



US009708358B2

(12) **United States Patent**  
**Ju et al.**

(10) **Patent No.:** **US 9,708,358 B2**  
(45) **Date of Patent:** **\*Jul. 18, 2017**

(54) **MASSIVE PARALLEL METHOD FOR  
DECODING DNA AND RNA**

(71) Applicant: **The Trustees of Columbia University  
in the City of New York**, New York,  
NY (US)

(72) Inventors: **Jingyue Ju**, Englewood Cliffs, NJ (US);  
**Zengmin Li**, Flushing, NY (US); **John  
Robert Edwards**, St. Louis, MO (US);  
**Yasuhiro Itagaki**, New York, NY (US)

(73) Assignee: **THE TRUSTEES OF COLUMBIA  
UNIVERSITY IN THE CITY OF  
NEW YORK**, New York, NY (US)

(\* ) Notice: Subject to any disclaimer, the term of this  
patent is extended or adjusted under 35  
U.S.C. 154(b) by 0 days.

This patent is subject to a terminal dis-  
claimer.

(21) Appl. No.: **15/380,284**

(22) Filed: **Dec. 15, 2016**

(65) **Prior Publication Data**

US 2017/0088574 A1 Mar. 30, 2017

**Related U.S. Application Data**

(60) Continuation of application No. 14/670,748, filed on  
Mar. 27, 2015, which is a continuation of application  
No. 13/959,660, filed on Aug. 5, 2013, now Pat. No.  
9,133,511, which is a continuation of application No.  
13/672,437, filed on Nov. 8, 2012, now abandoned,  
which is a continuation of application No.  
13/339,089, filed on Dec. 28, 2011, now abandoned,  
which is a continuation of application No.  
12/804,284, filed on Jul. 19, 2010, now Pat. No.  
8,088,575, which is a continuation of application No.  
11/810,509, filed on Jun. 5, 2007, now Pat. No.  
7,790,869, which is a continuation of application No.  
10/702,203, filed on Nov. 4, 2003, now Pat. No.  
7,345,159, which is a division of application No.  
09/972,364, filed on Oct. 5, 2001, now Pat. No.  
6,664,079, which is a continuation-in-part of  
application No. 09/684,670, filed on Oct. 6, 2000,  
now abandoned.

(60) Provisional application No. 60/300,894, filed on Jun.  
26, 2001.

(51) **Int. Cl.**  
**C07H 19/10** (2006.01)  
**C12Q 1/68** (2006.01)

(52) **U.S. Cl.**  
CPC ..... **C07H 19/10** (2013.01); **C12Q 1/6872**  
(2013.01); **C12Q 1/6874** (2013.01)

(58) **Field of Classification Search**

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

4,711,955 A 12/1987 Ward et al.  
4,772,691 A 9/1988 Herman  
4,804,748 A 2/1989 Seela  
4,824,775 A 4/1989 Dattagupta et al.  
4,863,849 A 9/1989 Melamede  
5,043,272 A 8/1991 Hartley  
5,047,519 A 9/1991 Hobbs, Jr. et al.  
5,118,605 A 6/1992 Urdea  
5,151,507 A 9/1992 Hobbs, Jr. et al.  
5,174,962 A 12/1992 Brennan  
5,175,269 A 12/1992 Stavrianopoulos  
5,242,796 A 9/1993 Prober et al.  
5,302,509 A 4/1994 Cheeseman  
5,308,990 A 5/1994 Takahashi et al.  
5,328,824 A 7/1994 Ward et al.  
5,332,666 A 7/1994 Prober et al.  
5,383,858 A 1/1995 Reilly et al.  
5,436,143 A 7/1995 Hyman  
5,437,975 A 8/1995 McClelland et al.  
5,449,767 A 9/1995 Ward et al.  
5,476,928 A 12/1995 Ward et al.  
5,516,664 A 5/1996 Hyman  
5,534,424 A 7/1996 Uhlen et al.  
5,547,839 A 8/1996 Dower et al.  
5,547,859 A 8/1996 Goodman et al.  
5,556,748 A 9/1996 Douglas  
5,599,675 A 2/1997 Brenner  
5,602,000 A 2/1997 Hyman

(Continued)

**FOREIGN PATENT DOCUMENTS**

CA 2425112 4/2002  
CA 2408143 11/2002

(Continued)

**OTHER PUBLICATIONS**

Office Action issued Sep. 21, 2007 in connection with U.S. Appl.  
No. 10/380,256.  
Office Action issued Oct. 25, 2002 in connection with U.S. Appl.  
No. 09/972,364.  
Office Action issued Mar. 14, 2003 in connection with U.S. Appl.  
No. 09/972,364.  
Office Action issued Dec. 20, 2006 in connection with U.S. Appl.  
No. 10/702,203.  
Amendment filed May 21, 2007 in response to Office Action issued  
Dec. 20, 2006 in connection with U.S. Appl. No. 10/702,203.  
Notice of Allowance issued Sep. 6, 2007 in connection with U.S.  
Appl. No. 10/702,203.  
Office Action issued Jun. 24, 2008 in connection with U.S. Appl.  
No. 11/894,690.

