



US010457984B2

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

(10) **Patent No.:** **US 10,457,984 B2**
(45) **Date of Patent:** ***Oct. 29, 2019**

- (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 disclaimer.

(21) Appl. No.: **16/150,180**
(22) Filed: **Oct. 2, 2018**

(65) **Prior Publication Data**
US 2019/0085015 A1 Mar. 21, 2019

Related U.S. Application Data
(60) Continuation of application No. 15/915,983, filed on Mar. 8, 2018, which is a 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.**
C12Q 1/68 (2018.01)
C07H 19/14 (2006.01)
C12Q 1/6869 (2018.01)
C07H 21/00 (2006.01)
C12Q 1/686 (2018.01)
C12Q 1/6874 (2018.01)

C12Q 1/6876 (2018.01)
C40B 40/00 (2006.01)
(52) **U.S. Cl.**
CPC *C12Q 1/6869* (2013.01); *C07H 19/10* (2013.01); *C07H 19/14* (2013.01); *C07H 21/00* (2013.01); *C12Q 1/68* (2013.01); *C12Q 1/686* (2013.01); *C12Q 1/6872* (2013.01); *C12Q 1/6874* (2013.01); *C12Q 1/6876* (2013.01); *C07B 2200/11* (2013.01); *C12Q 2525/117* (2013.01); *C12Q 2525/186* (2013.01); *C12Q 2535/101* (2013.01); *C12Q 2535/122* (2013.01); *C12Q 2563/107* (2013.01); *C12Q 2565/501* (2013.01); *C40B 40/00* (2013.01)

(58) **Field of Classification Search**
CPC C12Q 1/6869; C07H 19/14
USPC 536/4.1; 435/6.1
See application file for complete search history.

(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 |
| 4,888,274 A | 12/1989 | Radding 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 |
| 5,242,796 A | 9/1993 | Prober et al. |

(Continued)

FOREIGN PATENT DOCUMENTS

| | | |
|----|---------|---------|
| CA | 2425112 | 4/2002 |
| CA | 2408143 | 11/2002 |

(Continued)

OTHER PUBLICATIONS

U.S. Pat. No. 09/266,187, filed Mar. 10, 1999, Stemple et al.
(Continued)

Primary Examiner — Jezia Riley
(74) *Attorney, Agent, or Firm* — John P. White; 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 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.

2 Claims. 28 Drawing Sheets



(56)

References Cited

U.S. PATENT DOCUMENTS

| | | | | | | | |
|-----------|----|---------|------------------------|--------------|----|---------|------------------------|
| 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 et al. | 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. |
| 6,255,083 | B1 | 7/2001 | Williams | 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. |
| | | | | 2002/0168642 | A1 | 11/2002 | Druker |

(56)

References Cited

U.S. PATENT DOCUMENTS

| | | | |
|--------------|----|---------|-------------------|
| 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 91/06678 | 5/1991 |

| | | |
|----|----------------|---------|
| 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 2004/18493 | 3/2004 |
| WO | WO 2004/018493 | 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

