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28 December 2000

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.

WO 00/56872 A3

(54) Title: HIGH-THROUGHPUT GENE CLONING AND PHENOTYPIC SCREENING

(57) Abstract: The invention relates to the use of high-throughput methods for gene targeting, recombination, phenotype screening and biovalidation of drug targets utilizing enhanced homologous recombination (EHR) techniques. These methods utilize robotically driven multichannel pipetters to perform liquid, particle, cell and organism handling, robotically controlled plate and sample handling platforms, magnetic probes and affinity probes to selectively capture nucleic acid hybrids, and thermally regulated plates or blocks for temperature controlled reactions.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/07626

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/10 G01N35/00 //C12Q1/68,C12M1/40

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 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)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 99 37755 A (PANGENE CORP) 29 July 1999 (1999-07-29) the whole document	1-34
X	EP 0 718 404 A (TAKARA SHUZO CO) 26 June 1996 (1996-06-26) the whole document	1-34
A		35-37,46
X	WO 98 42727 A (STANFORD RES INST INT) 1 October 1998 (1998-10-01) abstract examples 1-6	1-34
A		35-37,46

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[X] Further documents are listed in the continuation of box C.

[X] 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.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 September 2000	29 SEP 2000

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	Galli, I

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

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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.
X	Geschäftsbericht 1998, MWG Biotech A.G. XP002147677 page 9 page 16	35-37,46
X	-& Application Notes MWG Biotech AG, 1998. "Automatisierung in forensischen Molekulargenetik: Einsatz des RoboAmp 4200 in der Laborroutine". (Dr. Michael Gerhard, IKA Niedersachsen, Fachgruppe 501). XP002147678 the whole document	35-37,46
P,X	-& WO 99 26070 A (HEIMBERG W.; WEICHSELGARTNER M.; GREBER M.) 27 May 1999 (1999-05-27) the whole document	35-37,46
T	-& Roboamp4200 specifications, available online at MWG's website: www.mwg-biotech.de/products/pcr/robots. Last modified december 1999. XP002147679 the whole document	35-37,46
X	WO 91 16675 A (APPLIED BIOSYSTEMS) 31 October 1991 (1991-10-31) abstract figure 1	35-37,46
A	HALL J M ET AL: "AN APPROACH TO HIGH-THROUGHPUT GENOTYPING" PCR METHODS AND APPLICATIONS,US,COLD SPRING HARBOR, NY, 1996, pages 781-790, XP000700236 ISSN: 1054-9803 the whole document	35-37,46

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/07626

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:

2. ☒ Claims Nos.: 38-45 and partly 46
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:

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: 1-34

A method of cloning a target nucleic acid comprising:

(a) providing an enhanced homologous recombination (EHR) comprising:

(i) a recombinase
(ii) a first and a second targeting polynucleotide, wherein said first polynucleotide comprises a fragment of said target nucleic acid and is substantially complementary to said second targeting polynucleotide, and
(iii) a separation moiety;

(b) contacting said EHR composition with a target library under conditions wherein said targeting polynucleotides can hybridize to said target nucleic acid; and

(c) isolating said target nucleic acid;

WHEREIN said providing and contacting are done using a robotic system.

A corresponding method of high throughput integrated genomics.

2. Claims: 35-46

A robotic system comprising means for producing a plurality of enhanced homologous recombination compositions.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 38-45 and partly 46

Claims 35 refers to a robotic system for producing a plurality of enhanced homologous recombinations. The description indicates that the system used is based on RoboAmp 4200, a product of MWG Biotech AG, which is of course known in prior art.

Claims 36-45 relate to a multitude of additional devices/means. 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 devices/means claimed. Furthermore, claim 46 relates to an extremely large number of possible additional devices/meams: there are so many options and possible permutations that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claim impossible.

In the present case, the claims in question so lack support, clarity and/or conciseness, 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 elements concretely described in the examples (especially example 2) and displayed in Fig. 1.

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/US 00/07626

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9937755 A	29-07-1999	AU 1913599 A	09-08-1999
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