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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: GLYCOPROTEINS AND METHODS OF USE THEREOF

MKLAFLLLG P MALLLLAGYG CLGASSGNLR TFGCAVREF TFLAKKPGCR
GLRITTDACW GRCETWEKPI LEPPYIEAHH RVCTYNETKQ VTKLPLNCAP
GVDPFYTYPV AIRCDCGACS TATTECETI (SEQ ID NO: 2)

MNKKRVKFPV LQLLVLLALCL STAAGSNISL RTFIGCAVRE FTFLAKKPGC
RGLRVTTDAC WGRCETCEKP SLDPYIEAH HRVCTYNETK LVTVILLPNC
SPDIDPFFTY PVAIRCDCMW STSTTEC (SEQ ID NO: 4)

(57) Abstract: The present invention provides novel isolated ARP/BRP polynucleotides and the membrane-associated or secreted polypeptides encoded by the ARP/BRP polynucleotides. Also provided are ARP and BRP protein multimers. Further provided are the antibodies that immunospecifically bind to a ARP/BRP polypeptide or any derivative, variant, mutant or fragment of the ARP/BRP polypeptide, a ARP/BRP multimer polynucleotide or antibody. The invention additionally provides methods in which the ARP/BRP polypeptide, multimer, polynucleotide and antibody are utilized in the detection and treatment of a broad range of pathological states, *e.g.* reproductive disorder, as well as to other uses.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07K14/59 C12N15/12 C07K16/26 G01N33/50 A61K31/7088 A61K39/395 A61K38/24		
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 C07K C12N G01N		
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.
X	DATABASE EMBL 'Online! CLIFTON, S. ET AL.: "db40d09.y1 Blackshear/Soares normalized Xenopus egg library Xenopus laevis cDNA clone IMAGE:3300977 5' similar to SW:GTHB_CYP CA P01235 GONADOTROPIN BETA CHAIN PRECURSOR. '2! SW:GTHB_CYPCA ;, mRNA sequence." Database accession no. BE131943 XP002210859	1-20, 22, 24-40
Y	the whole document --- -/--	1-22, 24-40
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> 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	"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	
"E" earlier document but published on or after the international filing date	"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	
"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)	"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.	
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	
"P" document published prior to the international filing date but later than the priority date claimed		
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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 Smalt, R	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE EMBL 'Online! 24 September 1999 (1999-09-24) HEILIG, R. ET AL.: "Human chromosome 14 DNA sequence BAC C-2011M8 of library CalTech-D from chromosome 14 of Homo sapiens (Human)" Database accession no. AL118555 XP002210860 cited in the application see nt 112862-113119 ---	1-20, 22, 24-40
X	WO 96 05224 A (UNIV WASHINGTON) 22 February 1996 (1996-02-22)	31, 33, 35-40
Y	the whole document	21
X	WO 00 23473 A (BEN MENAHEM DAVID ;BOIME IRVING (US); UNIV WASHINGTON (US)) 27 April 2000 (2000-04-27) the whole document ---	21, 31, 33, 35-40
X	WO 99 41377 A (ZYMOGENETICS INC) 19 August 1999 (1999-08-19) the whole document ---	23, 31, 33, 35-40
X	US 5 508 261 A (CAMPBELL ROBERT K ET AL) 16 April 1996 (1996-04-16) the whole document ---	23, 31, 33, 35-40
A	NARAYAN PREMA ET AL: "A biologically active single chain human chorionic gonadotropin analog with altered receptor binding properties." ENDOCRINOLOGY, vol. 141, no. 1, January 2000 (2000-01), pages 67-71, XP008007175 ISSN: 0013-7227 the whole document ---	
P,X	WO 01 53346 A (AKZO NOBEL NV ;MOSELNAN SIETSE (NL); SPEK VAN DER PETRUS JOHANNES) 26 July 2001 (2001-07-26) the whole document ---	1-40
P,X	WO 01 44475 A (FUJII RYO ;HOSOYA MASAKI (JP); FUKUSUMI SHOJI (JP); HINUMA SHUJI () 21 June 2001 (2001-06-21) the whole document ---	1-40
P,X	WO 01 40291 A (BURGESS CATHERINE E ;PRAYAGA SUDHIRDAS K (US); MEZES PETER S (US);) 7 June 2001 (2001-06-07) see NOVGON ---	1-40
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International Application No