(Continued)

*Primary Examiner* — Layla Berry

(74) *Attorney, Agent, or Firm* — John P. White; Gary J.  
Gershik; Cooper & Dunham LLP

(57) **ABSTRACT**

This invention provides methods for attaching a nucleic acid  
to a solid surface and for sequencing nucleic acid by  
detecting the identity of each nucleotide analog after the  
nucleotide analog is incorporated into a growing strand of  
DNA in a polymerase reaction. The invention also provides  
nucleotide analogs which comprise unique labels attached to  
the nucleotide analog through a cleavable linker, and a  
cleavable chemical group to cap the —OH group at the  
3' position of the deoxyribose.

(56)

## References Cited

## U.S. PATENT DOCUMENTS

5,637,469	A	6/1997	Wilding et al.	6,787,308	B2	9/2004	Balasubramanian et al.
5,654,419	A	8/1997	Mathies et al.	6,818,395	B1	11/2004	Quake et al.
5,658,736	A	8/1997	Wong	6,833,246	B2	12/2004	Balasubramanian
5,709,999	A	1/1998	Shattuck-Eidens et al.	6,858,393	B1	2/2005	Anderson et al.
5,714,330	A	2/1998	Brenner et al.	6,864,052	B1	3/2005	Drmanac et al.
5,728,528	A	3/1998	Mathies et al.	6,911,345	B2	6/2005	Quake et al.
5,763,594	A	6/1998	Hiatt et al.	6,934,636	B1	8/2005	Skierczynski et al.
5,770,365	A	6/1998	Lane et al.	6,982,146	B1	1/2006	Schneider et al.
5,770,367	A	6/1998	Southern et al.	7,037,687	B2	5/2006	Williams et al.
5,789,167	A	8/1998	Konrad	7,056,661	B2	6/2006	Korlach et al.
5,798,210	A	8/1998	Canard et al.	7,056,666	B2	6/2006	Dower et al.
5,804,386	A	9/1998	Ju	7,057,026	B2	6/2006	Barnes et al.
5,808,045	A	9/1998	Hiatt et al.	7,057,031	B2	6/2006	Olejnik et al.
5,814,454	A	9/1998	Ju	7,074,597	B2	7/2006	Ju
5,821,356	A	10/1998	Khan et al.	7,078,499	B2	7/2006	Odedra et al.
5,834,203	A	11/1998	Katzir et al.	7,105,300	B2	9/2006	Parce et al.
5,844,106	A	12/1998	Seela et al.	7,270,951	B1	9/2007	Stemple et al.
5,849,542	A	12/1998	Reeve et al.	7,279,563	B2	10/2007	Kwiatkowski
5,853,992	A	12/1998	Glazer et al.	7,329,496	B2	2/2008	Dower et al.
5,856,104	A	1/1999	Chee et al.	7,345,159	B2	3/2008	Ju et al.
5,869,255	A	2/1999	Mathies et al.	7,414,116	B2	8/2008	Milton et al.
5,872,244	A	2/1999	Hiatt et al.	7,427,673	B2	9/2008	Balasubramanian et al.
5,876,936	A	3/1999	Ju	7,459,275	B2	12/2008	Dower et al.
5,885,775	A	3/1999	Haff et al.	7,566,537	B2	7/2009	Balasubramanian et al.
5,908,755	A	6/1999	Kumar et al.	7,622,279	B2	11/2009	Ju
5,945,283	A	8/1999	Kwok et al.	7,635,578	B2	12/2009	Ju et al.
5,948,648	A	9/1999	Khan et al.	7,713,698	B2	5/2010	Ju et al.
5,952,180	A	9/1999	Ju	7,790,869	B2	9/2010	Ju et al.
5,959,089	A	9/1999	Hannessian	7,883,869	B2	2/2011	Ju et al.
5,962,228	A	10/1999	Brenner	7,982,029	B2	7/2011	Ju et al.
6,001,566	A	12/1999	Canard et al.	8,088,575	B2	1/2012	Ju et al.
6,001,611	A	12/1999	Will	8,158,346	B2	4/2012	Balasubramanian et al.
6,008,379	A	12/1999	Benson et al.	8,298,792	B2	10/2012	Ju et al.
