

**Illumina, Inc. vs. The Trustees of Columbia
University in the City of New York**

**Videotaped Deposition of
FLOYD ROMESBERG, PH.D.
October 09, 2018**

Page 1	Page 2
<p>1 UNITED STATES PATENT AND TRADEMARK OFFICE</p> <p>2 BEFORE THE PATENT TRIAL AND APPEAL BOARD</p> <p>3</p> <p>4</p> <p>5 ILLUMINA, INC.,</p> <p>6 Plaintiff,</p> <p>7 Case No.: IPR2018-00797</p> <p>8 vs. Patent 9,868,985</p> <p>9 THE TRUSTEES OF COLUMBIA UNIVERSITY</p> <p>10 IN THE CITY OF NEW YORK</p> <p>11 Defendant.</p> <p>12</p> <p>13 VIDEOTAPED DEPOSITION OF FLOYD ROMESBERG, PH.D.</p> <p>14 SAN DIEGO, CALIFORNIA</p> <p>15 TUESDAY, OCTOBER 9, 2018</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23 Reported by:</p> <p>24 Linda E. Marquette</p> <p>25 RPR, CLR, CSR No. 11874</p> <p>Job No. 10048075</p>	<p>1 UNITED STATES PATENT AND TRADEMARK OFFICE</p> <p>2 BEFORE THE PATENT TRIAL AND APPEAL BOARD</p> <p>3</p> <p>4</p> <p>5 ILLUMINA, INC.,</p> <p>6 Plaintiff,</p> <p>7 Case No.: IPR2018-00797</p> <p>8 vs. Patent 9,868,985</p> <p>9 THE TRUSTEES OF COLUMBIA UNIVERSITY</p> <p>10 IN THE CITY OF NEW YORK</p> <p>11 Defendant.</p> <p>12</p> <p>13</p> <p>14</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20 VIDEOTAPED DEPOSITION of FLOYD ROMESBERG, Ph.D.,</p> <p>21 taken on behalf of Patent Owner, at 12790 El Camino</p> <p>22 Real, San Diego, California, beginning at 12:31 p.m.,</p> <p>23 and ending at 4:36 p.m., on Tuesday, October 9, 2018,</p> <p>24 before Linda E. Marquette, RPR, CLR, Certified Shorthand</p> <p>25 Reporter No. 11874.</p>
Page 3	Page 4
<p>1 APPEARANCES:</p> <p>2</p> <p>3 For Petitioner:</p> <p>4 BY: WILLIAM R. ZIMMERMAN, ESQ.</p> <p>5 KNOBBE MARTENS</p> <p>6 1717 Pennsylvania Avenue</p> <p>7 Suite 900</p> <p>8 Washington, DC 20006</p> <p>9 bill.zimmerman@knobbe.com</p> <p>10 -and-</p> <p>11 BY: NATHANAEL R. LUMAN, ESQ.</p> <p>12 KNOBBE MARTENS</p> <p>13 12790 El Camino Real</p> <p>14 San Diego, California 92130</p> <p>15 858.707.4000</p> <p>16 nate.luman@knobbe.com</p> <p>17</p> <p>18</p> <p>19</p> <p>20 For Patent Owner:</p> <p>21 BY: ROBERT S. SCHWARTZ, ESQ.</p> <p>22 -and-</p> <p>23 BY: ZACHARY L. GARRETT, ESQ.</p> <p>24 FITZPATRICK, CELLA, HARPER & SCINTO</p> <p>25 1290 Avenue of the Americas</p> <p>New York, New York 10104-3800</p> <p>212.218.2298</p> <p>212.218.2200 fax</p> <p>rschwartz@fchs.com</p> <p>ALSO PRESENT:</p> <p>Videographer, Ryan Asanas</p> <p>Dr. Steven Menchen</p> <p>John Murnane, Esq.</p>	<p>1 I N D E X</p> <p>2 WITNESS: PAGE</p> <p>3 FLOYD ROMESBERG, Ph.D.</p> <p>4 EXAMINATION BY MR. SCHWARTZ 8</p> <p>5 EXAMINATION BY MR. ZIMMERMAN 135</p> <p>6</p> <p>7 EXHIBITS</p> <p>8 NO. DESCRIPTION PAGE</p> <p>9 Exhibit 1075 ** 11</p> <p>10 United States Patent 9,868,985 B2 dated</p> <p>11 1/16/2018</p> <p>12 Exhibit 2080 11</p> <p>13 Deposition transcript of Floyd Romesberg</p> <p>14 dated 1/14/2014 (260 pages)</p> <p>15 Exhibit 2007 18</p> <p>16 Declaration of Floyd Romesberg, Ph.D.,</p> <p>17 IPR2013-00517, dated 5/5/2014 (43 pages)</p> <p>18 Exhibit 2095 21</p> <p>19 United States Patent 6,664,079 B2 dated</p> <p>20 12/16/2003</p> <p>21 Exhibit 2035 26</p> <p>22 Deposition transcript of Floyd</p> <p>23 Romesberg, Ph.D., dated 7/8/2014 in</p> <p>24 IPR2013-00517 (190 pages)</p> <p>25</p> <p>Exhibit 1036 ** 49</p> <p>Unexpected Enzymatic Fucosylation of the</p> <p>Hindered Tertiary Alcohol of</p> <p>3-C-Methyl-N-Acetyllactosamine Produces</p> <p>a Novel Analogue of the</p> <p>LeX-Trisaccharide</p> <p>Exhibit 2102 49</p> <p>Manuscript "Enzymatic and Chemical</p> <p>Synthesis of Oligosaccharide Analogs by</p> <p>Xiangping Qian, Spring 2000</p>

Page 5				Page 6			
1	EXHIBITS			1	EXHIBITS		
2	NO. DESCRIPTION	PAGE		2	NO. DESCRIPTION	PAGE	
3	Exhibit 2097	61		3	Exhibit 2101	126	
4	Chemoenzymatic Synthesis of a-(1 arrow			4	Regioselective Oxidation of Internal		
5	3)-Gal(N Ac) - Terminating Glycosides of			5	Olefins Bearing Neighboring Oxygen		
6	Complex Tertiary Sugar Alcohols			6	Functions by Means of Palladium		
7	Exhibit 2054	65		7	Catalysts. Preparation of β-Alkoxy or		
8	A Sequencing Method Based on Real-Time			8	Acetoxy Ketones from Allyl and Homoallyl		
9	Pyrophosphate			9	Ethers or Esters		
10	Exhibit 2105	72		10	Exhibit 2106	127	
11	Isomerization and Cleavage of Allyl			11	Hypervalent (tert-Butylperoxy) iodanes		
12	Ethers of Carbohydrates by			12	Generate Iodine-Centered Radicals at		
13	Trans- [Pd(NH3)2 Cl2] Tadeusz Bieg and			13	Room Temperature in Solution: Oxidation		
14	Wieslaw Szeja			14	and Deprotection of Benzyl and Allyl		
15	Exhibit 2098	77		15	Ethers, and Evidence for Generation of		
16	Complete Reverse Regioselection in			16	a-Oxy Carbon Radicals		
17	Wacker Oxidation of Acetonides and			17	Exhibit 2107	129	
18	Cyclic Carbonates of Allylic Diols			18	The Origins of the Benzotriazole Project,		
19	Exhibit 1023 **	79		19	Its Versatility Illustrated by a New --C		
20	Syntheses of Nucleosides Designed for			20	=CHCH+OEt Synthons, and Novel Synthesis		
21	Combinatorial DNA Sequencing			21	of alpha beta-Unsaturated Aldehydes and		
22	Exhibit 2099	84		22	Ketones, Furans, Pyrroles and Allyl		
23	United States Patent 5,858,671 dated			23	Ethers		
24	1/12/1999			24	Exhibit 1013 **	131	
25	Exhibit 2100	92		25	International Application Published		
	United States Patent 6,013,445 dated				Under the Patent Cooperation Treaty		
	1/11/2000				(PCT) dated 16 May 1991 for USP		
	Exhibit 2103	98			9,868,985		
	Project Information "Evolving Novel				Exhibit 1078 **	10	
	Polymerases for Genome Sequencing"				Declaration of Floyd Romesberg, Ph.D.,		
	Exhibit 2104	99			Exhibit 1001 **		
	Helicos and Columbia to Test Scripps'				U.S. Patent 7,057,026 B2	13	
	Improved Polymerases for Next-Gen				Exhibit 1015 **		
	Sequencing dated 10/3/2006				U.S. Patent 5,547,839	120	
	Exhibit 2096	114			** (Marked in previous depositions,		
	Deposition transcript of Floyd				referenced herein and attached		
	Romesberg, Ph.D., dated 9/19/2018				hereto.)		
	Volume I						
Page 7				Page 8			
1	SAN DIEGO, CALIFORNIA; TUESDAY, OCTOBER 9, 2018			1	firm in New York City. And also with me is Dr. Steven		
2	12:31 P.M. to 4:36 P.M.			2	Menchen.		
3				3	MR. ZIMMERMAN: Bill Zimmerman of Knobbe		
4	THE VIDEOGRAPHER: We are now on the record.			4	Martens Olsen & Bear on behalf of Illumina and the		
5	Today's date is October 9, 2018, and the time is			5	witness. With me is my partner Nate Luman and Marcus		
6	12:31 p.m.			6	Birch of Illumina.		
7	This begins the video-recorded deposition of			7	THE VIDEOGRAPHER: Thank you.		
8	Floyd Romesberg, Ph.D., being taken on behalf of the			8	The court reporter today is Linda Marquette,		
9	plaintiff in the matter of Illumina, Inc. v. Trustees of			9	also with Aptus Court Reporting.		
10	Columbia University in the City of New York, pending in			10	And she may now swear in or affirm the		
11	the United States Patent and Trademark Office before the			11	deponent.		
12	Patent Trial and Appeal Board, Case No. IPR2018-00797.			12			
13	We are at the offices of Knobbe Martens,			13	FLOYD ROMESBERG, PH.D.,		
14	located at 12790 El Camino Real, San Diego, California			14	having been first duly administered an oath, was		
15	92130.			15	examined and testified as follows:		
16	My name is Ryan Asanas, the videographer of			16			
17	Aptus Court Reporting, located at 600 West Broadway,			17	EXAMINATION		
18	Suite 300, San Diego, California 92101.			18	BY MR. SCHWARTZ:		
19	Will all counsel present please identify			19	Q. Good afternoon, Dr. Romesberg.		
20	yourselves and state whom you represent, starting with			20	A. Good afternoon.		
21	the taking attorney.			21	Q. So we went over the ground rules for a		
22	MR. SCHWARTZ: I am Robert Schwartz. I			22	deposition the last time we met, so I won't go over them		
23	represent Columbia University in this matter. With me			23	again, except to say that if there's any reason you		
24	is my colleague, Zachary Garrett and John Murnane.			24	can't give truthful testimony today, just -- I'd just		
25	We're all from the Fitzpatrick Cella Harper & Scinto			25	prefer that you tell us now.		

<p align="right">Page 9</p> <p>1 Is there any reason you can't give truthful 2 testimony today? 3 A. No, there's not. 4 Q. Okay. Did you meet with your attorneys in 5 preparation for your deposition today? 6 And I'm only asking for a yes or no answer. 7 A. Yes. 8 Q. And what are the names of the attorneys you 9 met with? 10 A. Nate and Marcus and Bill. 11 Q. Okay. And how many times did you meet with 12 the attorneys in preparation for your deposition today? 13 A. One time. 14 Q. And when did that meeting take place? 15 A. Yesterday. 16 Q. And approximately how much time yesterday did 17 you spend preparing for your deposition? 18 A. Six hours. 19 Q. Outside of that meeting, did you meet with 20 your attorneys any other time? 21 A. I did not. 22 Q. Okay. And did you speak with anybody else 23 other than those attorneys you mentioned about your 24 deposition? 25 A. I did not.</p>	<p align="right">Page 10</p> <p>1 Q. And what did you do to prepare for today's 2 deposition? 3 A. In addition to meeting with them yesterday? 4 Q. Uh-huh. 5 A. I spent a couple of hours this morning 6 rereading, refreshing my memory on -- on selected 7 publications and -- and documents from the IPR. 8 Q. And you understand that today's deposition is 9 in relationship to IPR2018-00797, correct? 10 A. I do. 11 Q. Okay. And you've prepared an expert 12 declaration in that IPR, correct? 13 A. I did. 14 Q. And I'm going to put in front of you -- 15 putting in front of you Exhibit 10,000 -- sorry, 1078 16 entitled Declaration of Floyd Romesberg, Ph.D., In 17 Support of Petition for Inter Partes Review of U.S. 18 Patent No. 9,868,985. 19 And please turn to the last page of the 20 declaration. Is that your signature on that page? 21 A. It is. 22 Q. Okay. The next exhibit I'm going to put in 23 front of you is Exhibit 1075, which is U.S. Patent No. 24 9,868,985. 25 ///</p>
<p align="right">Page 11</p> <p>1 (Exhibit 1075 was previously marked 2 for identification by the Certified 3 Shorthand Reporter.) 4 BY MR. SCHWARTZ: 5 Q. The inven- -- the invention claimed in U.S. 6 Patent No. 9,868,985 relates to a method of sequencing 7 of nucleic acid SBS, correct? 8 A. Correct. Correct. 9 Q. I'm going to put in front of you Exhibit 2080, 10 which is the deposition transcript in IPR2013-00128. 11 (Exhibit 2080 was previously marked 12 for identification by the Certified 13 Shorthand Reporter.) 14 BY MR. SCHWARTZ: 15 Q. Please turn to page 37. Please draw your 16 attention to line 8. And starting at line 8, the 17 transcript reads: 18 "QUESTION: You see it also lists 19 other uses for the nucleotides in 20 the '026 patent. Correct? 21 "ANSWER: Yes, correct. 22 "QUESTION: And it provides 23 various examples of those, such as 24 polynucleotide synthesis, nucleic 25 acid hybridization, SNP studies,</p>	<p align="right">Page 12</p> <p>1 labeling dNTPs, et cetera. 2 Do you see that? 3 "ANSWER: I do." 4 I'm going to ask you to skip ahead to page 38, 5 please. I don't want to read everything into the 6 record. 7 And please draw your attention to line 11. 8 And certainly feel free to read the testimony in between 9 from where we left off to here if you need to. 10 A. Yes. Can I do that, please? 11 Q. Can I ask the question first and just see if 12 you need to? And certainly if you need to, you can. 13 But for now, I'll just read the following testimony that 14 starts at line 11. 15 "QUESTION: Okay. So then you 16 would agree that those other 17 techniques listed are things other 18 than SBS. Correct? 19 "ANSWER: Yes. Correct." 20 That was your testimony, correct? 21 A. That is what's written. 22 Q. It is your opinion that polynucleotide 23 synthesis, nucleic acid hybridization, SNP studies, and 24 labeling dNTPs are techniques that are not SBS, correct? 25 A. Could I take that minute now to read this?</p>

<p align="right">Page 13</p> <p>1 Q. Oh, sure.</p> <p>2 A. Could I ask for a refresher on what is the</p> <p>3 '026 patent?</p> <p>4 Q. Do you want to see the '026 patent?</p> <p>5 A. If you -- I may not need to, if you just tell</p> <p>6 me who it is.</p> <p>7 Q. I can't testify, so I can -- I can put the</p> <p>8 patent in front of you if you want to see it.</p> <p>9 A. Sure.</p> <p>10 Q. This is Exhibit 1001. It's the '026 -- oh,</p> <p>11 I'm sorry. This is not marked yet. I can put it in</p> <p>12 front of you. I won't mark it, and if you want me to,</p> <p>13 I'll mark it. But --</p> <p>14 A. I don't even -- I'm not sure I know what that</p> <p>15 means.</p> <p>16 Q. Put a number on it.</p> <p>17 A. Yeah, I guess I'm not sure why that would -- I</p> <p>18 don't mind if you don't mark it.</p> <p>19 MR. ZIMMERMAN: You don't have to worry about</p> <p>20 it.</p> <p>21 THE WITNESS: Okay.</p> <p>22 A. Okay. Could you repeat the question?</p> <p>23 BY MR. SCHWARTZ:</p> <p>24 Q. So we read your testimony. I won't reread</p> <p>25 your testimony in the -- in the deposition.</p>	<p align="right">Page 14</p> <p>1 My question was: From your testimony you said</p> <p>2 it was your opinion that polynucleotide synthesis,</p> <p>3 nucleic acid hybridization, SNP studies, and labeling</p> <p>4 dNTPs are techniques that are not SBS. That's what you</p> <p>5 testified, correct?</p> <p>6 A. Could you show me where I exactly testified?</p> <p>7 Because I think what I was being asked was whether or</p> <p>8 not this patent -- this '026 patent described things</p> <p>9 other than just sequencing by synthesis. And it goes</p> <p>10 out of its way to do so in spots where I agreed.</p> <p>11 So I don't know that I listed specific things</p> <p>12 and said whether or not they were sequencing by</p> <p>13 synthesis. What I was answering there was that this</p> <p>14 patent was about things in addition to sequencing by</p> <p>15 synthesis.</p> <p>16 So if you could ask me a specific question</p> <p>17 again.</p> <p>18 Q. Okay. Well, let's go back.</p> <p>19 A. And if you could clarify whether you're asking</p> <p>20 me about what this patent says or whether I think a</p> <p>21 specific technique is sequencing by synthesis.</p> <p>22 Q. It was the latter. But we can go back to the</p> <p>23 transcript at line 8. Do you want to go back and look</p> <p>24 at the transcript?</p> <p>25 A. Which -- which page?</p>
<p align="right">Page 15</p> <p>1 Q. Starting at line 8 at page 37. And the</p> <p>2 question was:</p> <p>3 "You see it also lists other uses</p> <p>4 for the nucleotides in the '026</p> <p>5 patent. Correct?"</p> <p>6 And your answer was:</p> <p>7 "Yes. Correct.</p> <p>8 And the question was:</p> <p>9 "And it provides various examples</p> <p>10 of those, such as polynucleotide</p> <p>11 synthesis, nucleic acid</p> <p>12 hybridization, SNP studies, labeling</p> <p>13 dNTPs, et cetera.</p> <p>14 "Do you see that?</p> <p>15 And your answer was:</p> <p>16 "I do."</p> <p>17 And I asked you to skip ahead to page 38,</p> <p>18 line 11, where there was a conclusory question. And the</p> <p>19 question was:</p> <p>20 "Okay. So you would -- so then</p> <p>21 you would agree that those other</p> <p>22 techniques listed are things other</p> <p>23 than SBS. Correct?"</p> <p>24 And your answer was:</p> <p>25 "Yes. Correct."</p>	<p align="right">Page 16</p> <p>1 That was your testimony, correct?</p> <p>2 A. That is what's written, yes.</p> <p>3 But I do believe that it's referring to what</p> <p>4 is listed in the patent, not any particular list that</p> <p>5 may have been part of a question which ends with</p> <p>6 "et cetera." Because where it ends with "et cetera,"</p> <p>7 the patent does describe other things.</p> <p>8 I just want to be clear that I don't want</p> <p>9 to -- I'd have to rethink the question if it was do I</p> <p>10 think these are about sequencing by synthesis.</p> <p>11 But what I was answering here was whether the</p> <p>12 patent was -- included things other than sequencing by</p> <p>13 synthesis, which it clearly does.</p> <p>14 Q. Your answer was that you -- you provided an</p> <p>15 opinion as to whether polynucleotide synthesis, nucleic</p> <p>16 acid hybridization, SNP studies, labeling dNTPs were</p> <p>17 things other than sequencing by synthesis, and your</p> <p>18 answer was "Yes. Correct."</p> <p>19 MR. ZIMMERMAN: Objection. Asked and</p> <p>20 answered.</p> <p>21 A. I -- I did not testify -- I believe what I was</p> <p>22 testifying was whether or not this patent which they're</p> <p>23 asking about, and they say "and it provides examples of</p> <p>24 those such as," and it ends with "et cetera." So what</p> <p>25 the question is referring to is the subject matter in</p>

