WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: C12Q 1/68, B01L 3/00, 7/00

A3 (11) 1

(11) International Publication Number:

WO 96/15269

(43) International Publication Date:

23 May 1996 (23.05.96)

(21) International Application Number:

PCT/US95/14823

(22) International Filing Date:

13 November 1995 (13.11.95)

(81) Designated States: AU, CA, CN, JP, MX, RU, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

(30) Priority Data:

08/338,728 14 November 1994 (14.11.94) US 08/338,380 14 November 1994 (14.11.94) US 08/338,369 14 November 1994 (14.11.94) US Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(71) Applicant: TRUSTEES OF THE UNIVERSITY OF PENN-SYLVANIA [US/US]; Suite 300, 3700 Market Street, Philadelphia, PA 19104 (US).

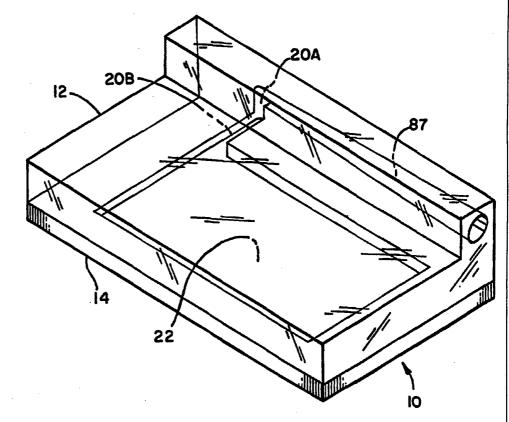
(72) Inventors: WILDING, Peter; 208 Darby Road, Paoli, PA 19301 (US). KRICKA, Larry, J.; 886 Nathan Hale Road, Berwyn, PA 19312 (US).

(74) Agents: HAGAN, Patrick, J. et al.; Dann, Dorfman, Herrell and Skillman, Suite 720, 1601 Market Street, Philadelphia, PA 19103-2307 (US). (88) Date of publication of the international search report: 21 November 1996 (21.11.96)

(54) Title: MESOSCALE POLYNUCLEOTIDE AMPLIFICATION DEVICES

(57) Abstract

Disclosed devices for amplifying a preselected polynucleotide in a sample by conducting a polynucleotide amplification reaction. The devices are provided with a substrate microfabricated to include a polynucleotide amplification reaction chamber, having at least one cross-sectional dimension of about 0.1 to 1000 μ m. The device also includes at least one port in fluid communication with the reaction chamber, for introducing a sample to the chamber, for venting the chamber when necessary, and, optionally, for removing products or waste material from the device. The reaction chamber may be provided with reagents required for amplification of a preselected polynucleotide. The device also may include means for thermally regulating the contents of the reaction chamber, to amplify



a preselected polynucleotide. Preferably, the reaction chamber is fabricated with a high surface to volume ratio, to facilitate thermal regulation. The amplification reaction chamber also may be provided with a composition which diminishes inhibition of the amplification reaction by material comprising a wall of the reaction chamber, when such treatment is required.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria				
AU	·	GB	United Kingdom	MR	Mauritania
	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	
BG	Bulgaria	IE	Ireland	NZ	Norway
BJ	Benin	IT	Italy		New Zealand
BR	Brazil	JP	Japan	PL	Poland
BY	Belarus	KE	Kenya	PT	Portugal
CA	Canada	KG	-	RO	Romania
CF	Central African Republic		Kyrgystan	RU	Russian Federation
CG	Congo	KP	Democratic People's Republic	SD	Sudan
CH	Switzerland		of Korea	SE	Sweden
CI		KR	Republic of Korea	SI	Slovenia
	Côte d'Ivoire	KZ	Kazakhstan	SK	Slovakia
CM	Cameroon	LI	Liechtenstein	SN	Senegal
CN	China	LK	Sri Lanka	TD	Chad
CS	Czechoslovakia	LU	Luxembourg	TG	Togo
CZ	Czech Republic	LV	Latvia	TJ	•
DE	Germany	MC	Monaco	TT	Tajikistan
DK	Denmark	MD	Republic of Moldova		Trinidad and Tobago
ES	Spain	MG	Madagascar	UA	Ukraine
FI	Finland	ML	Mali	US	United States of America
FR	France			UZ	Uzbekistan
GA	Gabon	MN	Mongolia	VN	Viet Nam
-Jra	Cacon				

