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Ju et al.

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

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(56) **References Cited**

U.S. PATENT DOCUMENTS

(21) Appl. No.: **16/150,185**

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
4,888,274 A 12/1989 Redding et al.
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

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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.

(Continued)

FOREIGN PATENT DOCUMENTS

CA 2425112 4/2002
CA 2408143 11/2002

(Continued)

OTHER PUBLICATIONS

U.S. Appl. No. 12/804,025, filed Jul. 13, 2010, Balasubramanian et
al.

(Continued)

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(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 analogue after the
nucleotide analogue is incorporated into a growing strand of
DNA in a polymerase reaction. The invention also provides
nucleotide analogues which comprise unique labels attached
to the nucleotide analogue through a cleavable linker, and a
cleavable chemical group to cap the —OH group at the
3'-position of the deoxyribose.

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(56)

References Cited

U.S. PATENT DOCUMENTS

5,242,796	A	9/1993	Prober et al.	6,274,320	B1	8/2001	Rothberg et al.
5,302,509	A	4/1994	Cheeseman	6,277,607	B1	8/2001	Tyagi et al.
5,308,990	A	5/1994	Takahashi et al.	6,287,821	B1	9/2001	Shi et al.
5,328,824	A	7/1994	Ward et al.	6,294,324	B1	9/2001	Bensimon et al.
5,332,666	A	7/1994	Prober et al.	6,309,829	B1	10/2001	Livak et al.
5,383,858	A	1/1995	Reilly et al.	6,309,836	B1	10/2001	Kwiatkowski
5,424,186	A	6/1995	Fodor et al.	6,312,893	B1	11/2001	Van Ness et al.
5,436,143	A	7/1995	Hyman	6,316,230	B1	11/2001	Egholm et al.
5,437,975	A	8/1995	McClelland et al.	6,335,155	B1	1/2002	Wells et al.
5,449,767	A	9/1995	Ward et al.	6,361,940	B1	3/2002	Van Ness et al.
5,476,928	A	12/1995	Ward et al.	6,380,378	B1	4/2002	Kitamura et al.
5,516,664	A	5/1996	Hyman	6,432,360	B1	8/2002	Church
5,534,424	A	7/1996	Uhlen et al.	6,495,680	B1	12/2002	Gong
5,547,839	A	8/1996	Dower et al.	6,524,829	B1	2/2003	Seeger
5,547,859	A	8/1996	Goodman et al.	6,555,349	B1	4/2003	O'Donnell
5,556,748	A	9/1996	Douglas	6,613,508	B1	9/2003	Ness et al.
5,599,675	A	2/1997	Brenner	6,613,513	B1	9/2003	Parce et al.
5,602,000	A	2/1997	Hyman	6,627,436	B2	9/2003	Sorge et al.
5,614,365	A	3/1997	Tabor et al.	6,627,748	B1	9/2003	Ju et al.
5,637,469	A	6/1997	Wilding et al.	6,632,655	B1	10/2003	Mehta et al.
5,654,419	A	8/1997	Mathies et al.	6,639,088	B2	10/2003	Kwiatkowski
5,658,736	A	8/1997	Wong	6,664,079	B2	12/2003	Ju et al.
5,709,999	A	1/1998	Shattuck-Eidens et al.	6,664,399	B1	12/2003	Sabesan
5,714,330	A	2/1998	Brenner et al.	6,713,255	B1	3/2004	Makino et al.
5,728,528	A	3/1998	Mathies et al.	6,780,591	B2	8/2004	Williams et al.
5,763,594	A	6/1998	Hiatt et al.	6,787,308	B2	9/2004	Balasubramanian et al.
5,770,365	A	6/1998	Lane et al.	6,818,395	B1	11/2004	Quake et al.
5,770,367	A	6/1998	Southern et al.	6,833,246	B2	12/2004	Balasubramanian