<p style="text-align: right;">Page 17</p> <p>1 the patent, which I was familiar with at that time, and</p> <p>2 I was answering questions about that.</p> <p>3 BY MR. SCHWARTZ:</p> <p>4 Q. Is it your opinion that polynucleotide</p> <p>5 synthesis is a form of SBS?</p> <p>6 A. Polynucleotide synthesis is often involved in</p> <p>7 SBS. That's the "by synthesis" part. But you can</p> <p>8 certainly do polynucleotide synthesis without</p> <p>9 sequencing. So it does not have to involve sequencing.</p> <p>10 Q. All right. So when you said that you agree</p> <p>11 that those other techniques listed are things other than</p> <p>12 SBS, and you agreed to that, you're withdrawing that</p> <p>13 testimony?</p> <p>14 A. No. I'm -- what that testimony was referring</p> <p>15 to was the subject matter that I was being asked about</p> <p>16 in this patent. And I believe that testimony -- I</p> <p>17 believe I would still answer that the same way.</p> <p>18 Q. Well, do you believe that polynucleotide</p> <p>19 synthesis, nucleic acid hybridization, SNP studies, and</p> <p>20 labeling dNTPs are things other than SBS?</p> <p>21 A. That's not what's asked.</p> <p>22 Q. Well, do you believe that? Is that your</p> <p>23 opinion?</p> <p>24 A. So you're now asking me a separate question?</p> <p>25 Q. Yes, because -- I am asking you that question.</p>	<p style="text-align: right;">Page 18</p> <p>1 A. Okay. So could you please ask that question</p> <p>2 again?</p> <p>3 Q. Is it your opinion that polynucleotide</p> <p>4 synthesis, nucleic acid hybridization, SNP studies,</p> <p>5 labeling dNTPs are things other than SBS?</p> <p>6 A. All of those things can involve -- can be</p> <p>7 related to SBS. They can all be parts of sequencing by</p> <p>8 synthesis. So I would not say that those are unrelated</p> <p>9 to sequencing by synthesis, no.</p> <p>10 Q. So those are techniques that are SBS; is that</p> <p>11 your opinion?</p> <p>12 A. They can be part of SBS. They can be</p> <p>13 independent of SBS as well.</p> <p>14 Q. I'm putting in front of you Exhibit 2007,</p> <p>15 which is your expert declaration IPR2013-00517.</p> <p>16 (Exhibit 2007 was previously marked</p> <p>17 for identification by the Certified</p> <p>18 Shorthand Reporter.)</p> <p>19 BY MR. SCHWARTZ:</p> <p>20 Q. Please turn to page 10.</p> <p>21 A. Can -- can I ask, when did I give this</p> <p>22 testimony? I'm just drawing -- I've given several of</p> <p>23 these, so I would like to make sure I know which one I'm</p> <p>24 talking about. This would have been 2014?</p> <p>25 Q. When did you sign this? Is that what you're</p>
<p style="text-align: right;">Page 19</p> <p>1 asking?</p> <p>2 A. Yeah, that would be enough --</p> <p>3 Q. You signed this May 5th of 2014.</p> <p>4 A. Thank you.</p> <p>5 Q. I mean, do you agree with that? I shouldn't</p> <p>6 be testifying so ...</p> <p>7 A. It's not written here, but I believe that's</p> <p>8 correct.</p> <p>9 Q. It should be.</p> <p>10 A. Oh, it is. Yeah. Then it's correct.</p> <p>11 Q. Okay. Please turn to page 10.</p> <p>12 On page 10 there is a section entitled Scope</p> <p>13 and Content of the Prior Art. Do you see that?</p> <p>14 A. I do.</p> <p>15 Q. And underneath that is a Section A, entitled</p> <p>16 U.S. Patent No. 6,664,079 to Ju, et al.</p> <p>17 Do you see that?</p> <p>18 A. I do.</p> <p>19 Q. And to make it easier going forward, I'll</p> <p>20 refer to the U.S. Patent No. 6,664,079 as the '079</p> <p>21 patent. Okay?</p> <p>22 A. Okay.</p> <p>23 Q. Please draw your attention to paragraph 28,</p> <p>24 which is the first paragraph in Section A. And please</p> <p>25 look at the last sentence in paragraph 28, which starts</p>	<p style="text-align: right;">Page 20</p> <p>1 with "One of ordinary skill." Do you see that?</p> <p>2 A. I do.</p> <p>3 Q. You write:</p> <p>4 "One of ordinary skill in the art</p> <p>5 would have understood these</p> <p>6 teachings of Ju as stating that Ju's</p> <p>7 invention was nucleotide sequence</p> <p>8 determination using a DNA polymerase</p> <p>9 and, in particular, using the method</p> <p>10 referred to as sequencing by</p> <p>11 synthesis."</p> <p>12 That is what you wrote, correct?</p> <p>13 A. That is correct. That is what I wrote.</p> <p>14 Q. It is your opinion that a reader of Ju's</p> <p>15 patent specification understood that the sequencing</p> <p>16 method in Ju's patent is SBS, correct?</p> <p>17 A. That is what is written. I'm not -- I don't</p> <p>18 have that patent in front of me, but that's certainly</p> <p>19 what is -- what is written here.</p> <p>20 Q. And in support for your opinion, you refer to</p> <p>21 portions of the '079 patent specification, specifically</p> <p>22 Column 4, lines 22 to 26, and Column 21, lines 1 through</p> <p>23 5, correct?</p> <p>24 A. I'm sorry. Where are you getting that?</p> <p>25 Q. I'm getting that within the paragraph.</p>

<p style="text-align: right;">Page 21</p> <p>1 Paragraph 28 you cite to in spec- --</p> <p>2 A. Oh, in paragraph -- yes.</p> <p>3 Q. So as support for your opinion that we just</p> <p>4 went over, you referred to the portions of the '079</p> <p>5 patent specification, specifically Column 4, lines 22 to</p> <p>6 26, and Column 21, lines 1 through 5, correct?</p> <p>7 A. Correct.</p> <p>8 Q. Okay. I'm going to put in front of you U.S.</p> <p>9 Patent No. 6,664,079 to Ju, et al. And this has been</p> <p>10 marked as Exhibit 2095.</p> <p>11 (Exhibit 2095 was marked for</p> <p>12 identification by the Certified</p> <p>13 Shorthand Reporter.)</p> <p>14 BY MR. SCHWARTZ:</p> <p>15 Q. This is the same patent you referred to in</p> <p>16 Section 5A of your declaration, correct?</p> <p>17 A. It appears to be.</p> <p>18 MR. ZIMMERMAN: The copy I have isn't marked.</p> <p>19 Has it been marked as 2095?</p> <p>20 MR. SCHWARTZ: It's been marked.</p> <p>21 MR. ZIMMERMAN: Okay.</p> <p>22 BY MR. SCHWARTZ:</p> <p>23 Q. And again, for convenience going forward, I</p> <p>24 will refer to this patent as the '079 patent. Okay?</p> <p>25 A. That is okay.</p>	<p style="text-align: right;">Page 22</p> <p>1 Q. Okay. Now, go back to your declaration,</p> <p>2 please, and draw your attention to paragraph 29. In</p> <p>3 paragraph 29 you write:</p> <p>4 "Ju's SBS methods have four</p> <p>5 'fundamental requirements.'</p> <p>6 (1) "The availability of four</p> <p>7 nucleotide analogues (aA, aC, aG, aT)</p> <p>8 each labeled with a unique label and</p> <p>9 containing a chemical moiety capping</p> <p>10 the 3'-OH group;</p> <p>11 (2) the four nucleotide analogues</p> <p>12 (aA, aC, aG, aT) need to be</p> <p>13 efficiently and faithfully</p> <p>14 incorporated by DNA polymerase as</p> <p>15 terminators in the polymerase</p> <p>16 reaction;</p> <p>17 (3) the tag and the group capping the</p> <p>18 3'-OH need to be removed with high</p> <p>19 yield to allow the incorporation and</p> <p>20 detection of the next nucleotide;</p> <p>21 and,</p> <p>22 (4) the growing strand of DNA should</p> <p>23 survive the washing, detection and</p> <p>24 cleavage processes to remain annealed</p> <p>25 to the DNA template."</p>
<p style="text-align: right;">Page 23</p> <p>1 And you cite to the Ju patent specification.</p> <p>2 That's Column 21, line 3 through 16.</p> <p>3 That is what you wrote, correct?</p> <p>4 A. That is what is written, yes.</p> <p>5 Q. And that is your opinion, correct?</p> <p>6 A. I -- I -- do you want me to go back into --</p> <p>7 into this '079 patent and refresh my memory on this? It</p> <p>8 was obviously my opinion then.</p> <p>9 Q. No, sir --</p> <p>10 A. It probably still is.</p> <p>11 Q. Okay. So it is -- it is your opinion that</p> <p>12 Ju's SBS methods have four fundamental requirements you</p> <p>13 list in paragraph 29 --</p> <p>14 A. Yes.</p> <p>15 Q. -- of your declaration, correct?</p> <p>16 And as support for your opinion, you cite to</p> <p>17 Column 21, lines 3 through 16, of the '079 patent,</p> <p>18 correct?</p> <p>19 A. I do.</p> <p>20 Q. And please direct your attention to</p> <p>21 paragraph 30 of your declaration. In paragraph 30 you</p> <p>22 write:</p> <p>23 "Thus, one of ordinary skill in</p> <p>24 the art would have understood that</p> <p>25 Ju's sequencing by synthesis methods</p>	<p style="text-align: right;">Page 24</p> <p>1 have the above four fundamental</p> <p>2 requirements, and if any of these</p> <p>3 requirements are not satisfied, then</p> <p>4 Ju's sequencing by synthesis method</p> <p>5 would not work for its intended</p> <p>6 purpose."</p> <p>7 That is your opinion and that is what you</p> <p>8 wrote, correct?</p> <p>9 A. Yes to both.</p> <p>10 Q. Please go to page 12 of your declaration. And</p> <p>11 draw your attention to paragraph 32. And please draw</p> <p>12 your attention to the sentence that begins four lines</p> <p>13 down in paragraph 32, where the sentence starts with "In</p> <p>14 discussing shortcomings."</p> <p>15 Do you see that?</p> <p>16 A. I do.</p> <p>17 Q. You write:</p> <p>18 "In discussing shortcomings of</p> <p>19 prior art pyrosequencing methods, Ju</p> <p>20 states that this method 'can only</p> <p>21 sequence up to 30 base pairs (bps)</p> <p>22 of nucleotide sequences' Id at</p> <p>23 Column 2, lines 10 through 25.</p> <p>24 "Thus, one of ordinary skill</p> <p>25 would understand Ju as teaching that</p>

<p style="text-align: right;">Page 25</p> <p>1 a method that can only sequence 30 2 base pairs is undesirable. 3 Regarding Ju's own method, Ju 4 teaches, 'in the DNA sequencing 5 system disclosed herein, more than 6 10,000 bases can be identified after 7 each cycle and after 100 cycles, a 8 million base pairs will be generated 9 from one sequencing chip' Id at 10 Column 21, lines 63 through 67. 11 "Thus, a person of ordinary skill 12 in the art would understand that the 13 desired read length of Ju's 14 sequencing method is more than 30 15 base pairs, and preferably up to a 16 hundred base pairs." 17 That is your opinion and that is what you 18 wrote, correct? 19 A. I -- I would have to rethink that exactly, but 20 I believe -- this is certainly what I wrote, and I 21 believe it's what I would believe, yes. 22 Q. If we focused on the last three lines of 23 paragraph 32 -- I'll strike that. Strike that question, 24 please. 25 I'm going to put in front of you your</p>	<p style="text-align: right;">Page 26</p> <p>1 deposition transcript in IPR2013-00517, which has been 2 marked as Exhibit 2035. 3 (Exhibit 2035 was previously marked 4 for identification by the Certified 5 Shorthand Reporter.) 6 THE WITNESS: Mine is not marked. 7 MR. ZIMMERMAN: Down here. 8 THE WITNESS: Oh, that's a mark? 9 BY MR. SCHWARTZ: 10 Q. Please turn to page 87. And please look at 11 line 5. Starting at line 5 -- 12 A. Oh, I'm sorry. Can I ask when this testimony 13 is from? Is this also from 2014? Yes, it is. I see. 14 Q. Please look at line 5. And starting at line 5 15 the transcript reads: 16 "QUESTION: Would you agree with 17 me that a person of ordinary skill 18 would understand that any alleged 30 19 base pair requirement as a goal? 20 "ANSWER: I think my reading was 21 that Ju had a much longer -- a goal 22 of being much longer than 30 23 nucleotides." 24 That was your testimony, correct? 25 A. That is what is written.</p>
<p style="text-align: right;">Page 27</p> <p>1 Q. Okay. Please turn to page 88 of that 2 transcript. Please look at line 1. And starting at 3 line 1, the transcript reads: 4 "ANSWER: I don't read it as 30 5 nucleotides being a goal of Ju. He 6 actually cites a pyrosequencing 7 method, and he cites the 30 8 nucleotides as a limitation -- the 9 fact that you can only get a read 10 length of 30 as a limitation. So I 11 think he's -- it's sort of -- it's 12 noted as a limitation, and he then 13 at a later -- at a different spot, 14 talks about much longer reads. 15 "So my read, I don't think he 16 actually gives a value of what he 17 says is his goal, but it was clearly 18 long -- in my read of it, it was 19 clearly longer than 30 because he is 20 disparaging the pyrosequencing 21 method as only providing 30 22 nucleotide read lengths." 23 That was your testimony, correct? 24 A. That is what is written. 25 Q. Please go to paragraph 33 on page 13 of your</p>	<p style="text-align: right;">Page 28</p> <p>1 declaration. That's Exhibit 2007 now. 2 A. The current dec? 3 Q. Exhibit 2007. It's the -- it's the 4 declaration in that IPR2013-00517. 5 A. This one? What page? 6 Q. Page 13, paragraph 33, please. 7 A. I'm there. 8 Q. And you write: 9 [As read] 10 "In order to achieve a read 11 length of more than 30 base pairs, 12 one of ordinary skill must have 13 understood that Ju's 3'-OH capping 14 group must be removed in nearly 15 quantitative yield through each 16 cycle of sequencing. For example, 17 the removal of efficiency of each 18 cycle must be greater than 19 95 percent to permit a read length 20 of 30 bases before phasing errors 21 cause the signal-to-noise ratio to 22 decrease beyond detectable limits 23 (i.e., 0.9530 = 21 %). 24 "One of ordinary skill would have 25 known that, in practice, Ju requires</p>

<p align="right">Page 29</p> <p>1 a removal efficiency significantly 2 higher than 95 percent to account 3 for inefficiencies associated with 4 other steps in the sequencing cycle 5 (such as inefficiencies with tag 6 removal and/or polymerase 7 incorporation of unnatural 8 nucleotides)."</p> <p>9 And you cite to the Ju patent specification at 10 Column 21, lines 8 through 13.</p> <p>11 That is what you wrote and that is your 12 opinion, correct?</p> <p>13 A. That is what is written, and I believe that 14 is -- would still be my opinion, yes.</p> <p>15 Q. And to support your opinion, you cite to 16 Column 21, lines 8 through 13 of the '079 patent, 17 correct?</p> <p>18 A. That is what is written, yes.</p> <p>19 Q. And following the portion of paragraph 33 that 20 I just read, you write:</p> <p>21 [As read] 22 "Likewise, one of ordinary skill 23 would have known that the removal 24 efficiency must be greater than 25 98.5 percent to yield Ju's desired</p>	<p align="right">Page 30</p> <p>1 read length of a hundred bases 2 (i.e., 0.85100 = 22%). [sic] 3 Therefore, a person of ordinary 4 skill in the art would have 5 understood that Ju's sequencing 6 method requires nearly quantitative 7 cleavage efficiency for the 3'-OH 8 capping group."</p> <p>9 That is your opinion and that is what you 10 wrote, correct?</p> <p>11 A. That is what is written, and I believe that 12 would still be my opinion, yes.</p> <p>13 Q. Please go to paragraph 34 of that declaration. 14 In paragraph 34 you write:</p> <p>15 "Ju also states that 'The success 16 of this [... sequencing by 17 synthesis] system will allow the 18 development of an ultra 19 high-throughput and high fidelity 20 DNA sequencing system for 21 polymorphism pharmacogenetics 22 applications and for whole genome 23 sequencing. This fast and accurate 24 DNA resequencing system is needed in 25 such fields as detection of single</p>
<p align="right">Page 31</p> <p>1 nucleotide polymorphisms (SNPs), 2 serial analysis of gene expression 3 (SAGE), identification in forensics 4 and genetic disease association 5 studies."</p> <p>6 And you cite to the Ju patent specification at 7 Column 4, lines 10 through 19.</p> <p>8 That is what you wrote and that is your 9 opinion, correct?</p> <p>10 MR. ZIMMERMAN: Objection. Mischaracterizes 11 the document.</p> <p>12 MR. SCHWARTZ: Did I misread something?</p> <p>13 MR. ZIMMERMAN: You did. You misread the 14 first sentence of the quote.</p> <p>15 BY MR. SCHWARTZ:</p> <p>16 Q. Okay. Let me read the beginning again. 17 "Ju also states that 'The success 18 of this [DNA sequencing by 19 synthesis] system will allow the 20 development of an ultra 21 high-throughput and high fidelity 22 DNA sequencing system for 23 polymorphism, pharmacogenetics 24 applications and for whole genome 25 sequencing."</p>	<p align="right">Page 32</p> <p>1 Did I read that correctly this time? 2 MR. ZIMMERMAN: You did not. 3 MR. SCHWARTZ: I'll try it again. 4 BY MR. SCHWARTZ:</p> <p>5 Q. Paragraph 34: 6 "Ju also states that, 'The 7 success of this [DNA sequencing]" -- 8 Are you -- are you -- are you saying I didn't record the 9 fact that he underlined some words? Is that what you're 10 saying?</p> <p>11 MR. ZIMMERMAN: No. 12 MR. SCHWARTZ: Oh. 13 MR. ZIMMERMAN: You keep leaving out the word 14 "the" DNA sequencing by the synthesis system. 15 MR. SCHWARTZ: I thought I had read that.</p> <p>16 BY MR. SCHWARTZ:</p> <p>17 Q. Let me read it again. Sorry about this. 18 A. I'm used to it.</p> <p>19 Q. [As read.] 20 "Ju also states that the success 21 of this [sic] [DNA sequencing by the 22 synthesis] system will allow the 23 development of an ultra 24 high-throughput and high fidelity DNA 25 sequencing system for polymorphism</p>