- Sep. 16, 2012 Petition for Inter Partes Review of U.S. Pat. No. 7,713,698, issued May 11, 2010.
- Sep. 16, 2012 Motion to Waive Page Limit and Proposed Petition in connection with Petition for Inter Partes Review of U.S. Pat. No. 7,713,698, issued May 11, 2010.
- Dec. 20, 2012 Preliminary Response under 37 C.F.R. 42.107 in connection with IPR2012-00006.
- Mar. 12, 2013 Decision on Petition for Inter Partes Review in connection with IPR2012-00006.
- Mar. 26, 2013 Request for Reconsideration in connection with IPR2012-00006.
- Apr. 26, 2013 Opposition to Request for Reconsideration (Rehearing) Under 37 C.F.R. 42.71. (C) in connection with IPR2012-00006.
- Sep. 27, 2013 Petitioner Opposition to Motion to Amend in connection with IPR2012-00006.
- Sep. 27, 2013 Petitioner Reply to Response to Petition in connection with IPR2012-00006.
- Nov. 18, 2013 Substitute Patent Owner Reply on Motion to Amend in Connection with IPR2012-00006.
- Prober et al. (1987), "A System for Rapid DNA Sequencing with Fluorescent Chain-Terminating Dideoxynucleotides", *Science* vol. 238, Oct. 16, 1987, pp. 336-341 (Exhibit 1003, filed Sep. 16, 2012 in connection with IPR2012-00006).
- Sep. 15, 2012 Declaration of George Weinstock Under Rule 37 C.F.R. §1.132 (Exhibit 1021, filed Sep. 16, 2012 in connection with IPR2012-00006).
- Excerpts of File History of U.S. Pat. No. 7,713,698 (Exhibit 1022, filed Sep. 16, 2012 in connection with IPR2012-00006).
- Columbia's Amended Complaint from *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, D. Del C.A. No. 12-376 (GMS), filed Apr. 11, 2012 (Exhibit 1025, filed Apr. 30, 2013 in connection with IPR2012-00006).
- Illumina's Answer to Amended Complaint from *The Trustees of Columbia University in the City of New York v. Illumina, Inc.*, D. Del C.A. No. 12-376 (GMS), filed Dec. 21, 2012 (Exhibit 1026, filed Apr. 30, 2013 in connection with IPR2012-00006).
- Rosenblum et al., "New Dye-Labeled Terminators for Improved DNA Sequencing Patterns," *Nucleic Acid Research*, 1997, vol. 25, No. 22, pp. 4500-4504 (Exhibit 1030, filed Jun. 18, 2013 in connection with IPR2012-00006).
- Jun. 8, 2013 Videotaped Deposition Transcript of George M. Weinstock, Ph.D. (Exhibit 1034, filed Jun. 18, 2013 in connection with IPR2012-00006).
- "Next Generation Genomics: World Map of High-throughput Sequencers," Sep. 1, 2013 (Exhibit 1036, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Videotaped Deposition Transcript of Dr. Xiaohai Liu, Mar. 20, 2013 (Exhibit 1039, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Excerpt from videotaped Deposition Transcript of George M. Weinstock, Ph.D., Jun. 8, 2013 (Exhibit 1040, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Seela et al., "Oligonucleotide Duplex Stability Controlled by the 7-Substituents of 7-Deazaguanine Bases," *Bioorganic & Medical Chemistry Letters*, vol. 5, No. 24, pp. 3049-3052, 1995 (Exhibit 1041, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Ramzaeva et al., "123. 7-Deazaguanine DNA: Oligonucleotides with Hydrophobic or Cationic Side Chains," *Helvetica Chimica Acta*, vol. 80, pp. 1809-1822, 1997 (Exhibit 1042, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Helvetica Chimica Acta, vol. 78, pp. 1083-1090, 1995 (Exhibit 1043, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Seela et al., "Duplex Stability of Oligonucleotides Containing 7-Substituted 7-Deaza- and 8-Aza-7-Deazapurine Nucleosides," *Nucleosides & Nucleotides*, 16(7-9), pp. 963-966, 1997 (Exhibit 1044, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Burgess et al., "Syntheses of Nucleosides