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(21) International Application Number: PCT/US99/06329 (22) International Filing Date: 23 March 1999 (23.03.99) (30) Priority Data: 60/078,969 23 March 1998 (23.03.98) US (71) Applicant: INVITROGEN CORPORATION [US/US]; 1600 Faraday Avenue, Carlsbad, CA 92008 (US). (72) Inventor: SHORT, Jay, M.; 320 DeLage Drive, Encinitas, CA 92024 (US). (74) Agents: BURKE, John, E. et al.; Pillsbury Madison & Sutro LLP, 1100 New York Avenue, N.W., Washington, DC 20005 (US).	(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims</i> <i>and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 25 November 1999 (25.11.99)	
(54) Title: MODIFIED NUCLEOTIDES AND METHODS USEFUL FOR NUCLEIC ACID SEQUENCING		
(57) Abstract The present invention relates to a method for sequencing nucleic acids. In particular, such method includes incorporating certain modified nucleotides referred to as Simtides into nucleic acid strands. These Simtides are complexes comprising a nucleotide base (or analog thereof), a linker, and a label capable of generating a detectable signal for sequencing. A Simtide may be incorporated into a sequencing fragment as a primer component, as a chain elongator, or as a chain terminator.		

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INTERNATIONAL SEARCH REPORT

Inter. Application No PCT/US 99/06329
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A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12Q1/68 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 C12Q 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.
X	WO 97 27331 A (DARWIN MOLECULAR) 31 July 1997 (1997-07-31) page 64, line 24 -page 65, line 5 page 69, line 7 -page 71, line 11; claims 1-14 page 79, line 6 -page 80, line 6 page 85, line 20 -page 88, line 18 ---	1,3-9
Y	---	2
X	EP 0 157 280 A (BOARD OF REGENTS OF THE UNIVERSITY OF NEBRASKA) 9 October 1985 (1985-10-09) page 3, line 10 -page 5, line 12 page 13, line 16 - line 23 page 30, line 2 - line 16; claim 5 --- -/--	1,10

 Further documents are listed in the continuation of box C.

 Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/06329

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 20591 A (PROLINX, INC.) 3 August 1995 (1995-08-03) cited in the application page 6, line 11 -page 7, line 12; claims; examples 25,26 ---	2
A	C. DUPLÅA: "Quantitative analysis of polymerase chain reaction products using biotinylated dUTP incorporation" ANALYTICAL BIOCHEMISTRY, vol. 212, 1993, pages 229-236, XP000377657 US the whole document ---	1,10
P,X	WO 98 16661 A (MORPHAGEN) 23 April 1998 (1998-04-23) page 48, line 24 -page 49, line 10 -----	1,2,5,6, 8-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/06329

Patent document cited in search report	A	Publication date	Patent family member(s)	Publication date
WO 9727331	A	31-07-1997	AU 2247397	20-08-1997
			CA 2243560	31-07-1997
			CN 1212021	24-03-1999
			CZ 9802184	16-12-1998
			EP 0868535	07-10-1998
			HU 9901321	28-07-1999
			NZ 331044	25-02-1999
			PL 328271	18-01-1999
EP 157280	A	09-10-1985	US 4729947	08-03-1988
			AU 588229	14-09-1989
			AU 4002185	03-10-1985
			CA 1230161	08-12-1987
			JP 2007209	11-01-1996
			JP 7043347	15-05-1995
			JP 61002077	08-01-1986
			US 5360523	01-11-1994
			US 5571388	05-11-1996
			US 5639874	17-06-1997
			US 5534125	09-07-1996
			US 5549805	27-08-1996
			US 5207880	04-05-1993
			US 5755943	26-05-1998
			US 5863403	26-01-1999
			US 5800995	01-09-1998
			US 5230781	27-07-1993
			US 5366603	22-11-1994
US 5346603	13-09-1994			
WO 9520591	A	03-08-1995	US 5594151	14-01-1997
			US 5594111	14-01-1997
			US 5623055	22-04-1997
			AU 702017	11-02-1999
			AU 1732495	15-08-1995
			CA 2181252	03-08-1995
			CZ 9602201	11-12-1996
			EP 0741734	13-11-1996
			JP 9508389	26-08-1997
			PL 315911	09-12-1996
			SK 98996	05-02-1997
			US 5852178	22-12-1998
			US 5648470	15-07-1997
			US 5688928	18-11-1997
			US 5668257	16-09-1997
			US 5668258	16-09-1997
			US 5837878	17-11-1998
			US 5847192	08-12-1998
			US 5744627	28-04-1998
			US 5777148	07-07-1998
			US 5872224	16-02-1999
			US 5859210	12-01-1999
			US 5877297	02-03-1999
US 5869623	09-02-1999			
US 5677431	14-10-1997			
WO 9816661	A	23-04-1998	AU 4993097	11-05-1998