<p align="right">Page 33</p> <p>1 pharmacogenetic application --</p> <p>2 pharmacogenetics applications and for</p> <p>3 whole genome sequencing. This fast</p> <p>4 and accurate DNA resequencing system</p> <p>5 is needed in such fields as detection</p> <p>6 of single nucleotide polymorphisms</p> <p>7 (SNPs) serial analysis of gene</p> <p>8 expression (SAGE), identification in</p> <p>9 forensics and genetic disease</p> <p>10 association studies."</p> <p>11 And you cite to the Ju patent specification at</p> <p>12 Column 4, lines 10 through 19.</p> <p>13 That is what you wrote and that is your</p> <p>14 opinion, correct?</p> <p>15 A. That is what is written, and I believe that</p> <p>16 would still be my opinion, yes.</p> <p>17 Q. And I'll note for the record that you</p> <p>18 underlined the words "ultra high-throughput" and "fast"</p> <p>19 in what you wrote, correct?</p> <p>20 A. That is correct.</p> <p>21 Q. Why did you emphasize the word "fast"?</p> <p>22 A. At this exact moment, I'm not -- I mean, this</p> <p>23 was -- I wrote this four years ago. I believe I was</p> <p>24 emphasizing that the deprotection need to be -- needed</p> <p>25 to be reasonably efficient. Or I might have been -- I</p>	<p align="right">Page 34</p> <p>1 might have been echoing what Ju said.</p> <p>2 I'm actually not -- I don't -- that was four</p> <p>3 years ago, and I don't remember.</p> <p>4 Q. And why did -- why did you emphasize the word</p> <p>5 "ultra high-throughput"?</p> <p>6 A. Same answer.</p> <p>7 Q. Going back to paragraph 34 of your declaration</p> <p>8 in Exhibit 2007.</p> <p>9 A. The same dec?</p> <p>10 Q. Yes.</p> <p>11 I just read paragraph 34 through the top of</p> <p>12 page 14. So following what I just read, we are now on</p> <p>13 the third line from the top of page 14, and you write:</p> <p>14 "Ju's characterization of its DNA</p> <p>15 sequencing system as 'fast'" -- and</p> <p>16 you put a quotes around fast -- "and</p> <p>17 'ultra high-throughput'" -- and you</p> <p>18 put quotes around ultra</p> <p>19 high-throughput -- "would have led a</p> <p>20 person of ordinary skill in the art</p> <p>21 to understand that speed was an</p> <p>22 important design consideration for</p> <p>23 Ju's sequencing system.</p> <p>24 "Thus, one of ordinary skill</p> <p>25 would have considered that each step</p>
<p align="right">Page 35</p> <p>1 of Ju's sequencing cycle should</p> <p>2 proceed as quickly as possible to</p> <p>3 increase the overall speed of the</p> <p>4 sequencing method.</p> <p>5 "Since removal of the 3'-OH</p> <p>6 capping group is one step in Ju's</p> <p>7 sequencing cycle," and you cite to</p> <p>8 the Ju patent specification at</p> <p>9 Column 21, lines 11 through 13, "a</p> <p>10 person of ordinary skill in the art</p> <p>11 would understand that rapid removal</p> <p>12 conditions would be required to</p> <p>13 develop a 'fast' sequencing system</p> <p>14 capable of the 'ultra</p> <p>15 high-throughput' of Ju's sequencing</p> <p>16 method."</p> <p>17 That is your opinion and that is what you</p> <p>18 wrote, correct?</p> <p>19 A. That is what is written, and I believe that</p> <p>20 would still be my opinion.</p> <p>21 Q. I'm going to ask you to go back to your</p> <p>22 deposition transcript in IPR2013-00517, which was marked</p> <p>23 as Exhibit 2035. And please turn to page 99, and please</p> <p>24 look at line 2. Starting at line 2, the transcript</p> <p>25 reads:</p>	<p align="right">Page 36</p> <p>1 [As read.]</p> <p>2 "But what I will say is that</p> <p>3 there are lots of polymerase</p> <p>4 reactions. There are lots of read</p> <p>5 lengths that would simply never be</p> <p>6 useful for sequencing by synthesis.</p> <p>7 "A read length of one is just an</p> <p>8 example. So [sic] you would never</p> <p>9 be able to do anything with that.</p> <p>10 So you're going to have to get read</p> <p>11 lengths of 25 or 30 in -- in a --</p> <p>12 with no more than an hour or so</p> <p>13 between reads to make it -- to --</p> <p>14 someone who's reading the Ju</p> <p>15 material, the Ju patent, and</p> <p>16 thinking about sequencing by</p> <p>17 synthesis is going to understand</p> <p>18 those as restrictions."</p> <p>19 That was your testimony and that is your</p> <p>20 opinion, correct?</p> <p>21 A. That is what is written. I would ask to read</p> <p>22 the context to make sure that I'm -- understand what I'm</p> <p>23 ask -- what I'm answering, though.</p> <p>24 Can I take a moment to read this or --</p> <p>25 Q. Sure.</p>

<p style="text-align: right;">Page 37</p> <p>1 A. Okay. Thank you.</p> <p>2 Okay. Could you repeat the question, please?</p> <p>3 Q. Starting at line transcript -- line 2 of the</p> <p>4 transcript, you stated:</p> <p>5 "But what I will say is that</p> <p>6 there are lots of polymerase</p> <p>7 reactions. There are lots of read</p> <p>8 lengths that would simply never be</p> <p>9 useful for sequencing by synthesis.</p> <p>10 "A read length of one is just an</p> <p>11 example. So [sic] you would never</p> <p>12 be able to do anything with that.</p> <p>13 So you're going to have to get read</p> <p>14 lengths of 25 or 30 in -- in a --</p> <p>15 with no more than an hour or so</p> <p>16 between reads to make it -- to --</p> <p>17 someone who's reading the Ju</p> <p>18 material, the Ju patent, and</p> <p>19 thinking about sequencing by</p> <p>20 synthesis is going to understand</p> <p>21 those as restrictions."</p> <p>22 And my question was, that is your opinion and</p> <p>23 that is your testimony, correct?</p> <p>24 A. That is what is written, but I would like to</p> <p>25 clarify. What I was -- the 25 to 30 is required for, as</p>	<p style="text-align: right;">Page 38</p> <p>1 I -- as we talked about last time, for genome</p> <p>2 reassembly. And so for de novo sequencing by synthesis,</p> <p>3 I should -- probably should have been more clear with</p> <p>4 this testimony. I was trying to look back to see if</p> <p>5 that was the subject matter. I'm not sure it was.</p> <p>6 The reason -- a reason that you need 25 to 30</p> <p>7 nucleotides is that you need to reassemble genomes. And</p> <p>8 one nucleotide, my point was that you could never -- if</p> <p>9 you simply had a one nucleotide read, you wouldn't know</p> <p>10 where in the genome you were.</p> <p>11 If you had two, you still don't know because</p> <p>12 there are too many places where two nucleotides are</p> <p>13 repeated. You have to get longer to have a unique</p> <p>14 sequence. And they're on the order of -- depending on</p> <p>15 the size of how much DNA you have, they're on the order</p> <p>16 of 15 to 30 nucleotides.</p> <p>17 And for the human genome, which is what I</p> <p>18 was -- in my mind at the time, 25 is about what you need</p> <p>19 for a unique placement of a sequence.</p> <p>20 Q. All right. But you did look back in the</p> <p>21 transcript, and there's nothing in the transcript where</p> <p>22 the question specifically was addressing genome</p> <p>23 sequencing, correct?</p> <p>24 A. I could not find it.</p> <p>25 Q. Okay. Okay. Please go back to page 14 of</p>
<p style="text-align: right;">Page 39</p> <p>1 your declaration.</p> <p>2 A. Same declaration?</p> <p>3 Q. Yes, please.</p> <p>4 MR. ZIMMERMAN: Just so we have a clear</p> <p>5 record, can you say which declaration it is?</p> <p>6 MR. SCHWARTZ: Exhibit 2007.</p> <p>7 BY MR. SCHWARTZ:</p> <p>8 Q. Please go to page 14.</p> <p>9 A. I'm there.</p> <p>10 Q. And draw your attention to about five lines</p> <p>11 down where you write:</p> <p>12 "Thus, one of ordinary skill</p> <p>13 would have considered that each step</p> <p>14 of Ju's sequencing" --</p> <p>15 A. I'm sorry. I'm in -- I'm in my dec. You said</p> <p>16 the declaration. I'm sorry. Could you hold on one</p> <p>17 second?</p> <p>18 Q. Sure.</p> <p>19 A. Which dec?</p> <p>20 Q. Exhibit 2007.</p> <p>21 A. Yeah. Page 5?</p> <p>22 Q. Yes -- page 14, line 5 -- five lines down.</p> <p>23 A. Mm-hmm, yes.</p> <p>24 Q. About five lines down you write:</p> <p>25 "Thus, one of ordinary skill</p>	<p style="text-align: right;">Page 40</p> <p>1 would have considered that each step</p> <p>2 of Ju's sequencing cycle should</p> <p>3 proceed as quickly as possible to</p> <p>4 increase the overall speed of the</p> <p>5 sequencing method."</p> <p>6 That is what you wrote and that is your</p> <p>7 opinion, correct?</p> <p>8 A. Yes.</p> <p>9 Q. Okay. Please go back to paragraph 29 of that</p> <p>10 declaration. In paragraph 29 of your declaration you</p> <p>11 refer to the '079 patent specification at</p> <p>12 Column 29 -- strike that.</p> <p>13 In paragraph 29 of your declaration, you refer</p> <p>14 to the '079 patent specification at Column 21, lines 3</p> <p>15 through 16. Do you see that?</p> <p>16 A. Yes.</p> <p>17 Q. And please go to the '079 patent, which is</p> <p>18 marked as Exhibit 2095.</p> <p>19 A. Column 21?</p> <p>20 Q. Yes, please. And lines 3 through 16. I'm</p> <p>21 just going to ask you to read that section to yourself</p> <p>22 and let me know when you're done.</p> <p>23 A. Lines 3 through 16?</p> <p>24 Q. It's what you refer to in your declaration.</p> <p>25 A. I read it.</p>

<p style="text-align: right;">Page 41</p> <p>1 Q. Okay. And with the '079 patent still in front 2 of you, please go to U.S. Patent No. 9,868,985, and 3 we're calling that the '985 patent. That's 4 Exhibit 1075. And so now you have in front of you both 5 the '079 patent and the '985 patent, correct? 6 A. Yes. 7 Q. And please turn to Column 20 of the '985 8 patent. And please look at line 65 and continue till 9 Column 21 at line 13. And just read that to yourself 10 and let me know when you're done. 11 And basically, my question is going to be -- I 12 think you can -- you can understand what I'm doing here 13 is I'm just asking you that the text that you refer to 14 in the '079 patent is identical to the text in the '985; 15 is that correct? 16 Please compare. 17 A. Yes, they seem to be identical. 18 Q. Okay. Please go to paragraph 32 of your 19 declaration, Exhibit 2007, and keep those patents in 20 front of you. 21 A. Which -- 22 Q. Paragraph 32 of your declaration, 23 Exhibit 2007. 24 A. Paragraph 32. Yes. 25 Q. And in paragraph 32 of your declaration, you</p>	<p style="text-align: right;">Page 42</p> <p>1 refer to the '079 patent specification at Column 2, 2 lines 10 through 25, and Column 21, lines 63 through 67, 3 correct? 4 A. I'm sorry. Could you repeat that? This is in 5 paragraph 32? 6 Q. Yes. 7 You refer to Column 2, lines 10 through 25, 8 sort of in the middle of the paragraph, and you refer to 9 Column 21, lines 63 through 67, towards the end, 10 correct? 11 A. Yes. I see. 12 Q. Okay. And so please go to the '079 patent, 13 which is Exhibit 2095. And let's start by looking at 14 Column 2, lines 10 through 25. Please read that to 15 yourself and let me know when you're done. 16 And basically, I'll ask you to do the same 17 thing of the '985 patent. 18 A. Column 2, I read line 10 through 25. 19 Q. Okay. Now, please open the '985 patent and go 20 to Column 2 as well, please. And please look at 21 lines 31 through 46. You can read that to yourself and 22 let me know when you're done. 23 A. You said lines 41 through 46? 24 Q. 31 through 46. 25 A. 31.</p>
<p style="text-align: right;">Page 43</p> <p>1 I have read them. 2 Q. So the text of the '079 patent specification 3 at Column 2, lines 10 through 25, is found word for word 4 in the '985 patent specification, correct? 5 A. It is. 6 Q. Please go to Column 21, lines 63 through 67 of 7 the '079. Column 21, lines 63 through 67. 8 A. So 2095. What -- what column? 9 Q. Of the '079 patent, Column 21, lines 63 10 through 67. 11 A. 63 through 67. 12 Q. Please read that to yourself and let me know 13 when you're done. 14 A. Yes. 15 Q. Okay. Now, please look at the '985 patent, 16 Column 21, and look at lines 60 through 64. Please read 17 that to yourself and let me know when you're done. 18 A. Column 21, line 60. 19 Q. Through 64. 20 A. I have read them. 21 Q. The text of the '079 patent specification at 22 Column 21, lines 63 through 67, is found word for word 23 in the '985 patent specification, correct? 24 A. They are not identical. 25 Q. And in what way are they different?</p>	<p style="text-align: right;">Page 44</p> <p>1 A. In the 2095, the '079 patent, the reference 2 "Schena et al. 1995 et al." has a period, whereas in the 3 '985 patent that we're discussing, now there's a comma. 4 Q. Okay. Otherwise they are identical? 5 A. Otherwise -- 6 MR. ZIMMERMAN: Objection. Mischaracterizes 7 the document. 8 BY MR. SCHWARTZ: 9 Q. Otherwise the portions that we read are 10 identical? 11 A. Otherwise the portion that you asked me to 12 read seems to be identical. 13 MR. ZIMMERMAN: Is now a good time for a 14 break? 15 MR. SCHWARTZ: Do you really need a break 16 right now? Because I'm going through -- 17 THE WITNESS: It will only take me a second. 18 I'll be -- I'll right back. 19 MR. SCHWARTZ: Sure. 20 MR. ZIMMERMAN: Can I just step out? 21 THE VIDEOGRAPHER: Going off the record at 22 1:28 p.m. 23 (Recess taken from 1:28 p.m. to 24 1:31 p.m.) 25 THE VIDEOGRAPHER: We are back on the record</p>

<p align="right">Page 45</p> <p>1 at 1:31 p.m.</p> <p>2 BY MR. SCHWARTZ:</p> <p>3 Q. Dr. Romesberg, during your break did you</p> <p>4 discuss today's deposition with your attorney?</p> <p>5 A. No, I did not.</p> <p>6 Q. Please go to paragraph 33 of your declaration,</p> <p>7 Exhibit 2007.</p> <p>8 A. Where?</p> <p>9 Q. Paragraph 33.</p> <p>10 A. Yes.</p> <p>11 Q. In paragraph 33 of your declaration you</p> <p>12 referred to the '079 patent specification at Column 21,</p> <p>13 lines 8 through 13. Do you see that?</p> <p>14 A. Where is this? 8 through 13?</p> <p>15 Q. 21, 8 through 13.</p> <p>16 A. Yes, I see it.</p> <p>17 Q. And please go to the '079 patent, which is</p> <p>18 Exhibit 2095 and look at Column 21, lines 8 through 13.</p> <p>19 Please read that to yourself and let me know when you</p> <p>20 are done.</p> <p>21 A. I have read it.</p> <p>22 Q. Please turn to the '985 patent and look at</p> <p>23 Column 21 of that patent. And please look at lines 5</p> <p>24 through 10 of the '985 patent at Column 21. And please</p> <p>25 read that to yourself and let me know when you're done.</p>	<p align="right">Page 46</p> <p>1 A. I have read it.</p> <p>2 Q. The text of the '079 patent specification at</p> <p>3 Column 21, lines 8 through 13, is found word for word in</p> <p>4 the '985 patent specification, correct?</p> <p>5 A. The specification in the '079 patent is found</p> <p>6 word for word in the '985, the parts that you just asked</p> <p>7 me to read, yes.</p> <p>8 Q. Okay. Please go to paragraph 34 of your</p> <p>9 declaration, which is Exhibit 2007. In paragraph 34 of</p> <p>10 your declaration you refer to the '079 patent</p> <p>11 specification at Column 4, lines 10 through 19, and at</p> <p>12 Column 21, lines 11 through 13, correct?</p> <p>13 A. Correct.</p> <p>14 Q. Okay. Please go to the '079 patent,</p> <p>15 Exhibit 2095, and look at, starting with Column 4,</p> <p>16 lines 10 through 19.</p> <p>17 A. The '079?</p> <p>18 Q. Yes. Column 4, lines 10 through 19. And read</p> <p>19 that to yourself and let me know when you're done.</p> <p>20 A. I am complete.</p> <p>21 Q. Please go back to the '985 patent and look at</p> <p>22 Column 4 and draw -- Column 4. And draw your attention</p> <p>23 to lines 31 through 41. And please read that section to</p> <p>24 yourself and let me know when you're done.</p> <p>25 A. I'm done.</p>
<p align="right">Page 47</p> <p>1 Q. The text of the '079 patent specification at</p> <p>2 Column 4, lines 10 through 19, are found word for word</p> <p>3 in the '985 patent specification, correct?</p> <p>4 A. Yes, they are.</p> <p>5 Q. And now please go to the '079 patent and look</p> <p>6 at Column 21, lines 11 through 13.</p> <p>7 A. Yes.</p> <p>8 Q. And please read that to yourself and let me</p> <p>9 know when you're done.</p> <p>10 A. 11 through 14?</p> <p>11 Q. 11 through 13.</p> <p>12 A. 13. I'm done.</p> <p>13 Q. And please go back to the '985 patent and turn</p> <p>14 to Column 21 and look at lines 8 through 10. Please</p> <p>15 read that to yourself and let me know when you're done.</p> <p>16 A. I'm done.</p> <p>17 Q. The text of the '079 patent specification at</p> <p>18 Column 21, lines 11 through 13, is found word for word</p> <p>19 in the '985 patent specification, correct?</p> <p>20 A. It is not identical.</p> <p>21 Q. Okay. And the difference being what?</p> <p>22 A. I believe it's called a superstrike. It's a</p> <p>23 longer hyphen between the 3' and the OH versus a dash,</p> <p>24 which the '985 patent has.</p> <p>25 Q. Do you understand both of them to mean the</p>	<p align="right">Page 48</p> <p>1 3'-OH group?</p> <p>2 A. I understand them both to mean the identical</p> <p>3 thing.</p> <p>4 Q. Okay. And other than that difference, the</p> <p>5 specifications are the same in that section, correct?</p> <p>6 A. Correct.</p> <p>7 MR. SCHWARTZ: Would this be a good time for</p> <p>8 you to take a break? It's been about an hour.</p> <p>9 MR. ZIMMERMAN: Sure.</p> <p>10 THE VIDEOGRAPHER: Going off the record at</p> <p>11 1:37 p.m.</p> <p>12 (Recess taken from 1:37 p.m. to</p> <p>13 1:55 p.m.)</p> <p>14 THE VIDEOGRAPHER: We are back on the record</p> <p>15 at 1:55 p.m.</p> <p>16 BY MR. SCHWARTZ:</p> <p>17 Q. Okay. Dr. Romesberg, during the break did you</p> <p>18 have any conversations with your attorneys relating to</p> <p>19 this case?</p> <p>20 A. No, I did not.</p> <p>21 Q. Please go back to the declaration in the</p> <p>22 present IPR, which is Exhibit 10,000 -- 1078. It's the</p> <p>23 declaration in IPR2018-00797. And please turn to</p> <p>24 page 49. Please draw your attention to the first two</p> <p>25 lines on page 49.</p>

<p style="text-align: right;">Page 49</p> <p>1 You rely on the Qian 1998 paper to support 2 your statement on page 49, and also elsewhere in your 3 declaration, that in O-O-allyl ether is removed using 4 palladium chloride in quantitative yield, correct? 5 A. That is what is written, yes. 6 Q. I'm going to put in front of you Exhibit 1036, 7 which is the Qian 1998 paper, correct? 8 (Exhibit 1036 was previously marked 9 for identification by the Certified 10 Shorthand Reporter.) 11 A. Yes. It is. 12 BY MR. SCHWARTZ: 13 Q. Okay. I'm going to put another document in 14 front of you. 15 (Exhibit 2102 was marked for 16 identification by the Certified 17 Shorthand Reporter.) 18 BY MR. SCHWARTZ: 19 Q. This is marked as Exhibit 2102. 20 A. Are you marking this now or it's been 21 previously? 22 Q. It's been premarked [sic]. And please look at 23 the second page of the document. And it's entitled 24 Enzymatic and Chemical Synthesis of Oligosaccharide 25 Analogs by Xiangping Qian.</p>	<p style="text-align: right;">Page 50</p> <p>1 Do you see that? 2 A. I do. 3 Q. And please turn to the fourth page of that 4 exhibit, the page that is entitled Library Release Form. 5 Do you see that? 6 A. I do. 7 Q. At the bottom of the page there's a signature, 8 it appears to be by Qian, that was signed on 9 January 25th, 2000. Do you see that? 10 A. I do. 11 Q. Okay. So please go back to the Qian 1998 12 paper, which was Exhibit 1036. And Xiangping Qian, who 13 was the first author of Exhibit 1036, is the same 14 Xiangping Qian who was the author of Exhibit 2102, 15 correct? 16 A. Well, they have the same name, so yeah, I 17 would assume there's the same name and the same 18 affiliation, so it would seem likely. 19 Q. Please turn to page 2185 of the Qian 1998 20 paper. And please draw your attention to Scheme 2. 21 And you rely on Scheme 2 in the Qian 1998 22 paper to support your opinion that an O-allyl ether is 23 removed using palladium chloride in quantitative yield 24 in a two-hour reaction at room temperature, correct? 25 A. Yes. I cite that.</p>
<p style="text-align: right;">Page 51</p> <p>1 Q. Okay. Please keep that paper in front of you 2 and go back to the thesis. When I say "thesis," I'm 3 referring to Qian Ph.D. thesis, Exhibit 2102. And 4 please turn to page 42. And please draw your attention 5 to compound 65. 6 Compound 65 in Qian's Ph.D. thesis is the same 7 O-allyl protected compound as compound 7 in the Scheme 2 8 in Qian 1998, correct? 9 A. He explicitly writes out what R must be in 10 compound 65 in the thesis, where he leaves it as an R in 11 compound 7. 12 Q. I believe if you look a little bit to the 13 right, you'll see O -- you'll see R is O-octyl in the 14 thesis. 15 A. It is written as octyl in the thesis, but it's 16 written as R in the text -- in the manuscript, in the 17 paper. My guess is that -- 18 Q. And look -- please look at the paper again, 19 and right under compound 6, do you see R octyl? 20 A. Yes, that's correct. Yep. 21 Q. So they are the same compound? 22 A. They would appear to be the same compound. 23 Q. Okay. Now, look at compound 66 in the thesis, 24 Qian's Ph.D. thesis. And that is the same allyl 25 deprotected compound as compound 8 in Qian 1998,</p>	<p style="text-align: right;">Page 52</p> <p>1 correct? 2 A. Yes. It would seem to be, yes. 3 Q. And please turn to page 77 of Qian's thesis. 4 A. I'm there. 5 Q. Page 77 of Qian's Ph.D thesis provides 6 experimental details for the allyl deprotection of 7 compound 65, correct? 8 A. It would appear to. 9 Q. And Qian writes -- 10 A. I haven't read it carefully, but that would 11 appear to be the case. 12 Q. Qian writes on that page: 13 "Compound 65 (220 mg, 0.23 mmol) 14 was treated with palladium chloride 15 in the same fashion as described for 16 17." 17 That's what Qian writes, correct? 18 A. That is what is written. 19 Q. And please turn to page 54 of Qian's thesis. 20 You might want to keep your finger where you were. 21 A. I'm there. 22 Q. And please draw your attention to the bottom 23 of the page where you see there are experimental details 24 provided for compound 17. Do you see that? 25 A. At the bottom of page 54?</p>