Designed for Combinatorial DNA Sequencing," *Chemistry—A European Journal*, vol. 5, No. 3, pp. 951-960, 1999 (Exhibit 1045, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Jan. 28, 2013 Declaration of Dr. Bruce P. Branchaud in Support of Petition for Inter Partes Review of U.S. Pat. No. 7,057,026 (Exhibit 1049, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Lee et al., "DNA sequencing with dye-labeled terminators and T7 DNA polymerase: effect of dyes and dNTPs on incorporation of dye-terminators and probability analysis of termination fragments," *Nucleic Acids Research*, vol. 20, No. 10, pp. 2471-2483, 1992 (Exhibit 1050, filed Sep. 27, 2013 in connection with IPR2012-00006).
- <http://www.answers.com/topic/incubate>, Accessed Sep. 27, 2013 (Exhibit 1051, filed Sep. 27, 2013 in connection with IPR2012-00006).
- http://en.wikipedia.org/wiki/Fluorenylmethoxycarbonyl_chloride, Accessed Sep. 27, 2013 (Exhibit 1052, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Sep. 27, 2013 Declaration of Kevin Burgess (Exhibit 1053, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Fuji, et al., "An Improved Method for Methoxymethylation of Alcohols under Mild Acidic Conditions," *Synthesis—The Journal of Synthetic Organic Chemistry*, pp. 276-277, Apr. 1975 (Exhibit 1054, filed Sep. 27, 2013 in connection with IPR2012-00006).
- Dower patent with highlights (Exhibit 2006, filed Apr. 26, 2013 in connection with IPR2012-00006).
- U.S. Pat. No. 7,713,698 (filed Aug. 20, 2007, issued May 11, 2010) (Exhibit 1001 in IPR2012-00006) (Exhibit 2011, filed Jun. 24, 2013 in connection with IPR2012-00006).
- U.S. Pat. No. 7,790,869 (filed Jun. 5, 2007, issued Sep. 7, 2010) (Exhibit 1001 in IPR2012-00007) (Exhibit 2012, filed Jun. 24, 2013 in connection with IPR2012-00006).
- Oct. 2, 2012 Declaration of George Weinstock Under 37 CFR 1.132 (Exhibit 1021 in IPR2013-00011) (Exhibit 2013, filed Jun. 24, 2013 in connection with IPR2012-00006).
- Petition for Inter Partes Review of U.S. Pat. No. 8,088,575 (Paper 4 in IPR2013-00011) (Exhibit 2014, filed Jun. 24, 2013 in connection with IPR2012-00006).
- Metzker et al. (1994) Termination of DNA synthesis by novel 3'-modified-deoxyribonucleoside 5'-triphosphates. *Nucleic Acids Res.* 22:4259-4267 (Exhibit 2015, filed Jun. 24, 2013 in connection with IPR2012-00006).
- Wu et al. (2007) Termination of DNA synthesis by N6-alkylated, not 3'-O-alkylated, photocleavable 2'-deoxyadenosine triphosphates. *Nucleic Acids Res.* 35:6339-6349 (Exhibit 2016, filed Jun. 24, 2013 in connection with IPR2012-00006).
- Sep. 15, 2012 Declaration of George Weinstock Under 37 CFR 1.132 (Exhibit 1021 in IPR2012-00007) (Exhibit 2017, filed Jun. 24, 2013 in connection with IPR2012-00006).
- Sep. 15, 2012 Declaration of George Weinstock Under 37 CFR 1.132 (Exhibit 1021 in IPR2012-00006) (Exhibit 2018, filed Jun. 24, 2013 in connection with IPR2012-00006).
- Definition of "DNA microarray." http://en.wikipedia.org/wiki/DNA_microarray (Exhibit 2019, filed Jun. 24, 2013 in connection with IPR2012-00006).
- Brettin et al. (2005) Expression capable library for studies of *Neisseria gonorrhoeae*, version 1.0 *BMC Microbiology*. 5:50 (Exhibit 2020, filed Jun. 24, 2013 in connection with IPR2012-00006).
- George M. Weinstock, *Handbook of Molecular Microbial Ecology*, vol. 1—Chapter 18: The Impact of Next-Generation Sequencing Technologies on Metagenomics 141-147 Frans J. de Bruijn ed., John Wiley & Sons, Inc. (2011) (Exhibit 2021, filed Jun. 24, 2013 in connection with IPR2012-00006).
- Sep. 16, 2012 Petition for Inter Partes Review of U.S. Pat. No.

