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US 60/160,096 (CIP) Filed on 15 October 1999 (15.10.1999) (71) Applicant (for all designated States except US): ORCHID BIOSCIENCES, INC. [US/US]; 303 College Road East, Princeton, NJ 08540 (US).

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[Continued on next page]

(54) Title: GENOTYPING REAGENTS, KITS AND METHODS OF USE THEREOF

Diagram of GBA Process



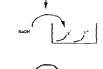
STEP 2: TargEx



STEP 3: HYBRIDIZATION



STEP 4: EXTENSION



STEP 5: DETECTION



substrace

11411

signal



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(57) Abstract: The present invention provides oligonucleotides that can be used to determine the presence, absence or identity of a single nucleotide polymorphism (SNP), kits containing such oligonucleotides, and methods of genotyping a nucleic acid sample using such oligonucleotides.

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IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK (utility model), SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

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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

tonal Application No

A. CLASS IPC 7	IFICATION OF SUBJECT MATTER C12Q1/68		,
According to	o International Patent Classification (IPC) or to both national cla	scification and IPC	
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	ocumentation searched (classification system followed by classification sy	fication symbols)	
IPC 7	C12Q		
Documenta	tion searched other than minimum documentation to the extent t	hat such documents are includ	ed in the fields searched
Electronic d	ata base consulted during the international search (name of dat	a base and, where practical, s	earch terms used)
EPO-In	ternal, SEQUENCE SEARCH, EMBL		
C DOCUME	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of th	a relevant nassanes	Relevant to claim No.
Category	Chairm of document, with indication, where appropriate, or an	- relevant passages	nelevant to Gain No.
X ·	NIKIFOROV T T ET AL: "Genetic Bit Analysis: A solid phase method for typing single nucleotide polymorphisms" NUCLEIC ACIDS RESEARCH,		18-29
	vol. 22, no. 20, 11 October 1994 (1994-10-11), 4167-4175, XP000606174 the whole document	pages	
P,A	DATABASE EMBL [Online] 22 December 1999 (1999-12-22) "SHGC-140185, human Homo sapiens STS genomic, sequence tagged site" Database accession no. G62521 XP002191442 SEQ ID 4 is at 179-229		1-17,30
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X Further documents are listed in the continuation of box C. Patent family members are list		nbers are listed in annex.	
° Special categories of cited documents : "T" lat		"T" later document publish	ed after the international filing date of in conflict with the application but
"A" documer	nt defining the general state of the art which is not rred to be of particular relevance	cited to understand th	of in conflict with the application but be principle or theory underlying the
"E" earlier document but published on or after the international			relevance; the claimed invention
"L" document which may throw doubts on priority claim(s) or		involve an inventive s	novel or cannot be considered to tep when the document is taken alone
citation	s cited to establish the publication date of another or other special reason (as specified)	cannot be considered	relevance; the claimed invention to involve an inventive step when the
other m		ments, such combina	d with one or more other such docu- tion being obvious to a person skilled
"P" documer later tha	nt published prior to the international filing date but an the priority date claimed	in the art. "&" document member of t	he same patent family
Date of the a	ctual completion of the international search	Date of mailing of the	nternational search report
26	5 February 2002	0 5	06. 02
Name and mailing address of the ISA Authorized officer			
	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	Teyssier	, В

INTERNATIONAL SEARCH REPORT

nal Application No
PCT/US 00/28436

	PCI/US 00/20430				
C.(Continua Category °	ntinuation) DOCUMENTS CONSIDERED TO BE RELEVANT ory Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No.				
P,A	DATABASE EMBL [Online] 22 December 1999 (1999-12-22) "SHGC-140184, human Homo sapiens STS genomic, sequence tagged site" Database accession no. G62520 XP002191443 The complementary strand of SEQ ID 4, with C->A polymorphism at position 26, is at		1-17,30		
	C->A polymorphism at position 26, is at 258-308.				
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INTERNATIONAL SEARCH REPORT

PCT/US 00/28436

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:					
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. X 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.: Invention 0: 1-27 and 30 partially; invention 935, claim 28, 29					
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:

Inventions n=0 to n=934: claims 1-27 and 30, all partially

A SNP site SEQ ID 4n+4, a genotyping reagent SEQ ID 4n+3, amplification primers SEQ ID 4n+1 and 4n+2, fragments or complementary strands therof; kits comprising these oligonucleotides; a method of genotyping using these oligonucleotides.

Invention 935: claims 28 and 29

A mixture of reagents and a method of amplifying a nucleic acid.