6,013,445	A	1/2000	Albrecht et al.	8,399,188	B2	3/2013	Zhao et al.
6,028,190	A	2/2000	Mathies et al.	8,796,432	B2	8/2014	Ju et al.
6,046,005	A	4/2000	Ju et al.	8,889,348	B2	11/2014	Ju
6,074,823	A	6/2000	Koster	9,115,163	B2	8/2015	Ju et al.
6,087,095	A	7/2000	Rosenthal et al.	9,133,511	B2	9/2015	Ju et al.
6,136,543	A	10/2000	Anazawa et al.	9,159,610	B2	10/2015	Zhang et al.
6,175,107	B1	1/2001	Juvinall	9,175,342	B2	11/2015	Ju et al.
6,197,557	B1	3/2001	Makarov et al.	9,255,292	B2	2/2016	Ju et al.
6,207,831	B1	3/2001	Auer et al.	9,297,042	B2	3/2016	Ju et al.
6,210,891	B1	4/2001	Nyren et al.	2002/0012966	A1	1/2002	Shi et al.
6,214,987	B1	4/2001	Hiatt et al.	2002/0168642	A1	11/2002	Drukier
6,218,118	B1	4/2001	Sampson et al.	2003/0008285	A1	1/2003	Fischer
6,218,530	B1	4/2001	Rothschild et al.	2003/0022225	A1	1/2003	Monforte et al.
6,221,592	B1	4/2001	Schwartz et al.	2003/0027140	A1	2/2003	Ju et al.
6,232,465	B1	5/2001	Hiatt et al.	2003/0044871	A1	3/2003	Cutsforth et al.
6,242,193	B1	6/2001	Anazawa et al.	2003/0054360	A1	3/2003	Gold et al.
6,245,507	B1	6/2001	Bogdanov	2003/0099972	A1	5/2003	Olejnik et al.
6,255,083	B1	7/2001	Williams	2003/0166282	A1	9/2003	Brown et al.
6,255,475	B1	7/2001	Kwiatkowski	2003/0180769	A1	9/2003	Metzker
6,274,320	B1	8/2001	Rothberg et al.	2003/0186256	A1	10/2003	Fischer
6,277,607	B1	8/2001	Tyagi et al.	2003/0190680	A1	10/2003	Rothschild et al.
6,287,821	B1	9/2001	Shi et al.	2003/0198982	A1	10/2003	Seela et al.
6,294,324	B1	9/2001	Bensimon et al.	2004/0014096	A1	1/2004	Anderson et al.
6,309,829	B1	10/2001	Livak et al.	2004/0096825	A1	5/2004	Chenna et al.
6,309,836	B1	10/2001	Kwiatkowski	2005/0032081	A1	2/2005	Ju et al.
6,312,893	B1	11/2001	Van Ness et al.	2005/0170367	A1	8/2005	Quake et al.
6,316,230	B1	11/2001	Egholm et al.	2005/0239134	A1	10/2005	Gorenstein et al.
6,335,155	B1	1/2002	Wells et al.	2006/0003352	A1	1/2006	Lipkin et al.
6,361,940	B1	3/2002	Van Ness et al.	2006/0057565	A1	3/2006	Ju et al.
6,380,378	B1	4/2002	Kitamura et al.	2006/0105461	A1	5/2006	Tom-Moy et al.
6,495,680	B1	12/2002	Gong	2006/0160081	A1	7/2006	Milton et al.
6,524,829	B1	2/2003	Seeger	2006/0160113	A1	7/2006	Korlach et al.
6,555,349	B1	4/2003	O'Donnell	2006/0240439	A1	10/2006	Smith et al.
6,613,508	B1	9/2003	Ness et al.	2006/0252038	A1	11/2006	Ju
6,613,513	B1	9/2003	Parce et al.	2007/0166705	A1	7/2007	Milton et al.
6,627,748	B1	9/2003	Ju et al.	2009/0088332	A1	4/2009	Ju et al.
6,632,655	B1	10/2003	Mehta et al.	2009/0240030	A1	9/2009	Ju et al.
6,639,088	B2	10/2003	Kwiatkowski	2010/0159531	A1	6/2010	Gordon et al.
6,664,079	B2	12/2003	Ju et al.	2011/0014611	A1	1/2011	Ju et al.
6,664,399	B1	12/2003	Sabesan	2011/0124054	A1	5/2011	Olejnik et al.
				2012/0052489	A1	3/2012	Gordon et al.
				2012/0142006	A1	6/2012	Ju et al.
				2013/0264207	A1	10/2013	Ju et al.
				2014/0315191	A1	10/2014	Ju et al.