<p style="text-align: right;">Page 53</p> <p>1 Q. At the bottom of page 54 there's experimental 2 details for compound 17. Do you see that? 3 A. Yeah. I don't know what the details are for, 4 but, yeah -- 5 Q. Okay. 6 A. -- I see some details. 7 Q. And Qian writes: 8 "To a solution of 16 (400 mg, 9 0.39 mmol) in methanol (15 ml) was 10 added palladium chloride (34 mg, 11 0.19 mmol). The mixture was stirred 12 at room temperature for four hours." 13 Qian writes that, right? 14 A. That is written, yes. 15 Q. Okay. The Qian Ph.D. thesis discloses that 16 the O-allyl deprotection of compound 65 to compound 66 17 using palladium chloride in methanol at room temperature 18 proceeds for four hours, correct? 19 A. No, it doesn't report that. The text says 20 "two hours," and I have no reason to believe that's 21 incorrect -- the manuscript from -- 22 Q. I'm asking you about the thesis. 23 A. Oh, the thesis does not define a time. Not -- 24 I mean, I can look and search more carefully, but I 25 don't see a time.</p>	<p style="text-align: right;">Page 54</p> <p>1 Q. We're -- we're looking at -- maybe we're -- 2 we're on page 54 of this thesis, right? We were looking 3 at compound 17. 4 A. Oh, I'm sorry. You were referring to compound 5 17? 6 Q. Yes. 7 A. He describes that it was treated in a solution 8 with methanol and palladium chloride that was stirred 9 for four hours. 10 Q. Okay. So the Qian Ph.D. thesis discloses that 11 the O-allyl deprotection of compound 65 to compound 66 12 using palladium chloride in methanol at room temperature 13 proceeds for four hours, correct? 14 MR. ZIMMERMAN: Objection. Mischaracterizes 15 the document. 16 MR. SCHWARTZ: It doesn't mischaracterize the 17 document. 18 A. It doesn't say that it was run for four hours. 19 As I said a minute ago, I don't see a time. If you want 20 me to look to see if -- 21 BY MR. SCHWARTZ: 22 Q. Well, can I just -- we looked at this before. 23 We were -- we were on page 77 of Qian, right, of his 24 thesis? 25 A. Yes.</p>
<p style="text-align: right;">Page 55</p> <p>1 Q. On page 77 he said "Compound 65" -- and I 2 won't read what's in parens -- "was treated with 3 palladium chloride in the same fashion as described for 4 17," correct? 5 A. Yes, that is what is written. 6 Q. Okay. And for compound 17, the reaction took 7 place at four hours, correct? 8 A. There is -- there is a time given for reaction 9 17. There's not a time given for reaction 65. 10 Q. Right. It says -- it says "in the same 11 fashion as described for 17," correct? 12 A. He says it was treated with palladium chloride 13 in the same fashion. 14 Q. Uh-huh. 15 A. There's no time dependence to treatment with 16 palladium chloride in that sentence. 17 Q. But he does indicate that it was treated with 18 palladium chloride in the same fashion as described for 19 17? 20 MR. ZIMMERMAN: Objection. Asked and 21 answered. 22 BY MR. SCHWARTZ: 23 Q. And in 17 he described using palladium 24 chloride for four hours, correct? 25 MR. ZIMMERMAN: Objection. Asked and</p>	<p style="text-align: right;">Page 56</p> <p>1 answered. 2 A. In -- he -- he explicitly says four hours for 3 compound 16 to 17 -- sorry, 15 to 16 -- no, wait. 4 On page 40 -- on page 54 he describes 5 treatment of compound 16 to yield 17 with palladium 6 chloride in methanol. And he then in a separate 7 sentence says it was stirred for four hours. 8 In a single sentence on page 77, he says, 9 "Compound 65 was treated with palladium chloride in the 10 same fashion as described for 17." I take that to be 11 the concentrations in the methanol. And in the text of 12 the paper where he reports this, it says two hours, and 13 I have no reason to think that that was not the time 14 that he used. 15 Q. In the thesis he says that he treated with 16 palladium chloride for four hours for 17, which was the 17 same fashion as compound 65, correct? 18 A. Where you and I are having problems 19 communicating is whether the statement refers to the 20 conditions of the reaction, the mixture of the reagents 21 present, or whether it implies a time. You are reading 22 it as it applies a time; I am not. So that's -- 23 Q. So you're saying that "in the same fashion" to 24 you means everything but the time? 25 A. It -- to tell you the truth, it's ambiguous.</p>

<p style="text-align: right;">Page 57</p> <p>1 Someone should have edited this and told him to put in 2 the time.</p> <p>3 Q. Okay. So again, I want to get your testimony 4 correct. So you're reading this thesis as saying that 5 when Qian said that he did it, the reaction for compound 6 17, the same way as compound 65, your interpretation of 7 that is that he means everything except for the four 8 hours that he explicitly states for 17, correct?</p> <p>9 MR. ZIMMERMAN: Objection. Mischaracterizes 10 the document.</p> <p>11 A. What I read that as is his treatment with 12 palladium chloride refers to the -- the -- the amount of 13 the palladium chloride and the -- and the methanol and 14 the temperature. Those are all things that chemists 15 would refer to conditions.</p> <p>16 Could they refer to time as a condition? 17 Sure. Maybe. It -- it -- it just leaves it ambiguous.</p> <p>18 BY MR. SCHWARTZ:</p> <p>19 Q. So a person of ordinary skill reading that 20 thesis could understand that he treated it for four 21 hours, correct?</p> <p>22 A. I think a person of ordinary skill in the art 23 would not have known, because it's simply not stated.</p> <p>24 Q. But they could have understood it to mean four 25 hours?</p>	<p style="text-align: right;">Page 58</p> <p>1 MR. ZIMMERMAN: Objection. Asked and 2 answered.</p> <p>3 A. I think they would not have known. I see 4 no -- I see no reason to assume the time of the 5 treatment was the same. I mean, it's just ambiguous. I 6 don't know -- I can't interpret how someone would have 7 interpreted something that's ambiguous.</p> <p>8 BY MR. SCHWARTZ:</p> <p>9 Q. So "in the same fashion" to you means it is 10 ambiguous?</p> <p>11 A. No. "In the same fashion" describes the 12 treatment, the -- so when a chemist talks about reaction 13 conditions, what they're talking about is the catalyst 14 added, the solvent, the ligands that are added. You let 15 that reaction go, and you monitor it for time typically, 16 and then find -- when the reaction is complete, you 17 would -- you would quench it and purify it. It is -- 18 it's ambiguous and a little odd that he didn't put the 19 time.</p> <p>20 Q. That he didn't put the time?</p> <p>21 A. That he seems to not to have -- I mean, I 22 haven't read this carefully, but he seems not to have 23 included the time.</p> <p>24 Q. He did for compound 17, correct?</p> <p>25 A. Yeah. That's not what I was talking about.</p>
<p style="text-align: right;">Page 59</p> <p>1 Q. Okay. For compound 17, he says four hours? 2 A. That is -- that is correct.</p> <p>3 Q. And then for compound 65, he says it was 4 treated in the same fashion as described for 17, 5 correct?</p> <p>6 MR. ZIMMERMAN: Objection. Asked and 7 answered, twice.</p> <p>8 BY MR. SCHWARTZ:</p> <p>9 Q. Does he say that?</p> <p>10 A. He says that he describes the reaction 11 conditions for the solution. And he gives how much 12 methanol and how much palladium chloride was used, the 13 molar equivalents and their weights. And then he says 14 that that mixture was stirred at room temperature for 15 four hours.</p> <p>16 I do -- that is not -- implicit in the 17 statement of the conditions being the same is not how 18 long the reaction was stirred.</p> <p>19 Q. Okay. We've already established that compound 20 65 and 66 in Qian's thesis are the same as compound 7 21 and 8 in Qian's 1998 paper, correct?</p> <p>22 A. That is correct.</p> <p>23 Q. Okay. Please turn to page 77 of Qian's 24 thesis.</p> <p>25 A. Page 77?</p>	<p style="text-align: right;">Page 60</p> <p>1 Q. Yes, please. 2 A. I'm there.</p> <p>3 Q. And starting at the third line Qian writes: 4 "Compound 65 (220 mg) --</p> <p>5 A. I'm sorry. Page 77? On the third line? Oh, 6 compound -- sorry. Could you start again?</p> <p>7 Q. All right.</p> <p>8 "Compound 65 (220 mg, 0.23 mmol) 9 was treated with palladium chloride 10 in the same fashion as described for 11 17. Purification by column 12 chromatography (4:1 hexanes/EtOAc) 13 gave 66 (202 mg, 96%) pass a whit 14 solid."</p> <p>15 And I believe "white" may have a typo. It 16 doesn't have the E at the end.</p> <p>17 A. That is correct.</p> <p>18 Q. That's what Qian writes, correct?</p> <p>19 A. That's correct.</p> <p>20 Q. Qian is reporting that the allyl deprotection 21 that results in compound 66 occurs at a 96 percent 22 yield, correct?</p> <p>23 A. No.</p> <p>24 Q. Why?</p> <p>25 A. He reports that it was purified at 9 -- that</p>

<p align="right">Page 61</p> <p>1 after purification he recovered 96 percent. There's</p> <p>2 inevitably loss during the recovery process.</p> <p>3 Q. Okay. I would like to mark another paper.</p> <p>4 A. Are we done with this one? We're just</p> <p>5 building up a lot of open documents.</p> <p>6 Q. I think so, yes.</p> <p>7 I'm putting in front of you a document</p> <p>8 entitled --</p> <p>9 A. I'm sorry. One second.</p> <p>10 Q. Let me just say that this was marked as</p> <p>11 Exhibit 2097.</p> <p>12 (Exhibit 2097 marked for</p> <p>13 identification by the Certified</p> <p>14 Shorthand Reporter.)</p> <p>15 A. Okay. Sorry. What?</p> <p>16 BY MR. SCHWARTZ:</p> <p>17 Q. So I just put in front of you a document that</p> <p>18 was marked as Exhibit 2097, and it's a paper entitled</p> <p>19 Chemoenzymatic Synthesis of alpha 1 - 3 Gal(NAc)</p> <p>20 Terminating Glycosides of Complex Tertiary Sugar</p> <p>21 Alcohols by Qian, et al. that was published in 1999.</p> <p>22 Both the Qian 1998 and the Qian 1999 papers</p> <p>23 list Xiangping Qian as the first author, correct?</p> <p>24 A. They do.</p> <p>25 Q. In fact, three of the four authors of Qian</p>	<p align="right">Page 62</p> <p>1 1998 are also authors of Qian 1999, correct?</p> <p>2 A. There are names -- I'm having trouble reading</p> <p>3 the names. There are four authors on the '98 paper, and</p> <p>4 let's see. This one is on it. Monica Palcic. Three of</p> <p>5 the four in the '98 paper seem to be on the '99 paper.</p> <p>6 Q. Please go to page 12065 of Qian 1999. And</p> <p>7 please draw your attention to Scheme 2 on the top of the</p> <p>8 page. Scheme 2 shows an allyl deprotection in reaction</p> <p>9 E, correct?</p> <p>10 A. That's correct.</p> <p>11 Q. And Qian 1999 reports that the allyl</p> <p>12 deprotection in Scheme 2 of Qian 1999 used palladium</p> <p>13 chloride in methanol, correct?</p> <p>14 A. Sorry. Could you repeat that question?</p> <p>15 Q. Qian 1999 reports that the allyl deprotection</p> <p>16 in Scheme 2 of that paper used palladium chloride in</p> <p>17 methanol, correct?</p> <p>18 A. Can you give me a minute to look at this? I</p> <p>19 haven't read this paper.</p> <p>20 Q. I think if you look at the legend of Scheme 2.</p> <p>21 A. Yeah, that's where I'm looking. That is</p> <p>22 correct.</p> <p>23 Q. And please turn to page 12069 of Qian 1999.</p> <p>24 And draw your attention to the right side of the page</p> <p>25 where there's an entry for -- and I won't read the whole</p>
<p align="right">Page 63</p> <p>1 thing. It starts with "Octyl 2,4, 6 Tri-O-benzyl."</p> <p>2 Do you see that on the top right?</p> <p>3 A. They actually all start that way on the right.</p> <p>4 Q. Sorry. It's the first full one, "Octyl 2, 4,</p> <p>5 6 Tri-O-benzyl beta D" --</p> <p>6 A. The one that ends with compound 9?</p> <p>7 Q. Correct.</p> <p>8 A. Yeah, I see it.</p> <p>9 Q. The allyl deprotection reaction in Scheme 2 is</p> <p>10 done at room temperature, correct?</p> <p>11 A. In the 1999 paper?</p> <p>12 Q. Yes.</p> <p>13 A. I don't see a temperature.</p> <p>14 Q. Well, in that section we just read, I didn't</p> <p>15 read the whole thing, but the one that ended in compound</p> <p>16 9, if you continue reading it -- I won't read it into</p> <p>17 the record -- do you see where it says "at room</p> <p>18 temperature for four hours"?</p> <p>19 A. Yes.</p> <p>20 Q. So that that reaction was done at room</p> <p>21 temperature, correct?</p> <p>22 A. That is what is written.</p> <p>23 Q. Okay. So please go back to the Qian 1998</p> <p>24 paper. And again, draw your attention to Scheme 2. And</p> <p>25 the allyl deprotection reaction in Scheme 2 in Qian 1998</p>	<p align="right">Page 64</p> <p>1 is also done using palladium chloride in methanol at</p> <p>2 room temperature, correct?</p> <p>3 A. That's correct.</p> <p>4 Q. All right. So going back to the Qian 1999</p> <p>5 paper, and looking again at Scheme 2, step E, Qian</p> <p>6 reports that the allyl deprotection yield is 83 percent</p> <p>7 after four hours, correct?</p> <p>8 A. In the 1999 paper, the deprotection of allyl</p> <p>9 is listed palladium chloride in methanol for four hours,</p> <p>10 83 percent.</p> <p>11 (Court reporter clarification.)</p> <p>12 A. In methanol for four hours, 83 percent.</p> <p>13 Q. So POSA in October 2000, having read Qian 1998</p> <p>14 and Qian 1999, understood that the allyl deprotection</p> <p>15 using Qian's deprotection chemistry varies between</p> <p>16 96 percent and 83 percent?</p> <p>17 A. No. That's not what I said.</p> <p>18 I would have -- between 83 percent and</p> <p>19 96 percent isolated yield. If you want to use the</p> <p>20 96 percent, the isolated yield was 96 percent, that is</p> <p>21 correct.</p> <p>22 Q. Okay. So it varies between 96 percent</p> <p>23 isolated yield and 83 percent?</p> <p>24 A. Yeah. I'm not sure of the 83 percent, whether</p> <p>25 it was an isolated yield or an in situ yield. I'm not</p>

<p style="text-align: right;">Page 65</p> <p>1 sure. I haven't read the paper.</p> <p>2 Q. Okay. But it reports it as 83 percent?</p> <p>3 A. Yes. In the figure caption, it reports it as</p> <p>4 83 percent.</p> <p>5 Q. And the reaction -- the allyl deprotection</p> <p>6 Scheme 2 in Qian's allyl deprotection in Qian 1999 takes</p> <p>7 place for four hours, correct?</p> <p>8 A. That is what it says, yes.</p> <p>9 MR. SCHWARTZ: I guess it's just been pointed</p> <p>10 out to me that, at least in LiveNote, there's a mistake</p> <p>11 at line 14 -- or time 14:18:33. It says: You want to</p> <p>12 use Ju's to 96 percent. And I think it was "if you want</p> <p>13 to use." If you want to use. So you have "Ju" when he</p> <p>14 said "use," I believe.</p> <p>15 Do we agree?</p> <p>16 MR. ZIMMERMAN: Yes. Thank you.</p> <p>17 THE WITNESS: There's no action item there for</p> <p>18 me, right?</p> <p>19 MR. ZIMMERMAN: No.</p> <p>20 BY MR. SCHWARTZ:</p> <p>21 Q. I'm going to put in front of you an exhibit</p> <p>22 that's been marked as Exhibit 2054.</p> <p>23 (Exhibit 2054 marked for</p> <p>24 identification by the Certified</p> <p>25 Shorthand Reporter.)</p>	<p style="text-align: right;">Page 66</p> <p>1 BY MR. SCHWARTZ:</p> <p>2 Q. Which is a paper entitled A Sequencing Method</p> <p>3 Based on Real-Time Pyrophosphate by Ronaghi, et al. It</p> <p>4 was published in 1998.</p> <p>5 Please draw your attention to the second</p> <p>6 paragraph on the first page of the paper, which is</p> <p>7 page 363. And the authors write:</p> <p>8 "Sequencing-by-synthesis is based</p> <p>9 on the detecting of nucleotide</p> <p>10 incorporation, using a</p> <p>11 primer-directed polymerase</p> <p>12 extension. The sequence can be</p> <p>13 deduced iteratively. During the</p> <p>14 last decade, many researchers,</p> <p>15 including the groups of Rosenthal,</p> <p>16 Gibbs and Jones, described various</p> <p>17 protocols based on fluorescently</p> <p>18 labeled nucleotides."</p> <p>19 That's what the authors write, correct?</p> <p>20 A. Yeah, that is what's written.</p> <p>21 Q. And so -- and then they continue to write, the</p> <p>22 authors continue to write:</p> <p>23 "The level of incorporation of</p> <p>24 these fluorescent nucleotides is</p> <p>25 low. However, as shown by Metzker,</p>
<p style="text-align: right;">Page 67</p> <p>1 et al." -- citing to reference 7 --</p> <p>2 "and therefore, the protocols only</p> <p>3 permit detection of a few bases."</p> <p>4 MR. ZIMMERMAN: I just want to object that it</p> <p>5 mischaracterizes the document. I don't know if your</p> <p>6 version is different, but mine has boxes and never an F.</p> <p>7 MR. SCHWARTZ: I agree. It does have a box</p> <p>8 there, but --</p> <p>9 MR. ZIMMERMAN: Throughout the document.</p> <p>10 Everything you're reading as an F is a box.</p> <p>11 BY MR. SCHWARTZ:</p> <p>12 Q. Okay. Would one understand that to be for the</p> <p>13 word "fluorescent"?</p> <p>14 A. Is that a question for me?</p> <p>15 Q. Yes.</p> <p>16 A. Yes.</p> <p>17 Q. Okay. And would you take a look at reference</p> <p>18 7. And reference 7 is the Metzker 1994 paper, correct?</p> <p>19 A. Correct.</p> <p>20 Q. The Ronaghi authors state that Metzker's 1994</p> <p>21 nucleotides have low levels of incorporation. That's</p> <p>22 what they say, right?</p> <p>23 A. That is what is written.</p> <p>24 Q. And the Ronaghi 1998 authors do not say</p> <p>25 anything in their paper -- and you can read it, the</p>	<p style="text-align: right;">Page 68</p> <p>1 whole thing if you want -- that they believe that</p> <p>2 Metzker's 1994 experiments were flawed. They don't say</p> <p>3 that, do they?</p> <p>4 A. I have -- I have -- I have read this paper.</p> <p>5 It has been a while. And I did not read it from that</p> <p>6 perspective. I would be very sur- -- let me put it this</p> <p>7 way. If they would have called that out, I would have</p> <p>8 remembered it, so I don't think they do.</p> <p>9 Q. So despite the fact that Metzker 1994 reported</p> <p>10 in that paper that there was a small amount of</p> <p>11 contaminating dATP in each of the 3' O protected amine</p> <p>12 nucleotides, the authors of Ronaghi 1998 still relied on</p> <p>13 that paper to draw conclusions about what the prior art</p> <p>14 taught, correct?</p> <p>15 A. It's -- it's a little difficult to answer that</p> <p>16 question, because they are not writing this in a legal</p> <p>17 document. They're writing this in a paper where they're</p> <p>18 trying to promote their technique. This is common in</p> <p>19 science. You try to highlight your work as being</p> <p>20 superior to others.</p> <p>21 It is certainly true that any 3' protected</p> <p>22 nucleotide is not going to go in as efficiently as an</p> <p>23 unprotected natural nucleotide. No doubt about that.</p> <p>24 They're -- and what they are trying to</p> <p>25 emphasize in that statement is that they're using</p>