(56)

References Cited

OTHER PUBLICATIONS

Sep. 16, 2012 Petition for Inter Partes Review of U.S. Pat. No. 7,790,869 (Paper 5 in IPR2012-00007) (Exhibit 2023, filed Jun. 24, 2013 in connection with IPR2012-00006).

Maxam and Gilbert (1977) A new method for sequencing DNA, Proc. Natl. Acad. Sci. USA. 74:560-564 (Exhibit 2024, filed Jun. 24, 2013 in connection with IPR2012-00006).

Sanger et al. (1977) DNA sequencing with chain-terminating inhibitors, Proc. Natl. Acad. Sci. USA. 74:5463-5467 (Exhibit 2025, filed Jun. 24, 2013 in connection with IPR2012-00006).

Pennisi (2000) DOE Team Sequences Three Chromosomes, Science. 288:417-419 (Exhibit 2026, filed Jun. 24, 2013 in connection with IPR2012-00006).

Welch and Burgess (1999) Synthesis of Fluorescent, Photolabile 3'-O-Protected nucleoside Triphosphates for the Base Addition Sequencing Scheme, nucleosides & Nucleotides. 18:197-201 (Exhibit 2027, filed Jun. 24, 2013 in connection with IPR2012-00006).

Hyman (1998) A New Method of Sequencing DNA, Analytical Biochemistry 174:423-436 (Exhibit 2028, filed Jun. 24, 2013 in connection with IPR2012-00006).

Canard and Sarfati (1994) DNA polymerase fluorescent substrates with reversible 3'-tags, Gene. 148:1-6 (Exhibit 2030, filed Jun. 24, 2013 in connection with IPR2012-00006).

Sarfati et al. (1987) Synthesis of Fluorescent or Biotinylated Nucleoside Compounds, Tetrahedron Letters. 43:3491-3497 (Exhibit 2032, filed Jun. 24, 2013 in connection with IPR2012-00006).

Jun. 25, 2013 Substitute Declaration of Dr. George L. Trainor [redacted] (Exhibit 2033, filed Aug. 30, 2013 in connection with IPR2012-00006).

Jingyue Ju et al. (2006) Four-color DNA sequencing by synthesis using/cleavable fluorescent nucleotide reversible terminators, Proceedings of the National Academy of Sciences. 103: 19635-19640 (Exhibit 2034, filed Jun. 25, 2013 in connection with IPR2012-00006).

Batista et al. (2008) PRG-1 and 21U-RNAs Interact to Form the piRNA Complex Required for Fertility in *C. elegans*. Molecular Cell 31:1-12 (Exhibit 2035, filed Jun. 25, 2013 in connection with IPR2012-00006).

Form 7 Review Context and Analysis, Biomedical Engineering and Research to Aid Persons with Disabilities Programs Dec. 19-20, 2000 Panel Review, Fluorescence Imaging Chip System for Massive Parallel DNA Sequencing. Proposal No. BES-0097793 (Exhibit 2036, filed Jun. 25, 2013 in connection with IPR2012-00006).

Oct. 1, 2006 Request for opinion on manuscript by J. Ju et al., Proceedings of National Academy of Sciences, U.S.A. (Exhibit 2037, filed Jun. 25, 2013 in connection with IPR2012-00006).

Correspondence between George Rupp, Chancellor, Columbia University and Richard T. Schlossberg, President, The David and Lucile Packard Foundation (2001) (Exhibit 2038, filed Jun. 25, 2013 in connection with IPR2012-00006).

The David and Lucile Packard Foundation, Packard Fellowships for Science and Engineering, <http://www.packard.org/what-wefund/conservation-and-science/packard-fellowships-for-science-and-engineering/> (last visited Jun. 25, 2013) (Exhibit 2039, filed Jun. 25, 2013 in connection with IPR2012-00006).

"Chemistry for Next-Generation Sequencing." http://www.illumina.com/technology/sequencing_technology.ilmn (Exhibit 2040, filed Jun. 25, 2013 in connection with IPR2012-00006).

Chiang et al. (2010) Mammalian microRNAs: experimental evaluation of novel and previously annotated genes, Genes & Dev. 24:992, 993 (Exhibit 2041, filed Jun. 25, 2013 in connection with IPR2012-00006).

Seo et al. (2004) Photocleavable fluorescent nucleotides for DNA sequencing on a chip constructed by site-specific coupling chemistry, Proc. Natl. Acad. Sci. 101(15):5488-5493 (Exhibit 2042, filed Jun. 25, 2013 in connection with IPR2012-00006).

Curriculum vitae of Mr. Raymond S. Sims (Exhibit 2043, filed Jun. 25, 2013 in connection with IPR2012-00006).

Documents reviewed by Mr. Raymond S. Sims in this Proceeding (Exhibit 2045, filed Jun. 25, 2013 in connection with IPR2012-00006).

Gary Schroth Proof of Chiang Paper (Exhibit 2052, filed Jun. 25, 2013 in connection with IPR2012-00006).

