



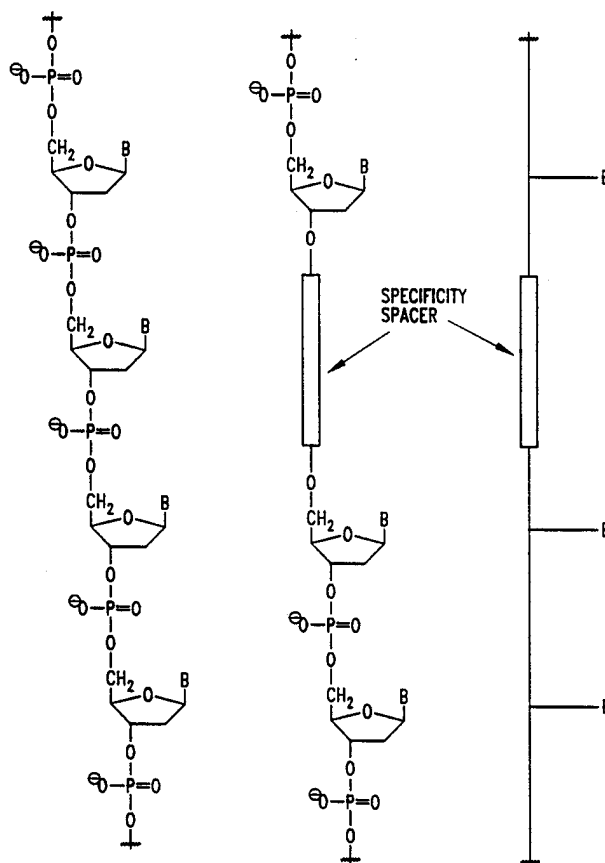
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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			(43) International Publication Date: 2 April 1998 (02.04.98)
(21) International Application Number: PCT/US97/17413 (22) International Filing Date: 24 September 1997 (24.09.97) (30) Priority Data: 60/026,621 24 September 1996 (24.09.96) US 08/719,132 24 September 1996 (24.09.96) US (71) Applicant: DARWIN MOLECULAR CORPORATION [US/US]; 1631 - 220th Street, S.E., Bothell, WA 98021 (US). (72) Inventors: VAN NESS, Jeffrey; 10020 - 49th Avenue, N.E., Seattle, WA 98125 (US). TABONE, John; 12117 N.E. 166th Place, Bothell, WA 98011 (US). GARRISON, Lori, K.; 4515 Evanston Avenue N., Seattle, WA 98103 (US). (74) Agents: PARKER, David, W. et al.; Seed and Berry LLP, 6300 Columbia Center, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).		(81) Designated States: AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 20 August 1998 (20.08.98)	

(54) Title: COMPOSITIONS AND METHODS FOR ENHANCING HYBRIDIZATION SPECIFICITY

(57) Abstract

Compositions and methods are provided for increasing the specificity of a probe nucleic acid for a target nucleic acid in a hybridization solution. An abasic residue, deoxyNebularine residue, or a hybotrope is used to increase specificity. A method is provided for identifying useful hybotropes, including salts, water miscible organic solvents, aprotic solvents and organic solvents, on the basis of enthalpy considerations. Hybotropic hybridization and modified oligonucleotides may be used in amplification reactions, such as PCR, sequence analysis methods, and genomic screening methods.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/17413

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12Q1/68

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 6 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 92 18649 A (MICROPROBE CORP) 29 October 1992	1,2, 12-14, 16-22, 28, 30-33, 39, 99-111, 125-131 112-124
Y	* see especially the claims * see the whole document --- -/-	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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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.