<p style="text-align: right;">Page 69</p> <p>1 natural triphosphates. That's what anyone who would 2 have read this would have read, that, boy, that's neat 3 because they don't have to use modified nucleotides. 4 Q. They do state expressly that the level of 5 incorporation of the nucleotides is low when they refer 6 to the Metzker 1994 paper, correct? 7 MR. ZIMMERMAN: Objection. Asked and 8 answered. 9 A. No one would read that with any knowledge of 10 what low meant. It's not wild type. Everyone would 11 have read that knowing that it wasn't as efficient as a 12 natural. Everyone would have read this. And this is no 13 doubt what the authors expect -- were intending, to 14 emphasize the use of their unmodified triphosphates, 15 which are incorporated faster. No doubt. 16 BY MR. SCHWARTZ: 17 Q. Okay. And so the authors of the Ronaghi paper 18 were able to make those interpretations of the Metzker 19 1994 paper despite the fact that it had small amounts of 20 contaminating dATP, correct? 21 A. They made these statements. The paper that 22 Metzker published, the experiments reported had those 23 contaminating amounts of ATP. So what you're stating is 24 factually true. It's written there. And that doesn't 25 change the fact that the Metzker experiments had the</p>	<p style="text-align: right;">Page 70</p> <p>1 contaminating dATP. So what you're saying is by 2 definition true. 3 Q. I think my question was, is that the authors 4 of Ronaghi 1998 made statements about Metzker 1994, 5 including the fact that the incorporation of the 6 nucleotides was low, but didn't say anything about the 7 fact that those -- those results were skewed by 8 contaminating dATP, correct? 9 A. That is factually correct. They write that, 10 and they do not cite the contaminating dATP. 11 Q. And Michael Metzker is not one of the authors 12 of Ronaghi 1998, correct? 13 A. He is not. 14 Q. And none of the authors of Ronaghi 1998 15 indicate any affiliation with Dr. Metzker's lab, 16 correct? 17 A. Not that I know of. 18 Q. And are you aware that Dr. Ronaghi is the 19 chief technology officer and senior vice president of 20 Illumina? 21 A. I was not aware of that. 22 Q. I'm going to switch subjects now. And I'm 23 going to ask you some questions about allyl ether 24 deprotection and palladium. 25 Before I hand out the article -- that's okay.</p>
<p style="text-align: right;">Page 71</p> <p>1 It's all right that you have it. 2 I just wanted to ask the -- the question. It 3 is your opinion that the allyl deprotection scheme 4 that's reported in Qian 1998, which was Exhibit 1036, 5 which uses palladium chloride in methanol, could be 6 modified so that it would work the same under aqueous 7 conditions as reported in Qian 1998, correct? 8 A. I don't exactly recall saying that, and that 9 seems like a little bit of an aggressive statement to 10 say. I think that a person of ordinary skill in the art 11 would have known that there were standard methods to get 12 a palladium chloride reaction of any sort into aqueous 13 environments that would have been compatible with DNA 14 stability and all the requirements for sequencing by 15 synthesis. They would have had the expectation, based 16 on the literature, that the yields might have been 17 quantitative, but they would not have known that. 18 So just to be clear, I didn't mean to testify 19 that they would have known that the reaction would have 20 been the same as reported in the 1998 paper in a 21 different environment. That would have required 22 checking. 23 Q. So if I understand your testimony, a skilled 24 artist in October 2000 wouldn't have known from the Qian 25 1998 paper that they would get quantitative yield of</p>	<p style="text-align: right;">Page 72</p> <p>1 allyl deprotection using Qian's conditions except under 2 aqueous conditions; is that -- 3 A. Because they were modifying the conditions, 4 they would have had an expectation of success based on 5 the Qian report. But would they have known? No one can 6 predict the future. So they would have had to run the 7 experiment. 8 I don't mean to be trite by that. Small 9 differences can have impact. So they would have -- 10 they would have run the experiment. 11 Q. Okay. I'm going to put in front of you a 12 paper that's been marked Exhibit 2105. 13 (Exhibit 2105 marked for 14 identification by the Certified 15 Shorthand Reporter.) 16 BY MR. SCHWARTZ: 17 Q. And it's a paper entitled Isomerization and 18 Cleavage of Allyl Ethers of Carbohydrates By 19 Trans-[Pd(NH3) 2 Cl2] by Bieg and Szeja. That was 20 published in 1985. 21 And please go to the first page of Bieg, page 22 441. And Bieg writes: 23 "Allyl ethers are widely used for 24 the 'temporary' protection of 25 hydroxy groups in carbohydrates.</p>

<p style="text-align: right;">Page 73</p> <p>1 The allyl group is conveniently 2 removed by isomerization and 3 subsequent cleavage of the labile 4 prop-1-enyl group." 5 That's what Bieg writes, correct? 6 A. That's correct, yes. 7 Q. And a POSA reading Bieg understood that the 8 deprotection of allyl ethers occurs in two steps where 9 the first step converts the allyl ether to an enyl ether 10 followed by a second step that converts the enyl ether 11 to the alcohol, correct? 12 A. I don't know if that's correct. These 13 reactions are complex. There are different variants of 14 them. One's called Tsuji-Trost, for example. 15 (Court reporter clarification.) 16 A. Tsuji-Trost. I think T-S-U-G-I [sic] dash 17 T-R-O-A-S-T [sic], I think. 18 If you want to make statements about the 19 mechanism of these reactions, you -- and people do this 20 all the time, and they are in papers where people study 21 the mechanisms, so that is a viable mechanism. It is 22 one of a variety -- one of a couple that are -- that 23 these reactions can precede through. 24 Q. Okay. But just focusing on this paper, this 25 paper specifically teaches that the -- "the allyl group</p>	<p style="text-align: right;">Page 74</p> <p>1 is removed by isomerization of subsequent cleavage of 2 the labile prop-1-enyl group? 3 A. It does say that. 4 Q. Okay. So that in this paper, the authors of 5 this paper teach that the deprotection occurs in two 6 steps, first, conversion to an enyl ether, followed by 7 conversion of the enyl ether to alcohol. That's what 8 they teach in this paper, right? 9 A. That is what it says. 10 Q. And please look down from where we were 11 reading in Bieg to the middle of the first page where 12 there is a sentence that starts with "Prop-1-enyl 13 ethers." Do you see that? 14 A. I do. 15 Q. And Bieg writes: 16 "Prop-1-enyl ethers are readily 17 cleaved under acidic conditions ..." 18 Do you see that? 19 A. I do. 20 Q. And a POSA in 2000 reading Bieg understood 21 that an enyl ether produced under acidic conditions 22 would cleave to produce an alcohol in a carbonyl 23 compound, correct? 24 A. That's a hard question. If there's -- I would 25 have to read this and see exactly what he's talking</p>
<p style="text-align: right;">Page 75</p> <p>1 about, but enyl ethers are stable, in general. In acid 2 they may not -- I mean, they are certainly going to 3 isomerize. I would have to think this mechanism through 4 carefully to make sure that I didn't misspeak. 5 Q. But a person reading this paper -- so my 6 question was, a person reading this paper in 2000 would 7 understand that Bieg is teaching that an enyl ether 8 produced under acidic conditions would cleave to produce 9 an alcohol in a carbonyl compound, correct? 10 A. Where does he say that? I see where he says 11 propine 1 -- prop-1-enyl ether are -- ethers are readily 12 cleaved under acidic conditions, ozonolysis followed by 13 alkaline hydrolysis, reaction with alkaline, 14 permanganate solution, or treatment with chloride ... is 15 that what you're talking about? 16 Q. I'm talking about he says earlier when we read 17 isomerization and subsequent cleavage. So the 18 isomerization would result in the carbonyl, correct? 19 A. No. The isomerization results in the enyl 20 ether, I think. And that then hydrolyzed -- I mean, 21 these mechanisms are complex. I would have to sit down 22 and, you know, draw out exactly what he's thinking about 23 here. 24 I mean, the way it usually happens is a 25 palladium chelates to the double bond of the enyl</p>	<p style="text-align: right;">Page 76</p> <p>1 ether -- of the allyl and then isomerizes to where the 2 palladium is palladium on the internal -- where a water 3 or a nucleophile attacks the least hindered carbon and 4 then you eliminate, and what's that produce? That 5 produces -- can I write that down? 6 Q. Yes. 7 A. Let's see. I don't think it produces a 8 carbonyl group. I might be missing something, but -- 9 despite what he's talking about, just an allyl group 10 deprotection by isomerization and cleavage. I don't 11 think there's a carbonyl group that ever appears there. 12 You're asking me a bit on the spot, and so I 13 hope I'm getting this right, but I think I am. It 14 produces an alcohol. 15 Q. Is a -- 16 MR. SCHWARTZ: Just give me a second here. 17 BY MR. SCHWARTZ: 18 Q. So what happens to enyl ethers in water and 19 acid? 20 A. An enyl ether will -- it will tautomerize to a 21 ketone. It's an enyl ether -- yeah. 22 Q. Okay. I'm going to put another paper in front 23 of you. 24 /// 25 ///</p>

<p style="text-align: right;">Page 77</p> <p>1 (Exhibit 2098 marked for 2 identification by the Certified 3 Shorthand Reporter.) 4 MR. SCHWARTZ: This has been marked as 5 Exhibit 2098. 6 MR. ZIMMERMAN: Marked as what number? 7 MR. SCHWARTZ: 2098. 8 BY MR. SCHWARTZ: 9 Q. And I've just put in front of you a paper 10 entitled Complete Reverse Regioselection in Wacker 11 Oxidation of Acetonides and Cyclic Carbonates of Allylic 12 Diols by Kang, et al., published in 1995. 13 And please refer to footnote 6 on the first 14 page of the paper. And are you looking at footnote 6? 15 A. I am. 16 Q. Looking at the reaction there as drawn. The 17 compound on the left side of the equation in footnote 6 18 where R is OBn or O-MOM is an allyl ether, correct? 19 A. Yeah. It's a substituted allyl ether, yes. 20 Q. The catalyst used in the first reaction in 21 that footnote is palladium chloride, correct? 22 A. Yes. 23 Q. And the solvent used in that first reaction in 24 footnote 6 contains water, correct? 25 A. It is DMF water, yes.</p>	<p style="text-align: right;">Page 78</p> <p>1 Q. And the reaction produced two products, one of 2 which is an alpha alkoxy ketone, correct? 3 A. Alpha alkoxy -- alpha alkoxy, yep. 4 Q. And the other product is a beta alkoxy 5 aldehyde, correct? 6 A. Yep. 7 Q. And so a person of ordinary skill in 2000 8 reading Kang, et al. in 1995, which is Exhibit 2098, 9 understood that when Kang used water and palladium 10 chloride with allyl ethers, they got oxidized products 11 and not enyl ethers or alcohols, correct? 12 MR. ZIMMERMAN: Objection. Mischaracterizes. 13 A. I haven't read this. What you're showing me 14 is a Wack -- I believe is a Wacker oxidation, and you 15 are -- they are showing the production of -- of an alpha 16 ketone and a beta aldehyde. 17 BY MR. SCHWARTZ: 18 Q. But not enyl ethers or alcohols, correct? 19 A. That's right. I mean, this is kind of what I 20 meant where the mechanisms can be complex. This is a 21 different mechanism than -- all palladium mechanisms are 22 not the same. 23 MR. SCHWARTZ: Again, it's being pointed out 24 to me, for the court reporter, that in my question which 25 was: A person of ordinary skill in 2000, it reads 2003.</p>
<p style="text-align: right;">Page 79</p> <p>1 I'm sure I didn't ask you a person of ordinary skill in 2 2003. 3 Do we agree that I meant 2000? It should have 4 said 2000? 5 MR. ZIMMERMAN: Yes. 6 That doesn't change your answer, does it? 7 THE WITNESS: No. 8 BY MR. SCHWARTZ: 9 Q. Okay. I'm putting in front of you a new 10 exhibit. And it's Exhibit 1023, which is a paper 11 entitled Syntheses of Nucleosides Designed for 12 Combinatorial DNA Sequencing by Welch, et al. that was 13 published in 1999. 14 (Exhibit 1023 marked for 15 identification by the Certified 16 Shorthand Reporter.) 17 BY MR. SCHWARTZ: 18 Q. Please turn to page 952. And please draw your 19 attention to the left side of the page and, in 20 particular, to the first full paragraph that starts with 21 "Our group and others." 22 Do you see that? 23 A. I do. 24 Q. And the authors write: 25 "Our group and others have been</p>	<p style="text-align: right;">Page 80</p> <p>1 exploring another way to facilitate 2 parallel analyses of multiple 3 samples in an array without gel 4 electrophoresis." 5 And they refer to references 38 to 43. 6 "We call this the Base Addition 7 Sequencing ... or BASS." 8 That's what the authors write, correct? 9 A. They call it the Base Additional Sequencing 10 Scheme or BASS, yes. 11 Q. And the authors cite to reference 38 to 43 to 12 support their statement, correct? 13 A. In the preceding sentence they cite -- 14 reference 38 to 43, yes. 15 Q. And please turn to the references page. And I 16 just want to confirm with you that reference 38 is the 17 Metzker 1994 paper. 18 A. It appears to be, yes. 19 Q. Okay. Now, please turn to page 956 of the 20 Welch paper. And please draw your attention to the left 21 side of the page where on the top of the page there's a 22 section entitled Conclusions. 23 Do you see that? 24 A. I do. 25 Q. Please draw your attention to line -- to six</p>

<p style="text-align: right;">Page 81</p> <p>1 lines down in the "Conclusions" section where there is a</p> <p>2 sentence that starts with "It seems clear that</p> <p>3 modifications." Do you see that?</p> <p>4 A. I do.</p> <p>5 Q. And the authors write:</p> <p>6 [As read.]</p> <p>7 "It seems clear that</p> <p>8 modifications to the polymerase</p> <p>9 enzyme, as well as to the nucleotide</p> <p>10 [sic] triphosphate are required if</p> <p>11 BASS is to be developed into a</p> <p>12 viable sequencing scheme."</p> <p>13 MR. ZIMMERMAN: Objection. Mischaracterizes</p> <p>14 the document.</p> <p>15 MR. SCHWARTZ: How does it mischaracterize the</p> <p>16 document?</p> <p>17 MR. ZIMMERMAN: You didn't read the sentence</p> <p>18 correctly.</p> <p>19 MR. SCHWARTZ: Let me read it again.</p> <p>20 BY MR. SCHWARTZ:</p> <p>21 Q. "It seems clear that modifications</p> <p>22 to the polymerase enzyme as well as</p> <p>23 to the nucleoside triphosphate are</p> <p>24 required if BASS is to be developed</p> <p>25 into a viable sequencing scheme."</p>	<p style="text-align: right;">Page 82</p> <p>1 Is that correct? That's what the authors,</p> <p>2 write, correct?</p> <p>3 A. That is what the authors write, yes.</p> <p>4 Q. And the BASS sequencing scheme is what was</p> <p>5 later called SBS, correct?</p> <p>6 A. I don't know whether it was also concurrently</p> <p>7 called SBS or not, but it is certainly today, as I</p> <p>8 understand BASS, it is -- I believe that is sequencing</p> <p>9 by synthesis. I mean, it's obviously very early.</p> <p>10 Q. So a person of ordinary skill in October 2000,</p> <p>11 reading the Welch 1999 paper, understood that</p> <p>12 modifications to the polymerase enzyme as well as to the</p> <p>13 nucleoside triphosphate are required if BASS is to be</p> <p>14 developed into a viable sequencing scheme, correct?</p> <p>15 A. That is not how I would read that sentence.</p> <p>16 Nor do I think a person of ordinary skill in the art</p> <p>17 would. Look, this is a conclusion. They're</p> <p>18 speculating. It seems clear as code for hey, maybe.</p> <p>19 Q. It actually directly states what I read,</p> <p>20 though, right?</p> <p>21 A. I'm telling you how a person of ordinary skill</p> <p>22 in the art would have read that. Science is just not</p> <p>23 like law like this. Just every sentence, every word</p> <p>24 doesn't mean some legal thing.</p> <p>25 I'm telling you in the "Conclusions" section,</p>
<p style="text-align: right;">Page 83</p> <p>1 what that sentence reads is they're speculating about</p> <p>2 what future progress would have to be accomplished,</p> <p>3 speculating, to -- to achieve that goal.</p> <p>4 Q. Okay. So -- and you're suggesting that a</p> <p>5 person of ordinary skill in 2000, reading those</p> <p>6 "Conclusions," would speculate that modifications to the</p> <p>7 polymerase enzyme as well as to the nucleoside</p> <p>8 triphosphate are required if BASS is to be developed</p> <p>9 into a viable sequencing scheme. Is that what you're</p> <p>10 saying?</p> <p>11 A. No. I'm saying -- I'm saying this paper is</p> <p>12 speculating about that.</p> <p>13 Q. So when it says "it seems clear that," you're</p> <p>14 saying that a POSA would read that as pure speculation?</p> <p>15 A. I would have to read this whole paper. In a</p> <p>16 conclusion section like this, a statement that --</p> <p>17 that -- I mean, it's such a forward-looking statement</p> <p>18 that -- if you want me to read it more carefully and --</p> <p>19 if this -- if this paper is about polymerase mutants,</p> <p>20 maybe, but it just -- it -- it is much more typical a</p> <p>21 sentence like that in the position that it's located in</p> <p>22 this "Conclusion" is just a forward-looking speculative</p> <p>23 statement.</p> <p>24 Q. But the reader would see that it says "it</p> <p>25 seems clear that," correct? The authors are saying "it</p>	<p style="text-align: right;">Page 84</p> <p>1 seems clear that." That's what they're saying, isn't</p> <p>2 it?</p> <p>3 MR. ZIMMERMAN: Objection. Compound.</p> <p>4 A. No. No, that's not what they're saying. I</p> <p>5 mean, those are the words written there, yes. Those</p> <p>6 words are written there.</p> <p>7 BY MR. SCHWARTZ:</p> <p>8 Q. And those authors wrote those words five years</p> <p>9 after the Metzker 1994 paper was published, correct?</p> <p>10 A. This paper was written in 1999. The Metzker</p> <p>11 paper was -- that you're referring to was written in</p> <p>12 1994.</p> <p>13 Q. Okay. I'm going to put in front of you -- I'm</p> <p>14 just looking at the time. I'm putting in front of you a</p> <p>15 document that carries Exhibit No. 2099.</p> <p>16 (Exhibit 2099 marked for</p> <p>17 identification by the Certified</p> <p>18 Shorthand Reporter.)</p> <p>19 MR. ZIMMERMAN: Have these been previously</p> <p>20 marked? Because, again, my copy isn't marked.</p> <p>21 MR. SCHWARTZ: We just marked one copy.</p> <p>22 MR. ZIMMERMAN: Okay.</p> <p>23 BY MR. SCHWARTZ:</p> <p>24 Q. I'm putting in front of you U.S. Patent</p> <p>25 No. 5,858,671 to Jones. Please turn to Column 2.</p>