5,789,167	A	8/1998	Konrad	6,858,393	B1	2/2005	Anderson et al.
5,798,210	A	8/1998	Canard et al.	6,864,052	B1	3/2005	Drmanac et al.
5,804,386	A	9/1998	Ju	6,911,345	B2	6/2005	Quake et al.
5,808,045	A	9/1998	Hiatt et al.	6,934,636	B1	8/2005	Skierczynski et al.
5,814,454	A	9/1998	Ju	6,982,146	B1	1/2006	Schneider et al.
5,821,356	A	10/1998	Khan et al.	7,037,687	B2	5/2006	Williams et al.
5,834,203	A	11/1998	Katzir et al.	7,056,661	B2	6/2006	Korlach et al.
5,844,106	A	12/1998	Seela et al.	7,056,666	B2	6/2006	Dower et al.
5,849,542	A	12/1998	Reeve et al.	7,057,026	B2	6/2006	Barnes et al.
5,853,992	A	12/1998	Glazer et al.	7,057,031	B2	6/2006	Olejnik et al.
5,856,104	A	1/1999	Chee et al.	7,074,597	B2	7/2006	Ju
5,858,671	A	1/1999	Jones	7,078,499	B2	7/2006	Odedra et al.
5,869,255	A	2/1999	Mathies et al.	7,105,300	B2	9/2006	Parce et al.
5,872,244	A	2/1999	Hiatt et al.	7,270,951	B1	9/2007	Stemple et al.
5,876,936	A	3/1999	Ju	7,279,563	B2	10/2007	Kwiatkowski
5,885,775	A	3/1999	Haff et al.	7,329,496	B2	2/2008	Dower et al.
5,885,813	A	3/1999	Davis et al.	7,345,159	B2	3/2008	Ju et al.
5,908,755	A	6/1999	Kumar et al.	7,393,533	B1	7/2008	Crotty et al.
5,945,283	A	8/1999	Kwok et al.	7,414,116	B2	8/2008	Milton et al.
5,948,648	A	9/1999	Khan et al.	7,427,673	B2	9/2008	Balasubramanian et al.
5,952,180	A	9/1999	Ju	7,459,275	B2	12/2008	Dower et al.
5,959,089	A	9/1999	Hannessian	7,541,444	B2	6/2009	Milton et al.
5,962,228	A	10/1999	Brenner	7,566,537	B2	7/2009	Balasubramanian et al.
6,001,566	A	12/1999	Canard	7,622,279	B2	11/2009	Ju
6,001,611	A	12/1999	Will	7,635,578	B2	12/2009	Ju et al.
6,008,379	A	12/1999	Benson et al.	7,713,698	B2	5/2010	Ju et al.
6,013,445	A	1/2000	Albrecht et al.	7,771,973	B2	8/2010	Milton et al.
6,028,190	A	2/2000	Mathies et al.	7,785,790	B1	8/2010	Church et al.
6,046,005	A	4/2000	Ju et al.	7,790,869	B2	9/2010	Ju et al.
6,074,823	A	6/2000	Koster	7,883,869	B2	2/2011	Ju et al.
6,087,095	A	7/2000	Rosenthal et al.	7,982,029	B2	7/2011	Ju et al.
6,111,116	A	8/2000	Benson et al.	8,088,575	B2	1/2012	Ju et al.
6,136,543	A	10/2000	Anazawa et al.	8,158,346	B2	4/2012	Balasubramanian et al.
6,175,107	B1	1/2001	Juvinall	8,298,792	B2	10/2012	Ju et al.
6,197,557	B1	3/2001	Makarov et al.	8,399,188	B2	3/2013	Zhao et al.
6,207,831	B1	3/2001	Auer et al.	8,796,432	B2	8/2014	Ju et al.
6,210,891	B1	4/2001	Nyren et al.	8,889,348	B2	11/2014	Ju
6,214,987	B1	4/2001	Hiatt et al.	9,115,163	B2	8/2015	Ju et al.
6,218,118	B1	4/2001	Sampson et al.	9,133,511	B2	9/2015	Ju et al.
6,218,530	B1	4/2001	Rothschild et al.	9,159,610	B2	10/2015	Zhang et al.
6,221,592	B1	4/2001	Schwartz et al.	9,175,342	B2	11/2015	Ju et al.
6,232,465	B1	5/2001	Hiatt et al.	9,255,292	B2	2/2016	Ju et al.
6,242,193	B1	6/2001	Anazawa et al.	9,297,042	B2	3/2016	Ju et al.
6,245,507	B1	6/2001	Bogdanov	9,708,358	B2	7/2017	Ju et al.
6,248,884	B1	6/2001	Lam et al.	9,718,852	B2	8/2017	Ju et al.
				9,719,139	B2	8/2017	Ju et al.
				9,725,480	B2	8/2017	Ju et al.
				9,868,985	B2	1/2018	Ju et al.
				2002/0012966	A1	1/2002	Shi et al.