(56)

**References Cited**

## U.S. PATENT DOCUMENTS

2015/0111759	A1	4/2015	Ju et al.
2015/0119259	A1	4/2015	Ju et al.
2015/0197800	A1	7/2015	Ju et al.
2015/0368710	A1	12/2015	Fuller et al.
2016/0024570	A1	1/2016	Ju et al.
2016/0024574	A1	1/2016	Ju et al.
2016/0041179	A1	2/2016	Ju et al.
2016/0090621	A1	3/2016	Ju et al.

## FOREIGN PATENT DOCUMENTS

DE	4141178	6/1993
DE	20122767	8/2007
DE	112007002932.3	8/2015
EP	0251786 B1	11/1994
EP	0995804	4/2000
EP	1182267	2/2002
EP	1291354	3/2003
EP	0808320	4/2003
EP	1337541 B1	3/2007
EP	1218391	4/2007
EP	0992511	3/2009
EP	2209911 B1	10/2013
GB	2000 0013276	6/2000
GB	2001 0029012	12/2001
GB	2446083	3/2011
GB	2446084	3/2011
GB	2457402	9/2011
WO	WO 89/09282	10/1989
WO	WO 89/11548	11/1989
WO	WO 90/13666	11/1990
WO	WO 91/06678	5/1991
WO	WO92/10587	6/1992
WO	WO 93/05183	3/1993
WO	WO 93/12340	10/1993
WO	WO 93/21340	10/1993
WO	WO 94/14972	7/1994
WO	WO 96/07669	3/1996
WO	WO 96/23807	8/1996
WO	WO 96/27025	9/1996
WO	WO 97/08183	3/1997
WO	WO 97/27317	7/1997
WO	WO 97/35033	9/1997
WO	WO 98/30720	7/1998
WO	WO 98/33939	8/1998
WO	WO 98/44151	10/1998
WO	WO 99/05315	2/1999
WO	WO 99/49082	9/1999
WO	WO 99/57321	11/1999
WO	WO 00/02895	1/2000
WO	WO 00/06770	2/2000
WO	WO 00/09753	2/2000
WO	WO 00/15844	3/2000
WO	WO 00/18956	4/2000
WO	WO 00/21974	4/2000
WO	WO 00/50172	8/2000
WO	WO 00/50642	8/2000
WO	WO 00/53805	9/2000
WO	WO 00/53812	9/2000
WO	WO 00/70073	11/2000
WO	WO 01/16375	3/2001
WO	WO 01/23610	4/2001
WO	WO 01/25247	4/2001
WO	WO 01/27625	4/2001
WO	WO 01/32930	5/2001
WO	WO 01/57248	8/2001
WO	WO 01/57249	8/2001
WO	WO 01/92284	12/2001
WO	WO 02/02813	1/2002
WO	WO 02/21098	3/2002
WO	WO 02/022883	3/2002
WO	WO 02/029003	4/2002
WO	WO 02/72892	9/2002

WO	WO 02/88382	11/2002
WO	WO 03/002767	1/2003
WO	WO 03/020968	3/2003
WO	WO 03/048178	6/2003
WO	WO 03/048387	6/2003
WO	WO 03/085135	10/2003
WO	WO 2004/018493	3/2004
WO	WO 2004/018497	3/2004
WO	WO 2004/055160	7/2004
WO	WO 2005/084367	9/2005
WO	WO 2006/073436	7/2006
WO	WO 2007/002204	1/2007
WO	WO 2007/062105	5/2007
WO	WO 2008/069973	6/2008
WO	WO 2012/083249	6/2012
WO	WO 2012/162429	11/2012
WO	WO 2013/154999	10/2013
WO	WO 2013/191793	12/2013
WO	WO 2014/144883	9/2014
WO	WO 2014/144898	9/2014
WO	WO 2015/123430	8/2015
WO	WO 2015/148402	10/2015
WO	WO 2015/179284	11/2015

## OTHER PUBLICATIONS

Amendment filed Oct. 16, 2008 in response to Office Action issued Jun. 24, 2008 in connection with U.S. Appl. No. 11/894,690.

Supplemental Amendment filed Jan. 16, 2009 in connection with U.S. Appl. No. 11/894,690.

Notice of Allowance issued Feb. 24, 2009 in connection with U.S. Appl. No. 11/894,690.

Office Action issued Jun. 5, 2009 in connection with U.S. Appl. No. 11/894,690.