<p style="text-align: right;">Page 85</p> <p>1 A. Have I read this? Have I seen this before?</p> <p>2 Q. Have you?</p> <p>3 A. I don't recall seeing this before.</p> <p>4 Q. Okay.</p> <p>5 A. Have I testified from this? Have I cited this</p> <p>6 in any of my writings?</p> <p>7 Q. I'm really not here to be asked questions, so</p> <p>8 you have to -- these are things that you need to be</p> <p>9 thinking about.</p> <p>10 MR. ZIMMERMAN: If it's not something you've</p> <p>11 seen, take as much time as you need to review it.</p> <p>12 THE WITNESS: Yeah. Thanks.</p> <p>13 BY MR. SCHWARTZ:</p> <p>14 Q. Please turn to Column 2. And please look at</p> <p>15 line 21 where there is a paragraph that starts with "The</p> <p>16 base addition DNA sequencing scheme." Do you see that?</p> <p>17 A. I do.</p> <p>18 Q. And Jones writes:</p> <p>19 "The base addition DNA sequencing</p> <p>20 scheme uses fluorescently labeled</p> <p>21 reversible terminators of polymerase</p> <p>22 extension, with a distinct and</p> <p>23 removable fluorescent label for each</p> <p>24 of the four ... analogs."</p> <p>25 And there's a citation to Metzker 1994.</p>	<p style="text-align: right;">Page 86</p> <p>1 Correct?</p> <p>2 MR. ZIMMERMAN: Objection. Mischaracterizes</p> <p>3 the document.</p> <p>4 MR. SCHWARTZ: You left out the word</p> <p>5 "nucleotide" in front of "analog."</p> <p>6 BY MR. SCHWARTZ:</p> <p>7 Q. Okay. With the word "nucleotide" in front of</p> <p>8 the word "analog," that's what Jones writes, and he</p> <p>9 refers to Metzker, et al. 1994, correct?</p> <p>10 A. That seems to be what's written.</p> <p>11 Q. And the Metzker, et al. 1994 paper cited by</p> <p>12 Jones is the same Metzker 1994 paper that's in your</p> <p>13 declaration, correct?</p> <p>14 A. It would seem to be.</p> <p>15 Q. And please look down a few lines to line 37.</p> <p>16 There's a sentence that starts with "A fundamental." Do</p> <p>17 you see that?</p> <p>18 A. I do.</p> <p>19 Q. And Jones writes:</p> <p>20 "A fundamental limitation to this</p> <p>21 approach is inherent in iterative</p> <p>22 methods that sequence consecutive</p> <p>23 nucleotides. That is, in order to</p> <p>24 sequence more than a handful of</p> <p>25 nucleotides, each cycle of analog</p>
<p style="text-align: right;">Page 87</p> <p>1 incorporation and deprotection must</p> <p>2 approach 100 percent efficiency.</p> <p>3 Even if the base addition sequencing</p> <p>4 scheme is refined so that each cycle</p> <p>5 occurs at 95 percent efficiency, one</p> <p>6 will have less than 75 percent of</p> <p>7 the product of interest after only</p> <p>8 six cycles ($0.956 = 0.735$). This</p> <p>9 will severely limit the ability of</p> <p>10 this method to sequence anything but</p> <p>11 very short DNA sequences. Only one</p> <p>12 cycle of template-directed analog</p> <p>13 incorporation and deprotection</p> <p>14 appears to have been demonstrated so</p> <p>15 far."</p> <p>16 And there is a citation to Metzker 1994.</p> <p>17 Do you see that?</p> <p>18 A. I do.</p> <p>19 Q. And again, the Metzker 1994 paper cited by</p> <p>20 Jones is the same to Metzker 1994 paper as in your</p> <p>21 declaration, correct?</p> <p>22 A. It seems to be.</p> <p>23 Q. And the approach that Jones is referring to</p> <p>24 when he states that there is a fundamental limitation to</p> <p>25 this approach, that's SBS he's referring to, correct?</p>	<p style="text-align: right;">Page 88</p> <p>1 A. It would seem to be. I -- I don't recall</p> <p>2 reading this document, so I'm not 100 percent certain,</p> <p>3 but it would seem to be. He opens the paragraph by</p> <p>4 saying "The base addition DNA sequencing scheme." That</p> <p>5 sounds like sequencing by synthesis.</p> <p>6 Q. So a POSA in 2000 reading Jones understood</p> <p>7 that, as Jones teaches, "In order to sequence more than</p> <p>8 a handful of nucleotides using the SBS method, each</p> <p>9 cycle of analog incorporation and deprotection must</p> <p>10 approach 100 percent efficiency," correct?</p> <p>11 A. Sequence more than a handful, is that what you</p> <p>12 said?</p> <p>13 Q. In order -- I'm just reading from what Jones</p> <p>14 is saying. So a person of ordinary skill reading Jones</p> <p>15 in October of 2000 understood that in order to sequence</p> <p>16 more than a handful of nucleotides using the SBS</p> <p>17 method --</p> <p>18 A. That is what Jones writes. That is what's</p> <p>19 written there.</p> <p>20 Q. And a POSA in 2000 reading Jones understood</p> <p>21 that if each cycle of SBS occurs at 95 percent</p> <p>22 efficiency, one will have less than 75 percent of the</p> <p>23 product of interest after only six cycles, correct?</p> <p>24 A. That is what is written, and I believe that is</p> <p>25 correct.</p>

<p align="right">Page 89</p> <p>1 Q. And Jones writes that that "will severely 2 limit the ability of this method to sequence anything 3 but very short DNA sequences." A POSA understood that 4 from reading Jones as well, correct? 5 A. That is certainly what is written. 6 Q. And if you'd turn to the front page of the 7 Jones patent and you look at the top right corner where 8 there's a date of patent, the patent issued in 9 January 1999, correct? 10 A. That is correct. 11 Q. And so a POSA in 2000 reading Jones understood 12 that at least as of January 1999, when Jones issued as a 13 patent, there had been only one cycle of 14 template-directed analog incorporation and deprotection 15 actually demonstrated for SBS, correct? 16 MR. ZIMMERMAN: Objection. Mischaracterizes. 17 A. I think they would have read that Jones says 18 something like there appears to have been. 19 BY MR. SCHWARTZ: 20 Q. And as support for that statement, Jones 21 refers to the Metzker 1994 paper, correct? 22 A. Again, I don't recall reading this, but he 23 must be referring -- that must be what he's referring to 24 as the demonstration of a single nucleotide 25 incorporation.</p>	<p align="right">Page 90</p> <p>1 Q. And the demonstration of a single nucleotide 2 incorporation in Metzker 1994 was for the two 3 nitrobenzyl capped nucleotide, correct? 4 A. Again, I don't know for sure that that's what 5 he's referring to here, but that is -- if he's referring 6 to Metzker for the demonstration of a single nucleotide 7 incorporation, then that I believe would be referring to 8 the nitrobenzyl case. 9 Q. Metzker 1994 did not demonstrate one cycle of 10 template-directed analog incorporation and deprotection 11 using an allyl capped nucleotide, correct? 12 A. That is correct. 13 Q. And Jones did not say anything, when he refers 14 to the Metzker 1994 paper, he didn't say anything about 15 Metzker's experiments being tainted by the presence of a 16 small amount of contaminating dATP, correct? 17 A. I haven't -- don't recall reading his patent, 18 so I can't -- 19 Q. In the portion we read. 20 A. In the portion -- 21 Q. Is it fair to say in the portion we read he 22 doesn't say anything about the Metzker 1994 experiments 23 being tainted by the presence of a small amount of 24 contaminating dATP? 25 A. In the portion we read, I did not see that.</p>
<p align="right">Page 91</p> <p>1 Q. And there's no indication on the face of the 2 Jones patent that Jones had any affiliation with 3 Michael Metzker or the Metzker lab, correct? 4 A. I have no idea. 5 Q. I'm just saying on the face of the patent. 6 A. Do you want me to read the entire front page? 7 Q. Well, just -- you can read the title, the 8 inventor, and the assignee. Do you see anything in 9 there that suggests that there's any relationship to 10 Michael Metzker or his lab? 11 A. Not that I see. 12 Q. Okay. 13 MR. ZIMMERMAN: Is now a good time for a 14 break? We've been going about an hour. 15 MR. SCHWARTZ: Sure. 16 THE VIDEOGRAPHER: Going off the record at 17 2:56 p.m. 18 (Recess taken from 2:56 p.m. to 19 3:17 p.m.) 20 THE VIDEOGRAPHER: We are back on the record 21 at 3:17 p.m. 22 BY MR. SCHWARTZ: 23 Q. And, Dr. Romesberg, thank you very much for 24 the cup of coffee. 25 Did you speak to your attorneys during your</p>	<p align="right">Page 92</p> <p>1 break about anything relating to this deposition? 2 A. No. 3 Q. I'm going to put a new document in front of 4 you. It's going to be marked as a new exhibit, 2100. 5 (Exhibit 2100 marked for 6 identification by the Certified 7 Shorthand Reporter.) 8 BY MR. SCHWARTZ: 9 Q. I just put in front of you U.S. Patent No. 10 6,013,445, to Albrecht, et al. And please turn to 11 Column 1. And please look at line 40. 12 Do you see there's a sentence that starts with 13 "As an alternative to the Sanger-based approaches"? Do 14 you see that, where it starts? 15 A. Sorry. Column 1? 16 Q. Column 1, around line 40. Do you see where it 17 starts out -- 18 A. Yes. 19 Q. -- "As an alternative"? 20 Albrecht writes: 21 "As an alternative to the 22 Sanger-based approaches to DNA 23 sequencing, several so-called 24 'base-by-base' or 'single base' 25 sequencing approaches have been</p>

<p style="text-align: right;">Page 93</p> <p>1 explored ..."</p> <p>2 And if you follow that sentence down a few</p> <p>3 lines, there's a citation to Metzker, et al. 1994.</p> <p>4 Do you see that?</p> <p>5 A. I do.</p> <p>6 Q. And the Metzker, et al. 1994 paper cited by</p> <p>7 Albrecht here is the same Metzker 1994 paper that is in</p> <p>8 your declaration, correct?</p> <p>9 A. It is Metzker 1994. I -- I don't have a</p> <p>10 reference list with any more information. I don't know</p> <p>11 of any other paper he published, so it would seem to be,</p> <p>12 yeah.</p> <p>13 Q. Please go to line 57 of Column 1. And there's</p> <p>14 a paragraph that begins with "unfortunately."</p> <p>15 Do you see that?</p> <p>16 A. I do.</p> <p>17 Q. Albrecht writes:</p> <p>18 "Unfortunately, 'base-by-base'</p> <p>19 sequencing schemes have not had</p> <p>20 widespread application because of</p> <p>21 numerous problems, such as</p> <p>22 inefficient chemistries which</p> <p>23 prevent determination of any more</p> <p>24 than a few nucleotides in a complete</p> <p>25 sequencing operation."</p>	<p style="text-align: right;">Page 94</p> <p>1 That's what's written in Albrecht, right?</p> <p>2 A. That is correct.</p> <p>3 Q. And again, another name for the base-by-base</p> <p>4 sequencing scheme referred to by Albrecht would be SBS,</p> <p>5 correct?</p> <p>6 A. I suspect so. I don't see a definition</p> <p>7 exactly, but it probably is. My -- I would guess that</p> <p>8 it is.</p> <p>9 Q. Okay. And if you'd turn to the front page of</p> <p>10 Albrecht and you look at the top right corner, there's</p> <p>11 an issue date of the patent of January 11th, 2000.</p> <p>12 Do you see that?</p> <p>13 A. I do.</p> <p>14 Q. So a POSA in 2000 reading Albrecht understood</p> <p>15 that, at least as of January 2000 when the Albrecht</p> <p>16 patent issued, SBS has problems such as inefficient</p> <p>17 chemistries which prevent determination of any more than</p> <p>18 a few nucleotides in a complete sequencing operation,</p> <p>19 correct?</p> <p>20 A. That is what this patent reads.</p> <p>21 Q. And one of the papers that Albrecht cites in</p> <p>22 reaching that conclusion is Metzker 1994, correct?</p> <p>23 A. I'd have to reexamine that. He -- he doesn't</p> <p>24 seem to cite Metzker on the spot where he says</p> <p>25 "Unfortunately, base-by-base sequencing schemes have not</p>
<p style="text-align: right;">Page 95</p> <p>1 received widespread application." That part that I</p> <p>2 think you're referring to, he doesn't cite Metzker</p> <p>3 there. He cites it above where he's just introducing</p> <p>4 so-called base-by-base or single base sequencing</p> <p>5 approaches have been explored. And then he lists</p> <p>6 several of which we're pretty all familiar with,</p> <p>7 including Tsien and Metzker.</p> <p>8 Q. Right.</p> <p>9 And then he goes on to say, talking still</p> <p>10 about base-by-base sequencing schemes, and the reference</p> <p>11 is that he relies on for base-by-base sequencing schemes</p> <p>12 are above, and that includes Metzker, correct?</p> <p>13 A. It -- Metzker is included in the group of</p> <p>14 citations that are general to the base-by-base. The --</p> <p>15 "unfortunately, the base-by-base sequencing schemes have</p> <p>16 not received widespread application" is a bit narrower</p> <p>17 of a statement. He doesn't provide any other reference.</p> <p>18 So the only thing -- the only references that</p> <p>19 anyone would have up to this point for sequencing by</p> <p>20 synthesis were the ones at the introductory level.</p> <p>21 Q. Okay. Please go back to Column 1, and just</p> <p>22 after the portion of the spec that we just read at</p> <p>23 line 61, there's a sentence that begins with "Moreover,</p> <p>24 in base-by-base." Do you see that?</p> <p>25 A. I do.</p>	<p style="text-align: right;">Page 96</p> <p>1 Q. Albrecht writes:</p> <p>2 "Moreover, in base-by-base</p> <p>3 approaches that requires enzymatic</p> <p>4 manipulations, further problems</p> <p>5 arise with instrumentation used for</p> <p>6 automated processing."</p> <p>7 And I'm going to ask you to skip to Column 2</p> <p>8 at line 1. And in the first full sentence on line 1</p> <p>9 Albrecht writes:</p> <p>10 "The accumulation of protein" -- excuse me.</p> <p>11 [As read.]</p> <p>12 "The accumulation of protein also</p> <p>13 affects molecular reporter systems,</p> <p>14 particularly those employing</p> <p>15 fluorescent labels, and renders the</p> <p>16 interpretation of measurements based</p> <p>17 on such systems difficult and</p> <p>18 inconvenient. These and other [sic]</p> <p>19 difficulties have significantly</p> <p>20 slowed the application of</p> <p>21 'base-by-base' sequencing schemes to</p> <p>22 parallel sequencing efforts."</p> <p>23 And it's been pointed out to me that I should</p> <p>24 have said:</p> <p>25 "These and similar difficulties</p>

<p align="right">Page 97</p> <p>1 have significantly slowed the</p> <p>2 application of 'base-by-base'</p> <p>3 sequencing schemes to parallel</p> <p>4 sequencing efforts."</p> <p>5 A. That's what it says.</p> <p>6 Q. And so a POSA in 2000, reading the portions of</p> <p>7 the Albrecht patent specification that we just looked</p> <p>8 at, understood that in addition to inefficient</p> <p>9 chemistries which prevent determination of any more than</p> <p>10 a few nucleotides in a complete sequencing operation,</p> <p>11 there were additional technical hurdles to successfully</p> <p>12 practice SBS that had yet to be solved as of</p> <p>13 January 2000 when the Albrecht patent issued, correct?</p> <p>14 A. That is what it says.</p> <p>15 Q. And of these technical issues that Albrecht</p> <p>16 teaches was yet to be solved as of January 2000 is the</p> <p>17 accumulation of protein, which renders interpretation of</p> <p>18 the SBS output difficult, particularly when the</p> <p>19 nucleotides have fluorescent labels.</p> <p>20 That's what he teaches, correct?</p> <p>21 A. That is what's written.</p> <p>22 Q. And if you would go back to the '985 patent,</p> <p>23 the patent at issue in this case, it was marked as</p> <p>24 Exhibit 1075. You may not need to look at it. If</p> <p>25 you -- I'm just going to ask you that the SBS method</p>	<p align="right">Page 98</p> <p>1 claimed in the '985 patent uses nucleotides with</p> <p>2 fluorescent labels, correct?</p> <p>3 A. Yes.</p> <p>4 MR. SCHWARTZ: I'm going to mark another</p> <p>5 exhibit. This is being marked as Exhibit 2103.</p> <p>6 (Exhibit 2103 marked for</p> <p>7 identification by the Certified</p> <p>8 Shorthand Reporter.)</p> <p>9 BY MR. SCHWARTZ:</p> <p>10 Q. I'm putting in front of you -- excuse me for a</p> <p>11 second. I'm putting in front of you a document entitled</p> <p>12 Project Information 1R21HG003977-01.</p> <p>13 Exhibit 2103 relates to a grant proposal you</p> <p>14 submitted to the National Human Genome Research</p> <p>15 Institute that was awarded to you in 2006, correct?</p> <p>16 A. Ah, yeah, I think so.</p> <p>17 Q. And if you look at the top left of</p> <p>18 Exhibit 2103, it indicates that the title of your grant</p> <p>19 is Evolving Novel Polymerases for Genome Sequencing; is</p> <p>20 that correct?</p> <p>21 A. Yes, that is correct.</p> <p>22 Q. That's what it says?</p> <p>23 A. Just to be clear, I'm not sure that this grant</p> <p>24 was funded. I don't remember. Are you saying that it</p> <p>25 was? In fact, I think it was not.</p>
<p align="right">Page 99</p> <p>1 Q. It says that the award notice date was the</p> <p>2 18th of May 2006. So you received an award notice?</p> <p>3 A. I think this was not funded. Special Emphasis</p> <p>4 Panel. Yeah, I'm virtually certain this was not funded.</p> <p>5 Yeah, an award notice, I think, is just a generic name.</p> <p>6 I'm not sure, but I guess I should -- it might have been</p> <p>7 funded. To be honest, I'm not sure.</p> <p>8 I certainly wrote this grant.</p> <p>9 Q. Okay. It does state that it was -- you</p> <p>10 received an award notice on 18th of May 2006, and it</p> <p>11 gives a project start and end date, correct?</p> <p>12 A. Yeah, I think -- I think this must have been</p> <p>13 funded.</p> <p>14 Q. Okay. I'm going to mark another exhibit.</p> <p>15 (Exhibit 2104 marked for</p> <p>16 identification by the Certified</p> <p>17 Shorthand Reporter.)</p> <p>18 BY MR. SCHWARTZ:</p> <p>19 Q. This exhibit is going to carry the number</p> <p>20 2104.</p> <p>21 A. Yeah, I think it must have been not funded and</p> <p>22 then funded, because it gives a project history.</p> <p>23 Q. So it's your recollection that this project</p> <p>24 information sheet refers to a funded project?</p> <p>25 A. I'm not 100 percent certain, but I think so.</p>	<p align="right">Page 100</p> <p>1 I apologize. I've had a lot of grants come and go.</p> <p>2 Q. Me too.</p> <p>3 So I just put in front of you Exhibit 2104 --</p> <p>4 oh, I'm putting in front of you another exhibit.</p> <p>5 Did I give it to you? I'm sorry. You've got</p> <p>6 me confused now about where we were. Exhibit 2104, and</p> <p>7 that's a document entitled Helicos and Columbia to Test</p> <p>8 Scripps' Improved Polymerases for Next Generation</p> <p>9 Sequencing. And it was published in Genome Web News on</p> <p>10 October 3rd, 2006.</p> <p>11 And you're the same Floyd Romesberg as is</p> <p>12 being quoted in Exhibit 2104, correct?</p> <p>13 A. Yeah. I -- I do not recall this at all, but,</p> <p>14 yeah, this would appear to be me.</p> <p>15 Q. And please go to the second-to-last paragraph</p> <p>16 on the first page that begins with "Romesberg, this</p> <p>17 spring." Do you see that?</p> <p>18 A. I do.</p> <p>19 Q. And it says -- the article reads:</p> <p>20 "Romesberg, this spring, won a</p> <p>21 two-year grant from the National</p> <p>22 Human Genome Research Institute</p> <p>23 entitled 'Evolving Novel Polymerases</p> <p>24 for Genome Sequencing,' he will work</p> <p>25 with Helicos, Ju's group, and</p>