(56)

References Cited

U.S. PATENT DOCUMENTS

2003/0022225	A1	1/2003	Monforte et al.
2003/0027140	A1	2/2003	Ju et al.
2003/0044871	A1	3/2003	Cutsforth et al.
2003/0054360	A1	3/2003	Gold et al.
2003/0099972	A1	5/2003	Olejnik et al.
2003/0166282	A1	9/2003	Brown et al.
2003/0180769	A1	9/2003	Metzker
2003/0186256	A1	10/2003	Fischer
2003/0190680	A1	10/2003	Rothschild et al.
2003/0198982	A1	10/2003	Seela et al.
2004/0014096	A1	1/2004	Anderson et al.
2004/0096825	A1	5/2004	Chenna et al.
2005/0032081	A1	2/2005	Ju et al.
2005/0170367	A1	8/2005	Quake et al.
2005/0239134	A1	10/2005	Gorenstein et al.
2006/0003352	A1	1/2006	Lipkin et al.
2006/0057565	A1	3/2006	Ju et al.
2006/0105461	A1	5/2006	Tom-Moy et al.
2006/0160081	A1	7/2006	Milton et al.
2006/0160113	A1	7/2006	Korlach et al.
2006/0240439	A1	10/2006	Smith et al.
2006/0252038	A1	11/2006	Ju
2007/0166705	A1	7/2007	Milton et al.
2009/0088332	A1	4/2009	Ju et al.
2009/0240030	A1	9/2009	Ju et al.
2010/0159531	A1	6/2010	Gordon et al.
2010/0323350	A1	12/2010	Gordon et al.
2011/0014611	A1	1/2011	Ju et al.
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.
2015/0037788	A1	2/2015	Ju
2015/0080232	A1	3/2015	Ju et al.
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.
2016/0264612	A1	9/2016	Ju et al.
2017/0088574	A1	3/2017	Ju et al.
2017/0088575	A1	3/2017	Ju et al.
2017/0088891	A1	3/2017	Ju et al.
2017/0313737	A1	11/2017	Ju et al.
2018/0201642	A1	7/2018	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 1989/09282	10/1989
WO	WO 89/10977	11/1989
WO	WO 1989/11548	11/1989
WO	WO 1990/13666	11/1990

WO	WO 1992/10587	6/1992
WO	WO 1993/05183	3/1993
WO	WO 93/12340	10/1993
WO	WO 1993/21340	10/1993
WO	WO 1994/14972	7/1994
WO	WO 1996/07669	3/1996
WO	WO 96/23807	8/1996
WO	WO 1996/23807	8/1996
WO	WO 96/27025	9/1996
WO	WO 1996/27025	9/1996
WO	WO 1997/08183	3/1997
WO	WO 1997/27317	7/1997
WO	WO 1997/35033	9/1997
WO	WO 1998/30720	7/1998
WO	WO 98/33939	8/1998
WO	WO 1998/33939	8/1998
WO	WO 1998/44151	10/1998
WO	WO 98/53300	11/1998
WO	WO 1999/05315	2/1999
WO	WO 1999/49082	9/1999
WO	WO 1999/57321	11/1999
WO	WO 2000/02895	1/2000
WO	WO 2000/06770	2/2000
WO	WO 2000/09753	2/2000
WO	WO 2000/15844	3/2000
WO	WO 2000/18956	4/2000
WO	WO 2000/21974	4/2000
WO	WO 2000/50172	8/2000
WO	WO 2000/50642	8/2000
WO	WO 00/53812	9/2000
WO	WO 2000/53805	9/2000
WO	WO 2000/53812	9/2000
WO	WO 2000/70073	11/2000
WO	WO 2001/16375	3/2001
WO	WO 2001/23610	4/2001
WO	WO 2001/25247	4/2001
WO	WO 2001/27625	4/2001
WO	WO 2001/32930	5/2001
WO	WO 2001/57248	8/2001
WO	WO 2001/57249	8/2001
WO	WO 01/92284	12/2001
WO	WO 2001/92284	12/2001
WO	WO 2002/02813	1/2002
WO	WO 02/21098	3/2002
WO	WO 2002/22883	3/2002
WO	WO 02/29003	4/2002
WO	WO 2002/29003	4/2002
WO	WO 2002/72892	9/2002
WO	WO 2002/079519	10/2002
WO	WO 2002/88381	11/2002
WO	WO 2002/88382	11/2002
WO	WO 2003/02767	1/2003
WO	WO 2003/20968	3/2003
WO	WO 2003/48178	6/2003
WO	WO 2003/48387	6/2003
WO	WO 2003/85135	10/2003
WO	WO 04/18493	3/2004
WO	WO 04/18497	3/2004
WO	WO 2004/018493	3/2004
WO	WO 2004/18493	3/2004
WO	WO 2004/18497	3/2004
WO	WO 2004/018497	3/2004
WO	WO 2004/055160	7/2004
WO	WO 2005/084367	9/2005
WO	WO 2006/73436	7/2006
WO	WO 2007/002204	1/2007
WO	WO 2007/62105	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