PCT/US 01/25240

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 73034 A (AMGEN INC) 4 October 2001 (2001-10-04) the whole document ----	1-40
E	WO 01 60850 A (MURDOCH PAUL R ; SMITHKLINE BEECHAM PLC (GB); SMITHKLINE BEECHAM CO) 23 August 2001 (2001-08-23) see sbghGTa ----	1-40
E	WO 02 30978 A (REGENERON PHARMA) 18 April 2002 (2002-04-18) the whole document ----	1-40
E	WO 01 85783 A (CAMPBELL ROBERT K ; SERONO INC (US); TAYAR NABIL EL (US)) 15 November 2001 (2001-11-15) the whole document -----	23, 31, 33, 35-40

INTERNATIONAL SEARCH REPORT

International application No.
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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:

Although claims 31 and 32 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.:
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:

see additional 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.:

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

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

1. Claims: 1-22, 24-30, 32, and 34 completely, and claims 23, 31, 33, 35-40 partially

Beta related protein (BRP) from human and Xenopus according to seq.ID's 1-4 and homologs thereof and their complexes, antibodies directed thereto, methods for their production, and their uses in treatment and diagnosis.

2. Claims: 23, 31, 33, 35-40, all partially

Alpha related protein (ARP) (e.g. according to seq.ID.18) and complexes thereof, nucleic acids encoding them, and their diagnostic and pharmaceutical uses.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9605224	A	22-02-1996	AU 703718 B2	01-04-1999
			AU 3206695 A	07-03-1996
			BR 9506313 A	05-08-1997
			CA 2173750 A1	22-02-1996
			CN 1131952 A	25-09-1996
			EP 0725795 A1	14-08-1996
			FI 961600 A	11-04-1996
			HU 75900 A2	28-05-1997
			JP 9505741 T	10-06-1997
			NO 961433 A	11-06-1996
			TR 960134 A2	21-06-1996
			WO 9605224 A1	22-02-1996
			US 6242580 B1	05-06-2001
			US 5705478 A	06-01-1998
			US 5958737 A	28-09-1999
			US 6028177 A	22-02-2000
US 6238890 B1	29-05-2001			
WO 0023473	A	27-04-2000	AU 1107200 A	08-05-2000
			BR 9914670 A	05-02-2002
			CN 1330665 T	09-01-2002
			CZ 20011388 A3	17-10-2001
			EP 1123315 A1	16-08-2001
			HU 0103760 A2	28-01-2002
			JP 2002533300 T	08-10-2002
			NO 20011925 A	18-06-2001
			PL 347375 A1	08-04-2002
			TR 200101463 T2	22-10-2001
			WO 0023473 A1	27-04-2000
			WO 9941377	A
CA 2320391 A1	19-08-1999			
EP 1053324 A1	22-11-2000			
JP 2002503467 T	05-02-2002			
WO 9941377 A1	19-08-1999			
US 5508261	A	16-04-1996	AT 193540 T	15-06-2000
			DE 69231129 D1	06-07-2000
			EP 0673383 A1	27-09-1995
			WO 9222568 A1	23-12-1992
WO 0153346	A	26-07-2001	AU 3732001 A	31-07-2001
			BR 0107655 A	15-10-2002
			WO 0153346 A1	26-07-2001
			EP 1254175 A1	06-11-2002
WO 0144475	A	21-06-2001	AU 1891301 A	25-06-2001
			EP 1239039 A1	11-09-2002
			WO 0144475 A1	21-06-2001
			JP 2001299362 A	30-10-2001
WO 0140291	A	07-06-2001	AU 1817201 A	12-06-2001
			EP 1259538 A2	27-11-2002
			WO 0140291 A2	07-06-2001
			US 2002068279 A1	06-06-2002
WO 0173034	A	04-10-2001	AU 4785801 A	08-10-2001
			WO 0173034 A2	04-10-2001

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/25240

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0173034	A		US 2002015981 A1	07-02-2002
WO 0160850	A	23-08-2001	AU 3976501 A	27-08-2001
			EP 1255771 A1	13-11-2002
			WO 0160850 A1	23-08-2001
WO 0230978	A	18-04-2002	WO 0230978 A1	18-04-2002
			AU 8001900 A	22-04-2002
WO 0185783	A	15-11-2001	AU 6137001 A	20-11-2001
			WO 0185783 A2	15-11-2001