Nov. 5, 2009 Amendment in response to Office Action issued Jun. 5, 2009 in connection with U.S. Appl. No. 11/894,690.

Office Action issued Sep. 3, 2008 in connection with U.S. Appl. No. 11/894,808.

Dec. 19, 2008 Amendment in response to Office Action issued Sep. 3, 2008 in connection with U.S. Appl. No. 11/894,808.

Amendment after Notice of Allowance filed Jun. 23, 2009 in connection with U.S. Appl. No. 11/894,808.

Office Action issued Jul. 10, 2009 in connection with U.S. Appl. No. 11/810,509.

Jan. 11, 2010 Amendment in response to Office Action issued Jul. 10, 2009 in connection with U.S. Appl. No. 11/810,509.

Jan. 26, 2010 Supplemental Amendment in connection with U.S. Appl. No. 11/810,509.

Notice of Allowance and Fee(s) Due issued Apr. 2, 2010 in connection with U.S. Appl. No. 11/810,509.

Office Action issued Oct. 28, 2010 in connection with U.S. Appl. No. 12/804,284.

Office Action issued Feb. 4, 2011 in connection with U.S. Appl. No. 12/804,284.

Aug. 4, 2011 Amendment in response to Office Action issued Feb. 4, 2011 in connection with U.S. Appl. No. 12/804,284.

Notice of Allowance issued Sep. 1, 2011 in connection with U.S. Appl. No. 12/804,284.

Office Action issued May 8, 2012 in connection with U.S. Appl. No. 13/339,089.

Notice of Abandonment issued Sep. 13, 2013 in connection with U.S. Appl. No. 13/672,437.

Office Action issued Dec. 1, 2014 in connection with U.S. Appl. No. 13/959,660.

Amendment filed Feb. 27, 2015 in connection with U.S. Appl. No. 13/959,660.

Notice of Allowance issued May 3, 2015 in connection with U.S. Appl. No. 13/959,660.

Official Action issued Mar. 17, 2009 in connection with Canadian Patent Application No. CA 2425112 OA.

Sep. 17, 2009 Response to Official Action issued Mar. 17, 2009 in connection with Canadian Patent Application No. CA 2425112 OA.

(56)

**References Cited**

## OTHER PUBLICATIONS

Sep. 16, 2010 Response to Official Action issued Mar. 16, 2010 in connection with Canadian Patent Application No. CA 2425112 OA. Partial European Search Report issued Apr. 26, 2007 in connection with European Patent Application No. 07004522.4.

Extended European Search Report issued Jul. 18, 2007 in connection with European Patent Application No. 07004522.4.

Official Action issued Mar. 14, 2008 in connection with European Patent Application No. 07004522.4.

Sep. 24, 2008 Response to Official Action issued Mar. 14, 2008 in connection with European Patent Application No. 07004522.4.

Communication Pursuant to Article 94(3) EPC issued Apr. 30, 2009 in connection with counterpart European Patent Application No. 07004522.4.

Nov. 10, 2009 Response to Communication Pursuant to Article 94(3) EPC issued Apr. 30, 2009 in connection with counterpart European Patent Application No. 07004522.4.

Communication Pursuant to Article 94(3) EPC issued Jun. 10, 2012 in connection with counterpart European Patent Application No. 07004522.4.

Oct. 20, 2010 Response to Communication Pursuant to Article 94(3) EPC issued Jun. 10, 2012 in connection with counterpart European Patent Application No. 07004522.4.

Communication Pursuant to Article 94(3) EPC issued Apr. 1, 2011 in connection with counterpart European Patent Application No. 07004522.4.

Oct. 11, 2011 Response to Communication Pursuant to Article 94(3) EPC issued Apr. 1, 2011 in connection with counterpart European Patent Application No. 07004522.4.

Communication Pursuant to Article 94(3) EPC issued May 24, 2012 in connection with counterpart European Patent Application No. 07004522.4.

Nov. 30, 2012 Response to Communication Pursuant to Article 94(3) EPC issued May 24, 2012 in connection with counterpart European Patent Application No. 07004522.4.

Communication Pursuant to Article 94(3) EPC issued Jun. 12, 2013 in connection with counterpart European Patent Application No. 07004522.4.

Dec. 31, 2013 Response to Communication Pursuant to Article 94(3) EPC issued Jun. 12, 2013 in connection with counterpart European Patent Application No. 07004522.4.

Jul. 9, 2014 Communication accompanying Summons to Attend Oral Proceedings in connection with counterpart European Patent Application No. 07004522.4.

Jan. 2, 2015 Written Submission in connection with counterpart European Patent Application No. 07004522.4.