(56) **References Cited**

FOREIGN PATENT DOCUMENTS

WO	WO 2015/148402	10/2015
WO	WO 2015/179284	11/2015

OTHER PUBLICATIONS

U.S. Appl. No. 10/227,131, filed Aug. 23, 2002, Barnes et al. May 4, 2013 Petition for Inter Partes Review of U.S. Pat. No. 8,158,346, issued Apr. 17, 2012.

Aug. 5, 2013 Patent Owner Preliminary Response to Petition for Inter Partes Review of U.S. Pat. No. 8,158,346, issued Apr. 17, 2012.

May 3, 2013 Declaration of Dr. Bruce Branchaud (Exhibit 1011, filed May 4, 2013 in connection with IPR2013-00266).

Excerpts from the '346 Patent File History (Exhibit 1012, filed May 4, 2013 in connection with IPR2013-00266).

Excerpts from the file history of European Patent Application No. 02781434.2 (Exhibit 1013, filed May 4, 2013 in connection with IPR2013-00266).

Oct. 28, 2013 Decision Instituting Inter Partes Review in connection with IPR2013-00266.

Dec. 30, 2013 Illumine Motion to Amend Under 37 C.F.R. §42.121 in connection with IPR2013-00266.

Floyd Romesburg Declaration, CV, and List of Documents Considered by Romesburg (Exhibits 2004, 2005, and 2028, filed Dec. 30, 2013 in connection with IPR2013-00266).

Bystrom, Branchaud et al., "ATP Analogs with Non-transferable Groups in the g Position as Inhibitors of Glycerol Kinase" *Bioorganic & Medicinal Chemistry Letters*, 7:2613-2616 (1997) (Exhibit 2021, filed Dec. 30, 2013 in connection with IPR2013-00266).

Pages from Handbook of Reagents for Organic Synthesis: Reagents for Silicon-Mediated Organic Synthesis (Philip L. Fuchs, ed.) (2011) (Exhibit 2022, filed Dec. 30, 2013 in connection with IPR2013-00266).

Eric Vermaas Declaration—Redacted version (Exhibit 2023, filed Dec. 30, 2013 in connection with IPR2013-00266).

Excerpts from Oct. 3, 2013 Bruce Branchaud Deposition Transcript in IPR2013-00128 (Exhibit 2024, filed Dec. 30, 2013 in connection with IPR2013-00266).

Petitioner's Feb. 28, 2014 Opposition to Patentee Motion to Amend in connection with IPR2013-00266.

Second Declaration of Dr. Bruce Branchaud in support of Intelligent Bio-Systems, Inc.'s Opposition to Illumina's Motion to Amend, from Feb. 28, 2014 (Exhibit 1021, filed Feb. 28, 2014 in connection with IPR2013-00266).

Deposition of Floyd Romesberg, Ph. D., from Jan. 14, 2014 (Exhibit 1022, filed Feb. 28, 2014 in connection with IPR2013-00266).

Deposition of Eric Vermaas from Jan. 13, 2014 (Exhibit 1029, filed Feb. 28, 2014 in connection with IPR2013-00266).

Excerpts from Protective Groups in Organic Synthesis (Theodora W. Greene & Peter G. M. Wuts eds., John Wiley & Sons, Inc. 3rd ed. 1999) (1991) (Exhibit 1035, filed Feb. 28, 2014 in connection with IPR2013-00266).

Zavgorodny et al., "1-Alkylthioalkylation of Nucleoside Hydroxyl Functions and Its Synthetic Applications: A New Versatile Method in Nucleoside Chemistry" *32 Tetrahedron Letters* 7593 (1991) (Exhibit 1038, filed Feb. 28, 2014 in connection with IPR2013-00266).

Mar. 21, 2014 Patent Owner's Reply to Petitioner's Opposition to Patent Owner's Motion to Amend in connection with IPR2013-00266.

Mar. 11, 2014 Bruce Branchaud Deposition Transcript (Exhibit 2030, filed Mar. 21, 2014 in connection with IPR2013-00266).