Inte. .onal Application No PCT/US 95/14823

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 C12Q1/68 B01L3/00 B01L7/00 According to International Patent Classification (IPC) or to both national classification and IPC Minimum documentation searched (classification system followed by classification symbols) IPC 6 B01L F16K 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 WO,A,93 22058 (TRUSTEES OF THE UNIVERSITY 1-9, OF PENNSYLVANIA) 11 November 1993 28-36 cited in the application see page 6 - page 7, line 3 see page 25, paragraph 3 see page 18, line 13 - line 16 see claims 1,5,12,13,19 Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: "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 "A" document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the international "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 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) "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 docu-"O" document referring to an oral disclosure, use, exhibition or other means ments, such combination being obvious to a person skilled in the art. document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search **1** 6. 10. 96 9 September 1996 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, Hocquet, A Fax: (+31-70) 340-3016

3

Inte onal Application No
PCT/US 95/14823

C(Continu	Story DOCHMENTS CONSIDERED TO BE BELEVANT	ENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
Х	WO,A,94 05414 (REGENTS OF THE UNIVERSITY OF CALIFORNIA) 17 March 1994	1-4,7	
Υ	cited in the application see page 10, line 12 - line 16	10,11, 13,15	
	see page 13, line 3 - line 11 see page 14, line 33 - line 35; figures 1,2		
	see page 18, line 3 - line 10; claims 42-45		
X X	see page 25, paragraph 2 see page 27, line 25 - line 29 	29,30,32 31,36	
Y	US,A,5 346 672 (STAPLETON) 13 September 1994 see column 10, line 8 - line 24	10,11,13	
A	EP,A,O 611 598 (PERKIN-ELMER) 24 August 1994	10-13,22	
	see column 9, line 41 - line 45 see column 10, line 58 - column 11, line 11		
Y	see column 21, line 5 - line 20 see column 21, line 27 - line 32	15	
A	NUCLEIC ACIDS RESEARCH, vol. 19, no. 15, page 4294 XP002012940 YAP ET AL.: "slide PCR" see page 4594, column 1, line 6 - line 7	20	
A	CLINICAL CHEMISTRY, vol. 40, no. 9, pages 1815-1818, XP002012941 WILDING ET AL.: "pcr in a silicon microstructure" see page 1817, column 1, line 7 - line 11	1-9	
A .	WO,A,93 13220 (TEPNEL) 8 July 1993 see page 1, last paragraph - page 2, paragraph 2 see page 7, paragraph 3 - page 8, paragraph 4 see page 10, last paragraph	15,20,21	
A	US,A,4 824 247 (TRUE) 25 April 1989 see column 4, line 8 - line 30; figure 2	37	
X	EP,A,O 318 255 (EASTMAN KODAK CO) 31 May 1989 see column 6, line 45 - column 7, line 32 see column 11, line 36 - column 12, line 46; claims 10-17; figures 12-15 see column 14, line 45 - line 51; claim 24; figures 9,20,21	38-43	
	-/- -		

3

Int ional Application No
PCT/US 95/14823

C.(Continuat	tion) DOCUMENTS CONSIDERED TO BE RELEVANT	PC1/US 95/14025
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
4	US,A,4 280 498 (JENSEN MARVIN E) 28 July 1981 see column 6, line 48 - column 7, line 17; figures 2-7	44

3

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

International application No.

PCT/US 95/14823

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This inte	ernational 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.: 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:
	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 Inte	rnational Searching Authority found multiple inventions in this international application, as follows:
	nims: 1-37 nims: 38-44
(Se	ee further PCT/ISA/206)
•	
1. X	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 searches 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 o	n Protest The additional search fees were accompanied by the applicant's protest.
	No protest accompanied the payment of additional search fees.
	· · · · · · · · · · · · · · · · · · ·