Jan. 15, 2015 Communication in connection with counterpart European Patent Application No. 07004522.4.

Jan. 29, 2015 Written Submission in connection with counterpart European Patent Application No. 07004522.4.

Feb. 5, 2015 Communication in connection with counterpart European Patent Application No. 07004522.4.

Mar. 23, 2015 Decision of Refusal in connection with counterpart European Patent Application No. 07004522.4.

Jun. 1, 2015 Notice of Appeal in connection with counterpart European Patent Application No. 07004522.4.

Aug. 3, 2015 Statement of Grounds of Appeal in connection with counterpart European Patent Application No. 07004522.4.

International Search Report issued May 13, 2002 in connection with PCT/US01/31243.

European Search Report issued Feb. 27, 2004 in connection with European Patent Application No. 01977533.7.

Supplementary European Search Report issued Feb. 16, 2004 in connection with European Patent Application No. 01977533.7.

Communication Pursuant to Article 94(3) EPC issued Mar. 30, 2005 in connection with European Patent Application No. 01977533.7.

Oct. 10, 2005 Response to Communication Pursuant to Article 94(3)

Communication Pursuant to Article 94(3) EPC issued Nov. 16, 2005 in connection with European Patent Application No. 01977533.7.

Mar. 22, 2006 Response to Communication Pursuant to Article 94(3) EPC issued Nov. 16, 2005 in connection with European Patent Application No. 01977533.7.

International Preliminary Examination Report issued on Jun. 13, 2003 in connection with PCT/US01/31243.

Official Action issued Mar. 31, 2006 in connection with European Patent Application No. 01968905.8.

Official Action issued May 21, 2007 in connection with European Patent Application No. 01968905.8.

International Preliminary Examination Report issued on Feb. 25, 2003 in connection with PCT/US01/28967.

Supplementary European Search Report issued Jun. 7, 2005 in connection with European Patent Application No. 01968905.8.

International Search Report issued Jan. 23, 2002 in connection with PCT/US01/28967.

European Search Report issued May 18, 2016 in connection with European Patent Application No. EP15195765.1, Ju et al.

Notification of Transmittal of International Search Report and the Written Opinion of the International Searching Authority, or the Declaration issued Sep. 9, 2008 in connection with International Application No. PCT/US06/24157.

Notification of Transmittal of International Search Report and Written Opinion, issued Feb. 6, 2008 in connection with International Application No. PCT/06/042739.

Notification Concerning Transmittal of International Preliminary Report on Patentability issued May 15, 2008 in connection with International Application No. PCT/US2006/042698.

Notification of Transmittal of the International Search Report and Written Opinion, issued Aug. 12, 2008 in connection with International Application No. PCT/US07/24646.

Office Action issued Nov. 14, 2007 in connection with U.S. Appl. No. 10/735,081.

Office Action issued Jul. 8, 2008 in connection with U.S. Appl. No. 10/591,520.

Restriction Requirement issued Oct. 1, 2007 in connection with U.S. Appl. No. 10/521,206.

U.S. Application for a Method for Direct Nucleic Acid Sequencing; U.S. Appl. No. 09/266,187, filed Mar. 10, 1999.

U.S. Appl. No. 90/008,149, filed Aug. 4, 2006, Gitten.

U.S. Appl. No. 90/008,152, filed Aug. 3, 2006, Gitten.

International Search Report issued Sep. 26, 2003 in connection with PCT/US03/21818.

International Preliminary Examination Report issued on Mar. 18, 2005 in connection with PCT/US03/21818.

Notification of Transmittal of International Search Report and Written Opinion, issued May 22, 2008 in connection with International Application No. PCT/US06/45180.

International Preliminary Report on Patentability issued on Sep. 5, 2006 in connection with PCT/US05/06960.

International Search Report issued Oct. 29, 2007 in connection with PCT International Application No. PCT/US07/13559.

Supplementary European Search Report issued Feb. 9, 2007 in connection with European Patent Application No. 03764568.6.

Supplementary European Search Report issued Sep. 9, 2008 in connection with PCT International Application No. PCT/US05/06960.

International Search Report issued Sep. 18, 2002 in connection with PCT/US02/09752.

International Preliminary Examination Report issued on Mar. 17, 2003 in connection with PCT/US02/09752.

Supplementary European Search Report issued May 25, 2005 in connection with European Patent Application No. 02728606.1.

Written Opinion of the International Searching Authority issued Oct. 27, 2005 in connection with PCT/US05/06960.

Written Opinion of the International Searching Authority issued Dec. 15, 2006 in connection with PCT/US05/13883.