Excerpts from Feb. 11, 2014 Bruce Branchaud Deposition Transcript in related IPR2013-00128 (Exhibit 2032, filed Mar. 21, 2014 in connection with IPR2013-00266).

Phenols" *Tetrahedron*, 44:6055-6064 (1988) (Exhibit 2043, filed Mar. 21, 2014 in connection with IPR2013-00266).

Excerpts from Oct. 3, 2013 Bruce Branchaud Deposition Transcript in related Inter Partes Review IPR2013-00128 (Exhibit 2044, filed Mar. 21, 2014 in connection with IPR2013-00266).

Welch et al., "Syntheses of Nucleosides Designed for Combinatorial DNA Sequencing" *Chem. Eur. J.*, 5:951-960 (1999) (Exhibit 2045, filed Mar. 21, 2014 in connection with IPR2013-00266).

Welch et al., Corrigenda to "Syntheses of Nucleosides Designed for Combinatorial DNA Sequencing" *Chem. Eur. J.*, 11:7145 (2005) (Exhibit 2046, filed Mar. 21, 2014 in connection with IPR2013-00266).

Wu et al., "Termination of DNA synthesis by N6-alkylated, not 3'-0-alkylated, photocleavable 2'-deoxyadenosine triphosphates", *Nucleic Acids Research* 35:6339-6349 (2007) (Exhibit 2047, filed Mar. 21, 2014 in connection with IPR2013-00266).

Taylor et al., "Rise per base pair in helices of double-stranded rotavirus RNA determined by electron microscopy" *Virus Research*, 2:175-182 (1985) (Exhibit 2048, filed Mar. 21, 2014 in connection with IPR2013-00266).

Watson et al., *Molecular Biology of the Gene*, Fifth Edition, Chapter 6 (2004) (Exhibit 2049, filed Mar. 21, 2014 in connection with IPR2013-00266).

Shen et al., "RNA structure at high resolution" *FASEB J.*, 9:1023-1033 (1995) (Exhibit 2050, filed Mar. 21, 2014 in connection with IPR2013-00266).

Holtzman et al., "Electron microscopy of complexes of isolated acetylcholine receptor, biotinyl-toxin, and avidin" *Proc. Natl. Acad. Sci. USA*, 79:310-314 (1982) (Exhibit 2051, filed Mar. 21, 2014 in connection with IPR2013-00266).

Pugliese et al., "Three-dimensional Structure of the Tetragonal Crystal Form of Egg-white Avidin in its Functional Complex with Biotin at 2.7 Angstrom Resolution" *Journal of Molecular Biology*, 231:698-710 (1993) (Exhibit 2052, filed Mar. 21, 2014 in connection with IPR2013-00266).

Fersht, "Fidelity of replication of phage ϕ X174 DNA by DNA polymerase III holoenzyme: Spontaneous mutation by misincorporation" *Proc. Natl. Acad. Sci. USA*, 76:4946-4950 (1979) (Exhibit 2053, filed Mar. 21, 2014 in connection with IPR2013-00266).

Fersht et al., "DNA polymerase accuracy and spontaneous mutation rates: Frequencies of purine-purine, purine-pyrimidine, and pyrimidine-pyrimidine mismatches during DNA replication" *Proc. Natl. Acad. Sci. USA*, 78:4251-4255 (1981) (Exhibit 2054, filed Mar. 21, 2014 in connection with IPR2013-00266).

Bebenek et al., "Frameshift errors initiated by nucleotide misincorporation" *Proc. Natl. Acad. Sci. USA*, 87:4946-4950 (1990) (Exhibit 2055, filed Mar. 21, 2014 in connection with IPR2013-00266).

Bebenek et al., "The Effects of dNTP Pool Imbalances on Frameshift Fidelity during DNA Replication" *J. Biol. Chem.*, 267:3589-3596 (1992) (Exhibit 2056, filed Mar. 21, 2014 in connection with IPR2013-00266).

Greene and Wuts, *Protective Groups in Organic Synthesis*, 3rd ed., Chapter 1 (1999) (Exhibit 2057, filed Mar. 21, in connection with IPR2013-00266).

Apr. 18, 2014 Petitioner Motion for Observations on the Cross-Examination Testimony of Dr. Romesberg, in connection with IPR2013-00266.

Apr. 18, 2014 Patentee Motion to Exclude Evidence in connection with IPR2013-00266.

