



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07H 21/00	A3	(11) International Publication Number: WO 96/32496 (43) International Publication Date: 17 October 1996 (17.10.96)
(21) International Application Number: PCT/US96/04559 (22) International Filing Date: 3 April 1996 (03.04.96) (30) Priority Data: 08/415,370 3 April 1995 (03.04.95) US (71) Applicant: MICROPROBE CORPORATION [US/US]; 1725 220th Street, S.E., No. 104, Bothell, WA 98021 (US). (72) Inventors: KUTYAVIN, Igor, V.; 16520 North Road #B101, Bothell, WA 98012 (US). LUKHTANOV, Eugeny, A.; Apartment #E-206, 16520 North Road, Bothell, WA 98012 (US). GAMPER, Howard, B.; 14048 212th Drive N.E., Woodinville, WA 98078 (US). MEYER, Rich, B., Jr.; 15533 61st Avenue N.E., Bothell, WA 98011 (US). (74) Agents: KLEIN, Howard, J. et al.; Klein & Szekeres, Suite 700, 4199 Campus Drive, Irvine, CA 92715 (US).		(81) Designated States: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), 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</i> <i>claims and to be republished in the event of the receipt of</i> <i>amendments.</i> (88) Date of publication of the international search report: 28 November 1996 (28.11.96)
(54) Title: COVALENTLY LINKED OLIGONUCLEOTIDE MINOR GROOVE BINDER CONJUGATES		
(57) Abstract Minor groove binding molecules are covalently bound to oligonucleotides which in their base sequence are complementary to a target sequence of single stranded or double stranded DNA, RNA or hybrids thereof. The covalently bound oligonucleotide minor groove binder conjugates strongly bind to the target sequence of the complementary strand.		

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.

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

INTERNATIONAL SEARCH REPORT

International Application No
PCT/JS 96/04559A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07H21/00

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 C07H

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.
A	TETRAHEDRON LETTERS, vol. 32, no. 49, 2 December 1991, OXFORD GB, pages 7171-7174, XP002014641 M.MANO HARAN ET AL.: "Novel Functionalization of the Sugar Moiety of Nucleic Acids for Multiple Labeling in the Minor Groove." see the whole document --- -/--	1

☒ Further documents are listed in the continuation of box C.☒ 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

3 October 1996

Date of mailing of the international search report

09. 10. 96

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

Scott, J

INTERNATIONAL SEARCH REPORT

International Application No

PCT, JS 96/04559

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EMBO JOURNAL, vol. 11, no. 1, January 1992, EYNSHAM, OXFORD GB, pages 225-232, XP002014642 M.SRIRAM ET AL.: "Conformation of B-DNA Containing 06-ethyl-G-C Base Pairs Stabilized by Minor Groove Binding Drugs : Molecular Structure of d(CGC(e6G)AATTCGCG) Complexed with Hoechst 33258 or Hoechst 33342." see the whole document ---	1
A	BIOCHEMISTRY, vol. 33, no. 6, 15 February 1994, EASTON, PA US, pages 1412-1418, XP002014643 H.GOULAOUIC ET AL.: "Selective Binding to Polynucleotides of the Hybrid Intercalating Groove Binder Bis(pyrrolocarboxamide)-Oxazolopyridocarba zole: A Molecular Modeling Study." see abstract ---	1
A	NUCLEIC ACIDS RESEARCH, vol. 18, no. 16, 25 August 1990, OXFORD GB, pages 4771-4778, XP002014644 R.COSSTICK ET AL.: "Molecular Recognition in the Minor Groove of the DNA Helix. Studies on the Synthesis of Oligonucleotides and Polynucleotides Containing 3-Deaza-2'-deoxyadenosine. Interaction of teh Oligonucleotides with the restriction of Endonuclease EcoRV." see the whole document ---	1
A	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 89, no. 16, 15 August 1992, WASHINGTON US, pages 7586-7590, XP002014645 M.MRKSICH ET AL.: "Antiparallel Side-by-side Dimeric Motif for Sequence-Specific Recognition in the Minor Groove of DNA by the Designed Peptide 1-methylimidazole-2-carboxamide Netropsin." see the whole document ---	1

-/--

INTERNATIONAL SEARCH REPORT

International Application No

PC1, JS 96/04559

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BIOCHEMISTRY, vol. 33, no. 10, 15 March 1994, EASTON, PA US, pages 3055-3062, XP002014646 B.H.GEIERSTANGER ET AL.: "Structural and Dynamic Characterization of the Heterodimeric and Homodimeric Complexes of Distamycin and 1-Methylimidazole-2-carboxamide-Netropsin Bound to the Minor Groove of DNA." see abstract ---	1
A	JOURNAL OF THE CHEMICAL SOCIETY, CHEMICAL COMMUNICATIONS, no. 15, 1 August 1989, LETCHWORTH GB, pages 1023-1025, XP002014647 J.A.PARKINSON ET AL.: "NMR Probing of Binding Interactions used by Minor Groove Binding, DNA-Directed Ligands : Assignment of the Binding Site of Hoechst 33258 on the Self-Complementary Oligonucleotide, d(CGCGAATTCGCG)." see the whole document ---	1
A	JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 112, no. 9, 25 April 1990, DC US, pages 3279-3289, XP002014648 F.L.BOYD ET AL. : "Characterization of the Structure of the Anthramycin-d(ATGCAT)2 Adduct by NMR and Molecular Modeling Studies. Determination of the Stereochemistry of the Covalent Linkage Site, Orientation in the Minor Groove of DNA, and Effect on Local DNA Structure." see abstract ---	1
A	US,A,4 942 227 (DERVAN ET AL.) 17 July 1990 see abstract ---	1
A	US,A,5 395 849 (WITTMAN ET AL.) 7 March 1995 see abstract ---	1
A	US,A,4 665 184 (DERVAN ET AL.) 12 May 1987 see abstract ---	1
P,X	WO,A,95 29184 (UNIVERSITE LOUIS PASTEUR) 2 November 1995 see the whole document ---	1,8-12, 22
3 P,A	WO,A,96 06831 (AUKLAND DIVISION CANCER SOCIETY OF NEW ZEALAND INC.) 7 March 1996 see the whole document -----	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT, JS 96/04559

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-4942227	17-07-90	US-A- 4529401 US-A- 4665184	16-07-85 12-05-87
US-A-5395849	07-03-95	NONE	
US-A-4665184	12-05-87	US-A- 4942227	17-07-90
WO-A-9529184	02-11-95	FR-A- 2719048	27-10-95
WO-A-9606831	07-03-96	AU-A- 3247595	22-03-96