<p align="right">Page 101</p> <p>1 Scripps' sequencing facility to test 2 polymerases with novel properties in 3 actual sequencing settings." 4 And again, you're the Romesberg that's being 5 referred to in this exhibit, correct? 6 A. Yeah, that's right. 7 Q. And does this refresh your recollection that 8 that patent was funded? 9 A. That -- the proposal, yeah. 10 Q. Okay. 11 A. It wasn't -- 12 Q. It -- I'm sorry. Strike that. 13 Does that refresh your recollection that that 14 proposal was funded -- was a funded patent -- funded 15 grant? 16 A. Well, it doesn't so much spark my recollection 17 as tell me that it was. 18 Q. And the grant that is being referred to in 19 Exhibit 2104 is the same one that was -- the same grant 20 as in Exhibit 2103, correct? 21 A. I believe that is the case, yes. 22 Q. And Dr. Ju was a collaborator with you on that 23 grant, correct? 24 A. Yes, I believe that's correct. That was a 25 long time ago. And I only vaguely remember that. But</p>	<p align="right">Page 102</p> <p>1 yeah, I think that -- I think that -- I think that he 2 wanted -- I think we -- we spoke briefly at a meeting, 3 and he was going to supply us with O-allyl nucleotides, 4 I think. And he never did. I think we never actually 5 ran those experiments. 6 Q. And the grant relates to SBS, correct? 7 A. Yep. Yes. 8 Q. And continuing in the Genome Web news article 9 where we left off in the article, it reads: 10 "It's no secret that nucleotides 11 labeled with a fluorescent dye are 12 poor substrates for natural 13 polymerases." 14 So when the Genome Web News article was 15 written, it was understood that nucleotides labeled with 16 a fluorescent dye are poor substrates for natural 17 polymerases, correct? 18 A. I'm not sure I'd take Genome Web to be a 19 definitive source of science. I don't even remember 20 this article. I have -- don't -- I don't know who wrote 21 this. I don't know. 22 Again, this is not so different than a lot of 23 other things we've talked about. There's no doubt that 24 fluorescent labeling -- nucleoside triphosphates with 25 linkers that attach fluorophores tend to reduce their</p>
<p align="right">Page 103</p> <p>1 recognition by polymerases. So certainly what they are 2 saying is not far off. 3 Q. Okay. And they say that "nucleotides labeled 4 with a fluorescent dye are poor substrates for natural 5 polymerases." That's what they say, right? 6 A. That is what it says. 7 Q. So please go back to Exhibit 2103, which is 8 the Project Information sheet. And please draw your 9 attention to the section entitled Abstract Text. The 10 abstract starts with a description and it says that it 11 is "provided by the applicant." Do you see that? 12 A. I do. 13 Q. That means that you wrote the text that is in 14 the description of this exhibit, right? 15 A. I did. 16 Q. And the description reads: 17 "There is great incentive for 18 developing low cost technologies for 19 sequencing genomes. While 20 significant advances have been made 21 in conventional sequencing methods, 22 the reductions in cost and time 23 required to make genome sequencing 24 more feasible require the 25 development of new methodologies.</p>	<p align="right">Page 104</p> <p>1 Indeed, many new and promising 2 methods are under development. 3 However, these new approaches are 4 generally limited by the inability 5 of DNA polymerases to synthesize DNA 6 with modified deoxynucleotide 7 triphosphate (dNTPs)." 8 That's what you wrote, correct? 9 A. That is correct. 10 Q. And when you refer to "new approaches," you're 11 including in those approaches SBS, correct? 12 A. Yes. 13 Q. And so it was your opinion in the 2005 -- 2000 14 time -- 2005-2006 time frame, when you submitted this 15 grant proposal, that new approaches, including those 16 of -- including SBS "are generally limited by the 17 inability of DNA polymerases to synthesize DNA with 18 modified deoxynucleotide triphosphates," correct? 19 A. That is what is written, but I mean -- but I 20 guess I would ask you to clarify what you think I meant 21 by "limited." 22 Q. Again, Dr. Romesberg, respectfully, I can't 23 testify. But those are -- 24 A. Sure. 25 Q. -- your words.</p>

<p style="text-align: right;">Page 105</p> <p>1 A. Just to clarify, "limited" means would be 2 improved by optimizing. 3 Q. So there were improvements that needed to be 4 made in methods, including SBS, as of the 2005-2006 time 5 frame when you used modified deoxynucleotide 6 triphosphates? 7 A. Yeah. And so I was specifically 8 collaborate -- trying to collaborate with industry, 9 because I wanted to be -- to be involved in a polymerase 10 that could help commercialize these ideas. So I wasn't 11 interested in -- in -- in reactions or people showing 12 sequencing of 10 or 20 or whatever nucleotide sequences 13 people could do. 14 I -- I -- by, I think 2005 it was beginning to 15 come clear -- become clear that people were going to do 16 things like human genomes, and that's why I actually am 17 talking about genome sequencing. And so that was still 18 challenging then and that sort of like big scale 19 commercialization. And certainly anything that 20 optimized polymerase recognition, polymerase 21 selectivity, the triphosphates, all of it, you know, all 22 hands on board, anything that makes things better. 23 Q. Okay. But these new approaches, which include 24 SBS, are generally limited by the inability of the 25 polymerases to synthesize DNA with modified dNTPs;</p>	<p style="text-align: right;">Page 106</p> <p>1 that's what you wrote? 2 A. "Limited" meaning that -- that they needed -- 3 that I was -- that I was asking the NIH to fund me to 4 optimize that. 5 Q. And would you agree that if you understood in 6 the 2005-2006 time frame that new approaches, including 7 SBS, are generally limited by the inability of DNA 8 polymerases to synthesize DNA with modified dNTPs, that 9 that was also true in 2000? 10 A. Again, it depends on how you define "limited." 11 I mean, for example, Metzker showed with two analogs in 12 principle that you could. No one had -- no one had 13 sequenced a human genome -- well, no one had sequenced a 14 human genome with the cost that people would soon be 15 able to. So people weren't sequencing like they were 16 today. So it hadn't sort of been commercialized or to 17 that point where it had become this notion that you 18 could get a genome for a grand, which the NIH had 19 already announced. 20 So that was kind of like the big incentive. 21 In fact, that was one of the big incentives of going to 22 the NIH, because the NIH had announced this program 23 because people around this time knew you could sequence. 24 But what the NIH wanted to do was to do -- to reduce the 25 cost. So when you think -- say things like "limited by"</p>
<p style="text-align: right;">Page 107</p> <p>1 whatever, a part of that is that you want to reduce 2 costs to the point to make progress towards that \$1,000 3 genome, because that's what the NIH was going to fund. 4 So any application to the NIH was going to try to 5 reflect. 6 Q. These are your words, though, right? 7 A. And I was -- and that's what I was trying to 8 do. 9 Q. Okay. So it was your -- in your words, these 10 new approaches, which included SBS, were generally 11 limited by the inability of DNA polymerases to 12 synthesize DNA with modified deoxynucleotide 13 triphosphates. Those are your words, correct? 14 MR. ZIMMERMAN: Objection. Asked and 15 answered, literally four times now. 16 A. They were my words. And since they were my 17 words, I can -- I can tell you what I meant by 18 "limited." I was talking about reducing the cost, 19 increasing the efficiency, making progress towards, 20 frankly, what Illumina eventually did. 21 BY MR. SCHWARTZ: 22 Q. Okay. And let's -- why don't we look down a 23 little bit further in the "Abstract Text" section and 24 look down at Specific Aim 2. Do you see Specific Aim 2? 25 A. I do.</p>	<p style="text-align: right;">Page 108</p> <p>1 Q. And Specific Aim 2 reads: 2 "Evolve polymerases that 3 efficiently incorporate reversibly 4 fluorophore tagged dNTPs with 5 3'-O-allyl protecting groups and 6 then continue synthesis after double 7 deprotection." 8 That's what you wrote, correct? 9 A. Yep, that is correct. 10 Q. So one of the goals of your grant proposal 11 that was submitted in the 2005-2006 time frame, as 12 funded in 2006, was to "evolve polymerases that 13 efficiently incorporate reversibly fluorophore tagged 14 dNTPs with 3'-O-allyl protecting groups," correct? 15 A. That is what I wrote. 16 Q. That was one of your Specific Aims, right? 17 A. That is listed under Specific Aim 2, yes. 18 Q. And that was -- so that was one of the goals 19 of the grant at that time? 20 A. That is listed as Specific Aim 2, yes. 21 Q. And the Specific Aim represents a goal of the 22 grant, right? 23 A. Yes. 24 Q. So if, as you contend in your declaration, in 25 IPR2018-00797, which is the declaration in this case,</p>

<p align="right">Page 109</p> <p>1 that a POSA would have been motivated by Metzker in 1994</p> <p>2 to use the 3'-O-allyl capped nucleotide for SBS because</p> <p>3 it was efficiently incorporated by Vent (exo-) DNA</p> <p>4 polymerase, then why are you asking the National Human</p> <p>5 Genome Research Institute in the 2005-2000 time -- 2006</p> <p>6 time frame to give you research money to discover new</p> <p>7 polymerases that will efficiently incorporate</p> <p>8 fluorophore tagged 3'-O-allyl protected nucleotides by a</p> <p>9 polymerase?</p> <p>10 A. Several reasons. One, "efficient" is a</p> <p>11 relative term. And so the question is efficiency</p> <p>12 relative to what. In my dec that we're discussing now,</p> <p>13 if I used the word "efficient," I don't remember using</p> <p>14 it, but I might have, and if you say I did, I believe</p> <p>15 you, but I can tell that you that what it would have</p> <p>16 been about, the subject matter of the declaration was</p> <p>17 sequencing by synthesis. So it would have been relative</p> <p>18 to that required for sequencing by synthesis.</p> <p>19 And in my estimation, what Metzker</p> <p>20 demonstrated was enough to give a POSA optimism,</p> <p>21 expectation of success that the O-allyl protected group</p> <p>22 would have been accepted. The modified analog with an</p> <p>23 O-allyl protecting group would have been accepted</p> <p>24 sufficiently for sequencing by synthesis.</p> <p>25 That is not to say that they accepted as well</p>	<p align="right">Page 110</p> <p>1 as a natural triphosphate. That is certainly true. And</p> <p>2 that was very much the goal in the grant I wrote.</p> <p>3 Because I wanted to help of all polymerases that would</p> <p>4 synthesize genomes and have relengths of just -- they --</p> <p>5 they would synthesize DNA as efficiently with the</p> <p>6 modified analogs as they did with unmodified of the sort</p> <p>7 that pyroseq- -- that only pyrosequencing could do.</p> <p>8 So I was not -- when I say "efficiently" here,</p> <p>9 I don't mean to say that they -- that -- that there was</p> <p>10 anything that wasn't efficient enough for some</p> <p>11 application already. I just believed, and I still</p> <p>12 believe, that the -- the proposal was meritorious. And</p> <p>13 we're still sort of working on this to make polymerases</p> <p>14 better for different things because your applications</p> <p>15 change. What you want to use them for changes.</p> <p>16 And so now what people want isn't sequencing</p> <p>17 30 nucleotides. It isn't sequencing 35 nucleotides.</p> <p>18 It's getting increasing long read lengths that will</p> <p>19 continue to drive down costs of sequencing. And they</p> <p>20 want to continue to get analogs that are cheaper and</p> <p>21 more affordable and brighter. And there's all sorts of</p> <p>22 applications that are still optimization, that are still</p> <p>23 increasing the efficiency of different recognitions.</p> <p>24 Has that clarified it?</p> <p>25 Q. Dr. Romesberg, if you believed in 2005 and</p>
<p align="right">Page 111</p> <p>1 2006 that the 3'-O-allyl capped nucleotide was</p> <p>2 efficiently incorporated, as taught by Metzker, then why</p> <p>3 are you asking the NIH in one of your goals of your</p> <p>4 grant to give you money to find an enzyme that</p> <p>5 efficiently incorporates exactly that capped nucleotide?</p> <p>6 MR. ZIMMERMAN: He just answered that very</p> <p>7 question. Objection. Asked and answered.</p> <p>8 BY MR. SCHWARTZ:</p> <p>9 Q. All right.</p> <p>10 A. I will try to answer it again if you want me</p> <p>11 to.</p> <p>12 MR. SCHWARTZ: Well, first off, I don't</p> <p>13 like -- I don't appreciate the coaching. So you've been</p> <p>14 coaching for a while now, and I'm going to ask you to</p> <p>15 stop coaching. You can object.</p> <p>16 MR. ZIMMERMAN: Objection. Asked and</p> <p>17 answered, because you're repeating the same question</p> <p>18 over and over to him.</p> <p>19 MR. SCHWARTZ: Dr. Romesberg isn't answering</p> <p>20 my question.</p> <p>21 MR. ZIMMERMAN: So you admit that you're</p> <p>22 asking the same question again --</p> <p>23 MR. SCHWARTZ: No.</p> <p>24 MR. ZIMMERMAN: -- and he's answered it.</p> <p>25 You can go ahead and answer his question,</p>	<p align="right">Page 112</p> <p>1 again.</p> <p>2 A. I will try to answer this question.</p> <p>3 "Efficiency" is a relative term. If you're</p> <p>4 asking were the 3' O-allyl protecting -- were</p> <p>5 nucleotides with 3' O-allyl protecting groups accepted</p> <p>6 by polymerases efficiently enough for them to perform</p> <p>7 any application that people would have wanted to use</p> <p>8 them for, and the answer is no. And that's what I was</p> <p>9 asking for funding to help do.</p> <p>10 For example, we were evolving them in a</p> <p>11 thermostable polymerase so that you would have been able</p> <p>12 to heat cycle it, and there's certain advantages that</p> <p>13 might have come with that. And so there's all sorts of</p> <p>14 applications that people might want to rec- -- be able</p> <p>15 to recognize these analogs to perform, to partici- -- to</p> <p>16 help with.</p> <p>17 As a -- as a basic sequencing by synthesis</p> <p>18 platform, O-allyls had been demonstrated to be</p> <p>19 recognized by polymerases reasonably well. And so I --</p> <p>20 I wasn't saying that they weren't recognized by</p> <p>21 polymerases at all and that you can't perform any</p> <p>22 sequencing by synthesis. I was talking about pushing</p> <p>23 forward and participating in what was coming, genome</p> <p>24 sequencing, the ability to sequence genomes for a</p> <p>25 thousand dollars, which I actually think this grant was</p>

<p style="text-align: right;">Page 113</p> <p>1 in response to, the call for the 1K genome.</p> <p>2 And that may not be true, but it was around</p> <p>3 the same time. And like I said, this was 12 years ago,</p> <p>4 but I think that's actually true. It was in response to</p> <p>5 the 1K genome or shortly thereafter.</p> <p>6 So that kind of goal -- let me be clear about</p> <p>7 that. O-allyls were not recognized well enough for that</p> <p>8 goal. But that goal was unimaginable in 2000. No one</p> <p>9 knew what was coming.</p> <p>10 Q. You're not denying that you told the NI -- the</p> <p>11 granting agency in Specific Aim 2 that you wanted to</p> <p>12 "evolve polymerases that efficiently incorporate</p> <p>13 reversibly fluorophore tagged dNTPs with 3'-O-allyl</p> <p>14 protecting groups? You're not denying that, are you?</p> <p>15 A. It is --</p> <p>16 MR. ZIMMERMAN: Objection. Asked and</p> <p>17 answered.</p> <p>18 A. It is written there.</p> <p>19 BY MR. SCHWARTZ:</p> <p>20 Q. Okay. You can put that away.</p> <p>21 I'm going to put the -- I'm going to ask you</p> <p>22 to look at the '985 patent. That's Exhibit 1075. And</p> <p>23 please go to the claims, which start at Column 34. And</p> <p>24 I want to focus on the Y element in Claim 1. So please</p> <p>25 turn to column -- you can keep your finger on the claim,</p>	<p style="text-align: right;">Page 114</p> <p>1 but please turn to Column 36. Are we -- 36 is the</p> <p>2 claim. Please turn to 36, Column 36 in the claim. At</p> <p>3 line 6 the claim reads:</p> <p>4 "... wherein in Y represents a chemically</p> <p>5 cleavable, chemical linker ..." Do you see that?</p> <p>6 A. I do.</p> <p>7 Q. And I asked you for your understanding of what</p> <p>8 Y meant in your deposition on September 19th, and it was</p> <p>9 your -- your testimony that Y represented a cleavable --</p> <p>10 part of a cleavable label, a link or part of a label</p> <p>11 that would attach what he calls the tag.</p> <p>12 Do you remember that testimony?</p> <p>13 A. No. That sounds correct, but I do not</p> <p>14 explicitly remember it.</p> <p>15 Q. Well, let's -- we'll look at it, then. I was</p> <p>16 just trying to save -- avoid having to mark another</p> <p>17 exhibit, but we will.</p> <p>18 I'm going to be marking an exhibit as 2096.</p> <p>19 (Exhibit 2096 marked for</p> <p>20 identification by the Certified</p> <p>21 Shorthand Reporter.)</p> <p>22 BY MR. SCHWARTZ:</p> <p>23 Q. And this is your deposition transcript in the</p> <p>24 four previous IPRs in this case, correct?</p> <p>25 A. I have not seen this before, but it would --</p>
<p style="text-align: right;">Page 115</p> <p>1 it is labeled as such.</p> <p>2 Q. Okay. And just so -- for your information,</p> <p>3 this is the Min-U-Script version of it, so it means that</p> <p>4 there's multiple pages on a single page. I don't know</p> <p>5 if you've seen them like this before --</p> <p>6 A. I have.</p> <p>7 Q. -- but it has multiple pages. I'm sure your</p> <p>8 counsel has seen something like this.</p> <p>9 Please turn to page 206. It will be on your</p> <p>10 top right corner. Do you see 206?</p> <p>11 A. I do.</p> <p>12 Q. And starting at line 8 of the transcript, it</p> <p>13 reads:</p> <p>14 "QUESTION: Do you see in the</p> <p>15 structure that is drawn for this</p> <p>16 particular adenine nucleotide that</p> <p>17 the tag is attached to the base via</p> <p>18 a structure called Y?</p> <p>19 "ANSWER: A box called Y, yes, I</p> <p>20 see that.</p> <p>21 "QUESTION: What is your</p> <p>22 understanding of the box called Y?</p> <p>23 "ANSWER: It would be a</p> <p>24 cleavable -- part of a cleavable</p> <p>25 label -- a link or part of a label</p>	<p style="text-align: right;">Page 116</p> <p>1 that would attach what he calls the</p> <p>2 tag.</p> <p>3 "QUESTION: So you understand</p> <p>4 that the tag is not directly</p> <p>5 connected to the base, correct?</p> <p>6 "ANSWER: Yes. I mean, we'll get</p> <p>7 a little semantic talking about why</p> <p>8 the tag and why start and stop,</p> <p>9 because they're all going to be</p> <p>10 chemical bonds, but clearly the</p> <p>11 spirit here is that there is a part</p> <p>12 that is cleavable that will separate</p> <p>13 the fluorophore or the tag from the</p> <p>14 nuclear base."</p> <p>15 That was your testimony, correct?</p> <p>16 A. There's a variety of typographical errors</p> <p>17 there. I have not edited this yet. But that seems to</p> <p>18 be what I said and certainly consistent with what I</p> <p>19 would say, but there are typographical errors.</p> <p>20 Q. Did the typographical errors change the</p> <p>21 substance of your answer?</p> <p>22 A. I don't know. I mean, they get -- it just</p> <p>23 gets a little confusing. Like where it says "we'll get</p> <p>24 a little semantic talking about why the tag" -- it's</p> <p>25 almost certainly I said about where the tag starts and</p>