Apr. 10, 2014 transcript of Deposition of Floyd Romesberg (Exhibit 1042, filed Apr. 18, 2014 in connection with IPR2013-00266).

Apr. 18, 2014 Patentee Motion to Exclude Evidence in connection with IPR2013-00266.

May 2, 2014 Patentee Response to Petitioner Motion for Observations on Romesberg Testimony, in connection with IPR2013-00266.

Petitioner Demonstratives for May 28, 2014 Oral Hearing (Exhibit 1045, filed May 22, 2014 in connection with IPR2013-00266).

Patentee Demonstratives for May 28, 2014 Oral Hearing (Exhibit 2060, filed May 22, 2014 in connection with IPR2013-00266).

Transcript of May 28, 2014 Oral Hearing in IPR2013-00266, entered Jul. 8, 2014.

(56)

References Cited

OTHER PUBLICATIONS

- Oct. 3, 2012 Petition for Inter Partes Review of U.S. Pat. No. 8,088,575.
- Oct. 3, 2012 Motion to Waive Page Limit and Proposed Petition in connection with Petition for Inter Partes Review of U.S. Pat. No. 8,088,575.
- Jan. 7, 2013 Preliminary Response under 37 C.F.R. 42.107 in connection with IPR2013-00011.
- Mar. 12, 2013 Decision on Petition for Inter Partes Review in connection with IPR2013-00011.
- Mar. 26, 2013 Request for Reconsideration in connection with IPR2013-00011.
- Mar. 26, 2013 Request for Rehearing under 37 C.F.R. 42.71 of Decision to Institute Inter Partes Review in connection with IPR2013-00011.
- Apr. 26, 2013 Opposition to Request for Reconsideration (Rehearing) Under 37 C.F.R. 42.71.(C) in connection with IPR2013-00011.
- May 10, 2013 Decision on Request for Rehearing in connection with IPR2013-00011.
- Jun. 25, 2013 Motion to Amend Under 37 C.F.R. 42.121 in connection with IPR2013-00011.
- Aug. 30, 2013 Substitute Patent Owner Response Under 37 C.F.R. 42.120 in connection with IPR2013-00011.
- Sep. 27, 2013 Petitioner Opposition to Motion to Amend in connection with IPR2013-00011.
- Sep. 27, 2013 Petitioner Reply to Response to Petition in connection with IPR2013-00011.
- Nov. 18, 2013 Substitute Patent Owner Reply on Motion to Amend in connection with IPR2013-00011.
- Oct. 2, 2012 Declaration of George Weinstock Under Rule 37 C.F.R. §1.132 (Exhibit 1021, filed Oct. 3, 2012 in connection with IPR2013-00011).
- Excerpts of File History of U.S. Pat. No. 8,088,575 (Exhibit 1022, filed Oct. 3, 2012 in connection with IPR2013-00011).
- Sep. 27, 2013 Declaration of Kevin Burgess (Exhibit 1053, filed Sep. 27, 2013 in connection with IPR2013-00011).
- Jun. 25, 2013 Substitute Declaration of Dr. George L. Trainor [redacted] (Exhibit 2033, filed Aug. 30, 2013 in connection with IPR2013-00011).
- Nov. 12, 2013 Petitioner Motion to Exclude Evidence in connection with IPR2012-00007.
- Nov. 12, 2013 Patent Owner Motion for Observations on the Cross-Examination Testimony of Kevin Burgess, Ph.D. in connection with IPR2012-00007.
- Nov. 12, 2013 Patent Owner Motion to Exclude Evidence in connection with IPR2012-00007.
- Nov. 26, 2013 Petitioner's Response to Motion for Observations in connection with IPR2013-00011.
- Nov. 26, 2013 Patent Owner's Opposition to Petitioner's Motion to Exclude in connection with IPR2013-00011.
- Nov. 26, 2013 Petitioner's Opposition to Motion to Exclude in connection with IPR2013-00011.
- Dec. 3, 2013 Petitioner Reply to Patent Owner's Opposition to Motion to Exclude in connection with IPR2013-00011.
- Dec. 3, 2013 Patent Owner Reply on Motion to Exclude in connection with IPR2013-00011.
- Mar. 6, 2014 Final Written Decision in connection with IPR2013-00011.
- 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
- 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 energy transfer: 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 α - to β -Mannopyranoside 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.
- Chee, M. et al. (1996) "Accessing genetic information with high density DNA arrays," *Science* 274:610-614.
- 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

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