Information on patent family members

Inte onal Application No
PCT/US 95/14823

			101/03	93/14023
Patent document cited in search report	Publication date		t family nber(s)	Publication date
W0-A-9322058	11-11-93	US-A-	5304487	19-04-94
		US-A-	5296375	22-03-94
		AT-T-	140025	15-07-96
		AT-T-	140880	15-08-96
		AU-B-	4222393	29-11-93
		AU-B-	4222593	29-11-93
		AU-B-	4222693	29-11-93
		AU-B-	4222793	29-11-93
		AU-B-	4223593	29-11-93
		CA-A-	2134474	11-11-93
		CA-A-	2134475	11-11-93
		CA-A-	2134476	11-11-93
	•	CA-A-	2134478	11-11-93
		DE-D-	69303483	08-08-96
		DE-D-	69303898	05-09-96
		EP-A-	0637996	15-02-95
		EP-A-	0637997	15-02-95
		EP-A-	0639223	22-02-95
•		EP-A-	0637998	15-02-95
		EP-A-	0637999	15-02-95
		JP-T-	7506430	13-07-95
		JP-T-	7506431	13-07-95
		JP-T-	7506256	13-07-95
		JP-T-	7506257	13-07-95
		JP-T-	7506258	13-07-95
		WO-A-	9322053	11-11-93
•		WO-A-	9322054	11-11-93
		WO-A-	9322421	11-11-93
		WO-A-	9322055	11-11-93
		US-A-	5427946	27-06-95
		US-A-	5498392	12-03-96
***************************************		US-A-	5486335	23-01-96
WO-A-9405414	17-03-94	AU-B-	5092193	29-03-94
		EP-A-	0711200	15-05-96
		JP-T-	7508928	05-10-95
US-A-5346672	13-09-94	US-A-	5188963	23-02-93
	 .	US-A-	5451500	19-09-95

Information on patent family members

Int. ional Application No PCT/US 95/14823

			/	/
Patent document cited in search report	Publication date		family ber(s)	Publication date
US-A-5346672		EP-A-	0632839	11-01-95
03 A 33400/L		WO-A-	9319207	30-09-93
		AU-B-	7787291	13-06-91
		CA-A-	2068891	18-05-91
		EP-A-	0502108	09-09-92
		JP-T-	5501647	02-04-93
		WO-A-	9107486	30-05-91
		US-A-	5436129	25-07-95
		U3-A-	3430129	20-07-35
EP-A-611598	24-08-94	US-A-	5364790	15-11-94
		AU-B-	5505494	18-08-94
		CA-A-	2106360	17-08-94
		CN-A-	1095759	30-11-94
		JP-A-	6245771	06-09 -9 4
		NZ-A-	248835	21-12-95
		US-A-	5527510	18-06-96
WO-A-9313220	08-07-93	AU-B-	3169493	28-07-93
		BR-A-	9206985	05-12-95
		CA-A-	2126748	25-06-93
		EP-A-	0620863	26-10-94
		FI-A-	943054	22-08-94
		JP-T-	7502405	16-03-95
		NO-A-	942399	12-08-94
		ZA-A-	9210008	03-08-93
US-A-4824247	25-04-89	EP-A-	0404776	02-01-91
00 // 102121/		WO-A-	9006724	28-06-90
EP-A-0318255	31-05-89	US-A-	4902624	20-02-90
LI A UJIULJJ	31 03 07	DE-A-	3876957	04-02-93
		DE-A-	3880632	03-06-93
		DE-T-	3880632	18-11-93
		EP-A-	0318256	31-05-89
		JP-A-	1266858	24-10-89
		JP-C-	1854459	07-07-94
		JP-A-	1168270	03-07-89
		JP-B-	7038788	01-05-95
~~~~~~~~		UF-D-	7030700	01-03-33
US-A-4280498	28-07-81	AU-B-	533306	17-11-83

Information on patent family members

Int ional Application No
PCT/US 95/14823

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US-A-4280498		AU-B-	6343680	30-04-81
		CA-A-	1160124	10-01-84
		CA-A-	1160126	10-01-84
		DE-A-	3039859	30-04-81
		FR-A-	2474858	07-08-81
		FR-A-	2474859	07-08-81
		GB-A.B	2061466	13-05-81
		GB-A.B	2125130	29-02-84
	•	JP-B-	1009865	20-02-89
		JP-C-	1522445	12-10-89
		JP-A-	56066265	04-06-81
		SE-B-	448514	02-03-87
		SE-A-	8007163	23-04-81

Form PCT/ISA/210 (patent family annex) (July 1992)