International Search Report issued Jun. 8, 2004 in connection with PCT/US03/39354.



(56)

## References Cited

## OTHER PUBLICATIONS

International Search Report issued Dec. 15, 2006 in connection with PCT/US05/13883.

Arbo et al. (1993) "Solid Phase Synthesis of Protected Peptides Using New Cobalt (III) Amine Linkers," *Int. J. Peptide Protein Res.* 42:138-154.

Axelrod, V.D. et al. (1978) "Specific termination of RNA polymerase synthesis as a method of RNA and DNA sequencing," *Nucleic Acids Res.* 5(10):3549-3563.

Badman, E. R. et al. (2000) "A Parallel Miniature Cylindrical Ion Trap Array," *Anal. Chem.* (2000) 72:3291-3297.

Badman, E. R. et al. (2000) "Cylindrical Ion Trap Array with Mass Selection by Variation in Trap Dimensions," *Anal. Chem.* 72:5079-5086.

Bai et al. (2003) "Photocleavage of a 2-nitrobenzyl Linker Bridging a Fluorophore to the 5' end of DNA," *PNAS*, vol. 100, No. 2, pp. 409-413.

Bai, X., Kim, S., Li, Z., Turro, N.J. and Ju, J. (2004) "Design and Synthesis of a Photocleavable Biotinylated Nucleotide for DNA Analysis by Mass Spectrometry," *Nucleic Acids Research*, 32(2):534-541.

Benson, S.C., Mathies, R.A., and Glazer, A.N. (1993) "Heterodimeric DNA-binding dyes designed for energy transfer: stability and applications of the DNA complexes," *Nucleic Acids Res.* 21:5720-5726.

Benson, S.C., Singh, P., and Glazer, A.N. (1993) "Heterodimeric DNA-binding dyes designed for synthesis and spectroscopic properties," *Nucleic Acids Res.* 21:5727-5735.

Bergmann et al. (1995) "Allyl As Internucleotide Protecting Group in DNA Synthesis to be Cleaved Off by Ammonia," *Tetrahedron*, 51:6971-6976.

Bergseid M., Baytan A.R., Wiley J.P., Ankener W.M., Stolowitz, Hughs K.A., and Chestnut J.D. (2000) "Small-molecule base chemical affinity system for the purification of proteins," *BioTechniques* 29:1126-1133.

Bi, L., Kim D.H., and Ju, J. (2006) "Design and Synthesis of a Chemically Cleavable Fluorescent Nucleotide, 3'-O-Allyl-dGTP-allyl-Bodipy-FL-510, as a Reversible Terminator for DNA Sequencing by Synthesis" *J. Am. Chem. Soc.*, 128:2542-2543.

Braslavsky I.; Hebert, B.; Kartalov, E.; et al. (2003) "Sequence information can be obtained from single DNA molecules." *Proc. Natl. Acad. Sci.* 100(7):3960-3964.

Brunckova, J. et al. (1994) "Intramolecular Hydrogen Atom Abstraction in Carbohydrates and Nucleosides: Inversion of an  $\alpha$ -to  $\beta$ -Manopyranoside and Generation of Thymidine C-4' Radicals." *Tetrahedron Letters*, vol. 35, pp. 6619-6622.

Buck, G.A. et al. (1999) "Design Strategies and Performance of Custom DNA Sequencing Primers," *BioTechniques* 27(3):528-536.

Burgess, K. et al. (1997) "Photolytic Mass Laddering for Fast Characterization of Oligomers on Single Resin Beads," *J. Org. Chem.* 62:5662-5663.

Buschmann et al. (1999) "The Complex Formation of alpha,omega-Dicarboxylic Acids and alpha,omega-Diols with Cucurbituril and alpha-Cyclodextrin," *Acta Chim. Slov.* 46(3):405-411.

Buschmann et al. (2003) "Spectroscopic Study and Evaluation of Red-Absorbing Fluorescent Dyes," *Bioconjugate Chem.*, 14:195-204.

Canard B. et al. (1994) "DNA polymerase fluorescent substrates with reversible 3'-tags," *Gene*, 148:1-6.

Canard, B. et al. (1995) "Catalytic editing properties of DNA polymerases," *Proc. Natl. Acad. Sci. USA* 92:10859-10863.

Caetano-Anolies (1994) "DNA Amplification Fingerprinting Using Arbitrary Mini-hairpin Oligonucleotide Primers." *Nature Biotechnology*, 12:619-623.

Caruthers, M.H. (1985) "Gene synthesis machines: DNA chemistry and its uses," *Science* 230:281-285.