Information about Dr. Ju's intellectual property sent to Illumina (Exhibit 2074, filed Jun. 25, 2013 in connection with IPR2012-00006).

IPR Default Protective Order (Exhibit 2090, filed Jun. 26, 2013 in connection with IPR2012-00006).

Declaration of Raymond S. Sims (Exhibit 2091, filed Jun. 26, 2013 in connection with IPR2012-00006).

Rough Transcript of the Sep. 4, 2013 deposition of Dr. George L. Trainor (Exhibit 2092, filed Oct. 10, 2013 in connection with IPR2012-00006).

Excerpt from Protective Groups in Organic Synthesis, 3rd Ed. (Theodora W. Greene and Peter G.M. Wuts ed., John Wiley & Sons, Inc. 1999) (Exhibit 2093, filed Oct. 1, 2013 in connection with IPR2012-00006).

Final transcript of the Sep. 4-6, 2013 deposition of Dr. George L. Trainor (Exhibit 2094, filed Oct. 1, 2013 in connection with IPR2012-00006).

Final transcript of the Sep. 3, 2013, deposition of Raymond S. Sims (Exhibit 2095, filed Oct. 1, 2013 in connection with IPR2012-00006).

Nov. 12, 2013 Petitioner Motion to Exclude Evidence in connection with IPR2012-00006.

Videotaped Deposition Transcript of Kevin Burgess, Ph.D., Oct. 28, 2013, signed with errata—(Exhibit 1056, filed Nov. 19, 2013 in connection with IPR2012-00006).

Nov. 12, 2013 Patent Owner Motion for Observations on the Cross-Examination Testimony of Kevin Burgess, Ph.D. in connection with IPR2012-00006.

Nov. 12, 2013 Patent Owner Motion to Exclude Evidence in connection with IPR2012-00006.

Welch, M., et al (2005) Corrigenda to Syntheses of Nucleosides Designed for Combinatorial DNA Sequencing Chem. Eur.J., 1999, 951-960. Published in Chem. Eur. J, 2005, 11, 7136-7145 (Exhibit 2099, filed Nov. 12, 2013 in connection with IPR2012-00006).

Welch, M (1999) "Base Additions Sequencing Scheme (BASS) and Studies Toward New Sequencing Methodologies." Ph.D. Dissertation, Texas A&M University (Exhibit 2100, filed Nov. 12, 2013 in connection with IPR2012-00006).

Lu and Burgess (2006) "A Diversity Oriented Synthesis of 3'-O-modified nucleoside triphosphates for DNA 'Sequencing by Synthesis'." Bioorganic & Medicinal Chemistry Letters, 16, 3902-3905 (Exhibit 2101, filed Nov. 12, 2013 in connection with IPR2012-00006).

Advanced Sequencing Technology Awards 2004. <http://www.genome.gov/12513162> (accessed Oct. 14, 2013) (Exhibit 2102, filed Nov. 12, 2013 in connection with IPR2012-00006).

Welch and Burgess (2006) Erratum to Synthesis of Fluorescent, Photolabile 3'-O-Protected Nucleoside Triphosphates for the Base Addition Sequencing Scheme, Nucleosides & Nucleotides, 18:197-201. Published in Nucleosides, Nucleotides and Nucleic Acids, 25:1, 119 (Exhibit 2103, filed Nov. 12, 2013 in connection with IPR2012-00006).

Nov. 26, 2013 Petitioner Response to Motion for Observations in connection with IPR2012-00006.

Nov. 26, 2013 Patent Owner Opposition to Petitioner's Motion to Exclude in connection with IPR2012-00006.

Nov. 26, 2013 Petitioner Opposition to Motion to Exclude in connection with IPR2012-00006.

Dec. 3, 2013 Petitioner Reply to Patent Owner's Opposition to Motion to Exclude in connection with IPR2012-00006.

Dec. 3, 2013 Patent Owner Reply on Motion to Exclude in connection with IPR2012-00006.

Columbia's Demonstratives Under 42.70(b) for Dec. 17, 2013 Oral Hearing in connection with IPR2012-00006, IPR2012-00007, and

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.