A (SIGNALGENE INC [CA]; ROUSSEAU FRANCOIS [CA]) 23 March 2000 (2000-03-23) see whole doc. esp. claims and examples -----	1-108
X	WO 97/27321 A (UNIV LAVAL [CA]) 31 July 1997 (1997-07-31) see whole doc. esp. claims and p.3,1.1 ff. -----	1-108
X	US 2006/057612 A1 (STYRKARSDOTTIR UNNUR [IS] ET AL) 16 March 2006 (2006-03-16) see whole doc. esp. claims and par.137 ff. -----	1-108
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<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.		
<input checked="" type="checkbox"/> 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. *G* document member of the same patent family	
Date of the actual completion of the international search  <p style="text-align: center;">18 April 2008</p>	Date of mailing of the international search report  <p style="text-align: center;">27/05/2008</p>	
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  <p style="text-align: center;">Mueller, Frank</p>	

## INTERNATIONAL SEARCH REPORT

 International application No  
 PCT/IB2007/002363

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KOBAYASHI S ET AL: "ASSOCIATION OF BONE MINERAL DENSITY WITH POLYMORPHISM OF THE ESTROGEN RECEPTOR GENE" JOURNAL OF BONE AND MINERAL RESEARCH, NEW YORK, NY, US, vol. 11, no. 3, 1 March 1996 (1996-03-01), pages 306-311, XP000671392 ISSN: 0884-0431 the whole document	1-108
X	GENNARI L ET AL: "Estrogen receptor gene polymorphisms and the genetics of osteoporosis: a HuGE review" AMERICAN JOURNAL OF EPIDEMIOLOGY, SCHOOL OF HYGIENE & PUBLIC HEALTH OF THE JOHNS, US, vol. 161, no. 4, 15 February 2005 (2005-02-15), pages 307-320, XP002357226 ISSN: 0002-9262 the whole document	1-108
X	WO 2004/097044 A (OXAGEN LTD [GB]; BENNETT . SIMON THOMAS [GB]; EDWARDS MARK [GB]) 11 November 2004 (2004-11-11) see whole doc. esp. claims and examples	1-108
X	WO 2004/046381 A (UNIV ABERDEEN [GB]; RALSTON STUART [GB]) 3 June 2004 (2004-06-03) see whole doc. esp. claims	1-108
X	IOANNIDIS J.P.A. ET AL.,: "Differential genetic effects of the ESR1 gen polymorphisms on osteoporosis outcomes" JAMA, vol. 292, no. 17, 3 November 2004 (2004-11-03), pages 2105-2114, XP002466770 see whole doc. esp. p.2106, 1.col.	1-108
X	SHIELDS J.J. ET AL.,: "DraII and XmnI polymorphisms at the human parathyroid hormone locus" NUCLEIC ACID RESEARCH, vol. 19, no. 15, 1992, pages 4312-4312, XP002476932 the whole document	1-108

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2007/002363

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HOSOI T. ET AL.,: "association study of parathyroid hormone gene polymorphism and bone density in japanese postmenopausal women" CALCIF. TISSUE INT., vol. 64, 1999, pages 205-208, XP002476933 the whole document -----	1-108
X	KATSUMATA K. ET AL.,: "association of gene polymorphisms and bone density in japanese girls" J BONE MINER METAB, vol. 20, 2002, pages 164-169, XP002476934 the whole document -----	1-108

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2007/002363

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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 18,82 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.: 19,58 (part)  
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 No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
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.:  

1-108 (part)
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 and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box II.1

Although claims 18,82 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.

## Continuation of Box II.2

Claims Nos.: 19,58 (part)

The present claims 19,58, relates to an extremely large number of possible methods by using different probe pairs. Support and disclosure in the sense of Article 6 and 5 PCT is to be found however for a restricted number of probes used in the methods claimed, see [e.g. Tables 2 and 3]. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 19 and 58 (PCT Guidelines 9.19 and 9.23).

The search of claims 19 and 58 was restricted to those claimed methods which appear to be supported by using probe sequences which are clearly defined by structural features, see Tables 2 and 3 and which are used for genotyping the genes listed in Table 1.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.

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

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-108 (part)

Probes, primers, microarrays and method for prognosing, genotyping and treating osteoporosis using polymorphism rs2234693 of estrogen receptor (ESR1) in Fig.9

Inventions 2-112: claims 1-108 (part)

Probes, primers, microarrays and method for prognosing, genotyping and treating osteoporosis using polymorphism listed in Fig.9 and Table 5, for each polymorphism in an identified gene separately, Table has been identified to refer to 57 different genes and 112 SNPs, see page 15, lines 21-31

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/IB2007/002363
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Patent document cited in search report	A	Publication date	Patent family member(s)	Publication date
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