Chen X. and Kwok, P.-Y. (1997) "Template-directed dye-terminator incorporation (TDI) assay: a homogeneous DNA diagnostic method based on fluorescence resonance energy transfer," *Nucleic Acids Res.* 25:347-353.

Chiu, N.H., Tang, K., Yip, P., Braun, A., Koster, H., and Cantor, C.R. (2000) "Mass spectrometry of single-stranded restriction fragments captured by an undigested complementary sequence," *Nucleic Acids Res.* 28:E31.

Collins, F. S.; Morgan, M.; Patrinos, A. (2003) "The Human Genome Project: Lessons from Large-Scale Biology." *Science*, 300, pp. 286-290.

Crespo-Hernandez et al., (2000) "Part I. Photochemical and Photophysical Studies of Guanine Derivatives: Intermediates Contributing to its Photodestruction Mechanism in Aqueous Solution and the Participation of the Electron Adduct," *Photochemistry and Photobiology*, 71(5):534-543.

Drmanac, S.; Kita, D.; Labat, I.; et al. (1998) "Accurate sequencing by hybridization for DNA diagnostics and individual genomics." *Nat. Biotech.*, 16:54-58.

Edwards, J. et al. (2001) "DNA sequencing using biotinylated dideoxynucleotides and mass spectrometry," *Nucleic Acids Res.* 29(21):1041-1046.

Elango, N. et al. (1983) "Amino Acid Sequence of Human Respiratory Syncytial Virus Nucleocapsid Protein," *Nucleic Acids Research* 11(17) : 5941-5951.

Fallahpour, R.A. (2000) "Photochemical and Thermal reactions of Azido-Oligopyridines: Diazepinones, a New Class of Metal-Complex Ligands," *Helvetica Chimica Acta.* 83:384-393.

Fei, Z. et al. (1998) "MALDI-TOF mass spectrometric typing of single nucleotide polymorphisms with mass-tagged ddNTPs," *Nucleic Acids Research* 26(11):2827-2828.

Finzi, L. et al. (1995) "Measurement of Lactose Repressor-Mediated Loop Formation and Breakdown in Single DNA Molecules." *Science*, 267:378-380.

Fu, D.J., Tang, K., Braun, A., Reuter, D., Darnhofer-Demar, B., Little, D.P., O'Donnell, M.J., Cantor, C.R., and Koster, H. (1998) "Sequencing exons 5 to 8 of the p53 gene by MALDI-TOF mass spectrometry," *Nat. Biotechnol.* 16:381-384.

Gibson, K.J. et al. (1987) "Synthesis and Application of Derivatizable Oligonucleotides," *Nucleic Acids Research*, 15(16): 6455-6467.

Godovikova, T.S. et al. (1999) "5-[3-(E)-(4-Azido-2,3,5,6-tetrafluorobenzamido)propenyl-1]-2'-deoxyuridine-5'-triphosphate Substitutes for Thymidine-5'triphosphate in the Polymerase Chain Reaction," *Bioconjugate Chem.*, 10: 529-537.

Green, T.W. et al. and Wuts, P.G.M. "Protective Groups in Organic Synthesis" 3rd ed. New York: John Wiley & Sons, Inc., 1999. 96-99, 190-191, 260-261, 542-543, and 750-751.

Griffin, T.J. et al. (1999) "Direct Genetic Analysis by Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry," *Proc. Nat. Acad. Sci. USA* 96:6301-6306.

Guibé (1997) "Allylic Protecting Groups and Their Use in a Complex Environment Part I: Allylic Protection of Alcohols," *Tetrahedron*, 53:13509-13556.

Guibé (1998) "Allylic Protecting Groups and Their Use in a Complex Environment Part II: Allylic Protecting Groups and their Removal through Catalytic Palladium  $\pi$ -Allyl Methodology," *Tetrahedron*, 54:2967-3042.

Hacia J.G., Edgemon K., Sun B., Stern D., Fodor S.A., and Collins F.S. (1998) "Two Color Hybridization Analysis Using High Density Oligonucleotide Arrays and Energy Transfer Dyes," *Nucleic Acids Res.* 26:3865-6.

Haff L.A., et al. (1997) "Multiplex Genotyping of PCR Products with Mass Tag-Labeled Primers," *Nucleic Acids Res.* 25(18):3749-3750.

Haffiger, D. et al. (1997) "Seminested RT-PCR Systems for Small Round Structured Viruses and Detection of Enteric Viruses in Seafood," *International Journal of Food Microbiology* 37:27-36.

Hanshaw et al. (2004) "An Indicator Displacement System for

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.