Z document member of the same patent family

Date of the actual completion of the international search

23 June 1998

Date of mailing of the international search report

03.07.98

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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	WO 93 20234 A (DU PONT) 14 October 1993	1,3-6, 12-14, 17-20, 99-101, 103-110
Y	see the whole document	46-49, 53-56, 60-63, 67-70, 74-78, 82-87, 93,94, 96-98
X	WO 90 12116 A (GENE TRAK SYSTEMS) 18 October 1990	1-6, 12-14, 17-22, 24,25, 28, 30-35, 99-110
Y	see the whole document	1,7-11, 21,26, 27,32, 36-38, 44,45
Y	EP 0 628 571 A (NIPPON STEEL CORP) 14 December 1994	1,7-11, 21,26, 27,32, 36-38, 44,45
	see abstract	
Y	WO 92 15708 A (AMOCO CORP) 17 September 1992	1,2,4-8, 12-26, 28-36, 39-45, 99-111, 125-131
	see abstract see page 4, paragraph 3 - page 5, paragraph 1 see page 7, paragraph 2 - page 8, paragraph 1 see page 9, paragraph 1 see page 11, paragraph 2 - page 14, paragraph 2; claims 1-3,7,12,15,16	
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International Application No

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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	WO 95 30774 A (BECKMAN INSTRUMENTS INC ;CASKEY CHARLES THOMAS (US)) 16 November 1995 see abstract see page 4, line 9 - line 33 see page 5, line 31 - page 6, line 28 see page 9, line 10 - page 11, line 4 see page 14, line 19 - page 15, line 19 see page 16, line 10 - page 17, line 21; claims 1,3,4,8,10-13,16; table 2 ---	1,2,4-8, 12-26, 28-36, 39-45, 99-111, 125-131
Y	WO 94 06815 A (ISIS PHARMACEUTICALS) 31 March 1994 see abstract see page 3, line 7 - line 12 see page 20, line 1 - page 21, line 22; claim 1 ---	46-49, 53-56, 60-63, 67-70, 74-78, 82-87, 93,94, 96-98
Y	WO 95 19776 A (TRUSTEES OF COLUMBIA UNIVERSIT ;UNIV WASHINGTON (US)) 27 July 1995 see abstract see page 16, line 18 - line 24 ---	112-124
A	WO 87 06621 A (GILLESPIE DAVID) 5 November 1987 see abstract see page 12, paragraph 2 - page 14, paragraph 1 see page 15, paragraph 3 - page 16, paragraph 1 see page 17, paragraph 2 - page 21, paragraph 1; claims 1-7,13-20,24-29,35 ---	
A	EP 0 420 260 A (HOFFMANN LA ROCHE) 3 April 1991 see abstract see page 2, line 43 - line 52 see page 3, line 25 - line 38 see page 4, line 13 - line 24 see page 5, line 37 - line 43; claims 1,8-11,15,27-33; example 10 -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 97/17413

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.:
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: 1,4-10,12-22,24-37,39-45,99-111,
125-131 (partial); 2,3,11,38 (complete)

Compositions comprising a nucleic acid and a salt, the corresponding salt comprising an ammonium derivative in combination with a halogenated acetate, and a method using them.

2. Claims: 1,4-10,12-22,24-32,34-37,39-43,99-111,
125-131 (partial)

Compositions comprising a nucleic acid and a salt, the corresponding salt comprising an ammonium derivative in combination with a propionate, and a method using them.

3. Claims: 1,4-10,12-22,24-32,34-37,39-43,99-111,
125-131 (partial)

Compositions comprising a nucleic acid and a salt, the corresponding salt comprising an ammonium derivative in combination with a halogenated propionate, and a method using them.

4. Claims: 21,22,24-37,39-45,99-111,
125-131 (partial); 23 (complete)

Compositions comprising a nucleic acid and a salt, the corresponding salt comprising an ammonium derivative in combination with an acetate, and a method using them.

5. Claims: 46-98 (complete), 112-124 (partial)

An oligonucleotide in solution, an array of oligonucleotides, a composition comprising an oligonucleotide and a salt, an array composition comprising oligonucleotides, the corresponding oligonucleotide(s) containing at least one abasic "specificity spacer", and a method using them.

6. Claims: 112-124 (partial)

A method of hybridization using probes containing at least one 2'-deoxyNebularine.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. Appl. No.

PCT/US 97/17413

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