<p style="text-align: right;">Page 117</p> <p>1 stops, because they are going to be chemical bonds. But</p> <p>2 clearly the spirit here is that there is part -- there</p> <p>3 is a part that is cleavable that will separate the</p> <p>4 fluorophore from the tag -- or the tag -- of the tag</p> <p>5 from the nucleobase, not nuclear base.</p> <p>6 Q. Okay. So --</p> <p>7 A. It's just a little hard to read.</p> <p>8 Q. Okay. But your testimony was that Y</p> <p>9 represents a component that is between the fluorophore</p> <p>10 and the base that is cleavable, correct? It's not</p> <p>11 directly attached, the fluorophore to the base?</p> <p>12 A. Yeah. Yeah. That's certainly the spirit of</p> <p>13 what I was saying.</p> <p>14 Q. And the chemically cleavable chemical linker</p> <p>15 that is denoted as Y in Claim 1 must be cleavable under</p> <p>16 conditions that are suitable for SBS, correct?</p> <p>17 A. If you're asking under the criteria of -- in</p> <p>18 general, no, but could you ask me -- I'm sure you're</p> <p>19 asking this from a specific criteria. If you're going</p> <p>20 to use it for sequencing by synthesis, then -- then</p> <p>21 yeah, sure.</p> <p>22 Q. So the conditions must be mild so as to allow</p> <p>23 continued DNA synthesis to occur after chemical</p> <p>24 cleavage, correct?</p> <p>25 A. For most applications you're going to have to</p>	<p style="text-align: right;">Page 118</p> <p>1 we reinitiate DNA synthesis, so you would have to</p> <p>2 reinitiate DNA synthesis. So if cleaving the linker did</p> <p>3 something that prevented that, then -- the reason I'm</p> <p>4 being a little hesitant here is because this is a</p> <p>5 specific requirement, I think, of some of the patents</p> <p>6 that we're talking about. And so it would be easier to</p> <p>7 sort of answer the question in their context as opposed</p> <p>8 to a vacuum.</p> <p>9 Q. Well, let's do that in the context of Claim 1</p> <p>10 of the '985 patent. The cleavage of the cleavable --</p> <p>11 chemically cleavable chemical linker must take place</p> <p>12 under conditions that would be compatible with SBS,</p> <p>13 correct?</p> <p>14 A. Correct.</p> <p>15 Q. Please go back to your declaration in</p> <p>16 IPR2018-00797. That's this case. That was marked as</p> <p>17 Exhibit 1078. So it's your declaration in this case.</p> <p>18 Exhibit 1078.</p> <p>19 MR. ZIMMERMAN: It's going to be a thick one</p> <p>20 with a binder clip.</p> <p>21 THE WITNESS: It must be this, right?</p> <p>22 MR. ZIMMERMAN: 1078, yes.</p> <p>23 THE WITNESS: 1078, yeah, I have it.</p> <p>24 BY MR. SCHWARTZ:</p> <p>25 Q. Okay. Please turn to page 130.</p>
<p style="text-align: right;">Page 119</p> <p>1 A. 130?</p> <p>2 Q. Yes, please.</p> <p>3 On page 130, towards the bottom of the page,</p> <p>4 there is a section entitled Section IX.A.9, "Limitation</p> <p>5 'wherein Y represents a chemically cleavable, chemical</p> <p>6 linker.'"</p> <p>7 Do you see that?</p> <p>8 A. I do.</p> <p>9 Q. Please keep your finger on that page, but I</p> <p>10 would ask that you turn to page 108 of that declaration.</p> <p>11 And Section IX relates to ground 3 in which you contend</p> <p>12 that the '985 claims are obvious over Dower, Prober, and</p> <p>13 Metzker, correct?</p> <p>14 A. Section IX, ground 3, that's right.</p> <p>15 Q. And please go back to page 131 of your</p> <p>16 declaration.</p> <p>17 A. 131?</p> <p>18 Q. Yes.</p> <p>19 And page 131 is part of paragraph 183, which</p> <p>20 is within the Section IX.A.9 that relates to your ground</p> <p>21 3 challenge, correct?</p> <p>22 A. Yes.</p> <p>23 Q. And please draw your attention to the sentence</p> <p>24 on the bottom of page 131 where three lines up from the</p> <p>25 bottom of the page you refer to Figure 9.</p>	<p style="text-align: right;">Page 120</p> <p>1 Do you see that?</p> <p>2 A. I do.</p> <p>3 Q. And if you would, please, turn to page 132 of</p> <p>4 your declaration. Starting at the top of the page you</p> <p>5 draw the structure depicted in Figure 9.</p> <p>6 Do you see that?</p> <p>7 A. I do.</p> <p>8 Q. I'm going to put in front of you the Dower</p> <p>9 reference. Just keep all of that in front of you. And</p> <p>10 here's the -- it's not easy. I understand.</p> <p>11 I'm putting in front of you Exhibit 1015,</p> <p>12 which is U.S. Patent No. 5,547,839, and that's the Dower</p> <p>13 reference in your declaration, correct?</p> <p>14 A. Yes, it is.</p> <p>15 Q. Please turn to Figure 9 in Dower. On the top</p> <p>16 right side of Figure 9 in Dower, that's the same</p> <p>17 structure you drew in your declaration, correct?</p> <p>18 A. That is right.</p> <p>19 Q. And the B in Figure 9 of Dower represents the</p> <p>20 nucleotide base, correct?</p> <p>21 A. That is correct.</p> <p>22 Q. And the FMOC in Figure 9 is what you are</p> <p>23 calling the label, correct?</p> <p>24 A. Where -- where do I -- probably, but could I</p> <p>25 ask you where I describe that as a label, to make sure</p>

<p style="text-align: right;">Page 121</p> <p>1 I'm on the same page?</p> <p>2 Q. Do you consider that to be the label?</p> <p>3 A. The FMOC?</p> <p>4 Q. Yes.</p> <p>5 A. It has the fluorophore and the linker in it.</p> <p>6 I -- I -- did I -- the label. So I think the label sort</p> <p>7 of generically refers to both the linker and the</p> <p>8 fluorophore. Is that right?</p> <p>9 I can't ask questions. Sorry.</p> <p>10 Yeah, that is -- the FMOC provides the label.</p> <p>11 Sure.</p> <p>12 Q. And the reaction scheme on top of Figure 9 in</p> <p>13 Dower for attachment of FMOC to the base results in</p> <p>14 direct attachment of FMOC to the base via a carbamate</p> <p>15 linkage, correct?</p> <p>16 (Court reporter clarification.)</p> <p>17 A. A carbamate will form from the amine of the</p> <p>18 base.</p> <p>19 Q. According to the Figure 9 teachings in Dower,</p> <p>20 correct?</p> <p>21 A. Well, it doesn't expressly say that, but it</p> <p>22 certainly is the only -- it's the only likely thing from</p> <p>23 as he's drawn it.</p> <p>24 Q. Okay. So FMOC is directly attached to the</p> <p>25 nucleotide base in Dower Figure 9, correct?</p>	<p style="text-align: right;">Page 122</p> <p>1 A. The FMOC is directly attached to the base in</p> <p>2 Figure 9, that's correct. It's -- the FMOC -- the</p> <p>3 fluorinenal -- fluorophore of the FMOC is attached to</p> <p>4 the base via the built-in FMOC linker. That's the</p> <p>5 carbamate that you mentioned.</p> <p>6 Q. Is directly attached by a covalent bond to the</p> <p>7 base? There isn't a Y structure in between, correct?</p> <p>8 A. No, there is.</p> <p>9 Q. There's not a chemically cleavable Y structure</p> <p>10 that's compatible with SBS, correct?</p> <p>11 A. No, there is. If you take FMOC and treat it</p> <p>12 with mild base, it eliminates.</p> <p>13 Q. You're saying you can take F -- you can take</p> <p>14 the Figure 9 FMOC carbamate linkage and treat it with a</p> <p>15 condition that would be compatible with SBS?</p> <p>16 A. Before I answer that, let me make sure.</p> <p>17 Yes.</p> <p>18 Q. And via what reaction?</p> <p>19 A. Would you like me to draw it for you or --</p> <p>20 it's a little hard to explain. So the FMOC forms</p> <p>21 carbamate, as you mentioned. In the FMOC there is a</p> <p>22 acidic proton that's on the other side of the oxygen.</p> <p>23 It's acidic so you can add mild base. It's often like</p> <p>24 a -- like a -- just a mild base like mor- -- like a --</p> <p>25 just like an aniline -- no. Like an aromatic amine,</p>
<p style="text-align: right;">Page 123</p> <p>1 like pyridine or something, some weak base.</p> <p>2 And that eliminates. It blows off CO₂, and</p> <p>3 that leaves an amine. So you would regenerate the amine</p> <p>4 that you used to form the carbamate.</p> <p>5 FMOCs are used in peptide protection all the</p> <p>6 time, of -- of primary amines, of alkylamines. And they</p> <p>7 are cleaved off that way.</p> <p>8 MR. SCHWARTZ: I'd like to take a quick break.</p> <p>9 Thank you.</p> <p>10 THE VIDEOGRAPHER: Going off the record at</p> <p>11 3:57 p.m.</p> <p>12 (Recess taken from 3:57 p.m. to</p> <p>13 4:09 p.m.)</p> <p>14 THE VIDEOGRAPHER: We are back on the record</p> <p>15 at 4:09 p.m.</p> <p>16 BY MR. SCHWARTZ:</p> <p>17 Q. Dr. Romesberg, I'm going to put in front of</p> <p>18 you what's been marked as Exhibit 1014. And that's the</p> <p>19 Prober reference site that you rely on in your</p> <p>20 declaration. That's the same Prober reference you rely</p> <p>21 on, correct?</p> <p>22 A. It is.</p> <p>23 Q. And please go to page 338 of Prober. And</p> <p>24 please draw your attention to Figure 2(A), which shows</p> <p>25 the structures of Prober's base labeled nucleotides.</p>	<p style="text-align: right;">Page 124</p> <p>1 The labels are attached to the base in Prober's</p> <p>2 nucleotides by an acetylenic linker, correct?</p> <p>3 A. A propargylamine, correct. Yes.</p> <p>4 Q. And a POSA in October -- a POSA in October</p> <p>5 2000 understood that that linker is not cleavable under</p> <p>6 conditions that are suitable for SBS, correct?</p> <p>7 A. No one -- so that part of any linker would not</p> <p>8 be cleavable, that is correct. The propargylamine part.</p> <p>9 The amine is a part that you would use to attach the</p> <p>10 cleavable part.</p> <p>11 Q. And a POSA in October 2000 understood that</p> <p>12 Prober does not disclose the use of the chemically</p> <p>13 cleavable chemical linker to attach the label to the</p> <p>14 base of a nucleotide, correct?</p> <p>15 A. Prober does not. That is correct.</p> <p>16 Q. And a POSA in October of 2000 understood that</p> <p>17 Prober's fluorescently labeled nucleotides are ddNTPs,</p> <p>18 correct?</p> <p>19 A. They are dideoxy, that is correct. DdNTPs,</p> <p>20 yes.</p> <p>21 Q. And a POSA in October 2000 understood that</p> <p>22 Prober's fluorescently labeled ddNTPs are permanent</p> <p>23 terminators and cannot be used for SBS, correct?</p> <p>24 A. They cannot restart synthesis. They are</p> <p>25 incorporated in much the same way, but because they're</p>

<p style="text-align: right;">Page 125</p> <p>1 missing the 3' hydroxyl group as opposed to it being</p> <p>2 protected, they by definition cannot restart synthesis.</p> <p>3 So that step of sequencing synthesis, they would have</p> <p>4 failed it, yes.</p> <p>5 Q. So in October of 2000, a POSA understood that</p> <p>6 it was not possible to convert a ddNTP into a dNTP by</p> <p>7 any chemical procedure that would not severely damage</p> <p>8 the nucleotide, correct?</p> <p>9 A. I would have to think about that, but almost</p> <p>10 certainly I would -- I would be very prone to agree with</p> <p>11 that. Yeah, I can't imagine doing that selectively, but</p> <p>12 I haven't thought about it.</p> <p>13 Q. And I don't know that I'm going to necessarily</p> <p>14 need to mark this exhibit. I just want to ask you one</p> <p>15 last question about Metzker 1994.</p> <p>16 Do you recall that Metzker 1994 does not</p> <p>17 disclose any nucleotides with labels attached to the</p> <p>18 base?</p> <p>19 A. Metzker does not. His -- the 1994 paper is</p> <p>20 focused on 3' blocking groups.</p> <p>21 Q. Okay. I'm going to put in front of you a</p> <p>22 document that -- let me -- this is going to be marked as</p> <p>23 2101.</p> <p>24 ///</p> <p>25 ///</p>	<p style="text-align: right;">Page 126</p> <p>1 (Exhibit 2101 marked for</p> <p>2 identification by the Certified</p> <p>3 Shorthand Reporter.)</p> <p>4 BY MR. SCHWARTZ:</p> <p>5 Q. Putting in front of you a document entitled</p> <p>6 Regioselective Oxidation of Internal Olefins Bearing</p> <p>7 Neighboring Oxygen Function by Means of -- by Means of</p> <p>8 Palladium Catalysts. Preparation of β-Alkoxy or Acetoxy</p> <p>9 Ketones from Allyl and Homoallyl Ethers or Esters by</p> <p>10 Tsuji, et al. as published in 1982.</p> <p>11 Please turn to page 2680. And please direct</p> <p>12 your attention to the first paragraph. And the authors</p> <p>13 write:</p> <p>14 "As shown in Table 1, the</p> <p>15 oxidation of various allyl ethers</p> <p>16 and acetates with palladium</p> <p>17 chloride, copper chloride, oxygen,</p> <p>18 or palladium chloride P,</p> <p>19 benzoquinone catalyst system gave</p> <p>20 the corresponding Beta alkoxy</p> <p>21 ketones regioselectively."</p> <p>22 That's what the authors write, correct?</p> <p>23 A. That is what is written.</p> <p>24 Q. And please direct your attention to Table 1 on</p> <p>25 page 2681. Compounds A, B, C, D, and E in Table 1 are</p>
<p style="text-align: right;">Page 127</p> <p>1 referred to as allyl ethers, correct?</p> <p>2 A. Those are allyl ethers. There's a substitute</p> <p>3 allyl ethers, yes.</p> <p>4 Q. So -- so allyl ethers in Table 1 -- strike</p> <p>5 that.</p> <p>6 The Tsuji 1982 paper refers to allyl ethers as</p> <p>7 a genus that includes substituted allyl ethers, correct?</p> <p>8 A. I haven't read this, but it appears to, and</p> <p>9 that would not surprise me.</p> <p>10 Q. Okay. And some of the com- -- the com- --</p> <p>11 some of the compounds contain four carbon atoms, six</p> <p>12 carbon atoms, seven, eight. They vary in size, correct?</p> <p>13 A. That is -- that is -- again, I have not read</p> <p>14 this, but it is not unusual to describe to that -- to</p> <p>15 describe that group as allyl ethers. And there are</p> <p>16 certainly analogs with the number of carbons you</p> <p>17 described.</p> <p>18 Q. Okay. You can put that away. I'm going to</p> <p>19 mark another exhibit.</p> <p>20 (Exhibit 2106 marked for</p> <p>21 identification by the Certified</p> <p>22 Shorthand Reporter.)</p> <p>23 BY MR. SCHWARTZ:</p> <p>24 Q. This is going to be marked as 2106.</p> <p>25 A. By the way, this was the Tsuji of the</p>	<p style="text-align: right;">Page 128</p> <p>1 Tsuji-Trost reaction that I brought up a few minutes</p> <p>2 ago.</p> <p>3 Q. I'm putting in front of you a document</p> <p>4 entitled Hypervalent (tert-Butylperoxy) Iodanes Generate</p> <p>5 Iodine-Centered Radicals at Room Temperature in</p> <p>6 Solution: Oxidation and Deprotection of Benzyl and Allyl</p> <p>7 Ethers, and Evidence for Generation of Alpha-Oxy Carbon</p> <p>8 Radicals by Ochiai, et al. that was published in 1996.</p> <p>9 Please turn to page 7719 and draw your</p> <p>10 attention to Table 3. And Table 3 is entitled Allylic</p> <p>11 Oxidation of Allyl Ethers with Peroxyiodane 1a, correct?</p> <p>12 A. It is.</p> <p>13 Q. And Table 3 discloses compounds 1 to 13, which</p> <p>14 are referred to in that paper as allyl ethers, correct?</p> <p>15 A. I have not read this, but the table heading</p> <p>16 would appear to suggest that's the case, yes.</p> <p>17 Q. Okay. And included in that group of allyl</p> <p>18 ethers are allyl ethers that contain anywhere from three</p> <p>19 to nine carbon atoms, and they are both substituted and</p> <p>20 unsubstituted, correct?</p> <p>21 A. There are both substituted and unsubstituted</p> <p>22 there, yes.</p> <p>23 Q. And there's -- and there's multiple carbon</p> <p>24 atoms, more than three?</p> <p>25 A. Yes.</p>

<p style="text-align: right;">Page 129</p> <p>1 Q. Okay. I'm going to put another paper in front 2 of you. This is going to be marked as 2107. 3 (Exhibit 2107 marked for 4 identification by the Certified 5 Shorthand Reporter.) 6 BY MR. SCHWARTZ: 7 Q. And I won't even read the title of this paper. 8 It's self-evident. 9 I'm going to ask you to turn to page 1319. 10 And please draw your attention to the right column on 11 page 1319 where there's a heading entitled Preparation 12 of Allyl Ethers. 13 Do you see that? 14 A. I'm sorry. 1319? 15 Q. 1319. 16 Has "Preparation of Allyl Ethers." 17 A. A paragraph heading, yes. 18 Q. Yes. 19 And if you look down in the section, you see 20 "Scheme 4." Do you see that? 21 A. I do. 22 Q. And please draw your attention to the three 23 compounds shown in the middle of Scheme 4 labeled 20a, 24 b, and c. Do you see those? 25 A. I do.</p>	<p style="text-align: right;">Page 130</p> <p>1 Q. And compounds 20a through c are referred to as 2 allyl ethers by these authors, correct? 3 A. I have not read this paper, but they -- 4 MR. ZIMMERMAN: Take your time to read 5 whatever you need to read. 6 BY MR. SCHWARTZ: 7 Q. Are they referred to as allyl ethers by these 8 authors? 9 A. Allyl ethers, 20a through c, so yes, those 10 are -- the compounds labeled 20a through c are being 11 referred to as allyl ethers. 12 Q. Okay. And compound 20a contains 12 carbon 13 atoms and 20b contains 10 and 20c contains 12. 14 Do you agree with that? 15 A. Do you want me to count them? 16 Q. Well, I just -- maybe the better question is 17 to say the compounds 20a and b -- a, b, and c are not 18 three carbon allyl ethers, correct? 19 A. They are not. 20 Q. Okay. And so the authors -- the authors of 21 this paper referred to allyl ethers as ethers containing 22 more than three carbon atoms, correct? 23 A. As is common, people can loosely refer to the 24 group of -- of compounds as allyl ethers, and people 25 would know what they meant, yes.</p>
<p style="text-align: right;">Page 131</p> <p>1 Q. Okay. 2 MR. SCHWARTZ: How much time do I have? 3 THE VIDEOGRAPHER: Seven minutes. 4 BY MR. SCHWARTZ: 5 Q. All right. I'm going to put one last exhibit 6 in front of you. And I'm putting in front of you what's 7 been marked previously as Exhibit 1013, which is the 8 Tsien patent application. 9 (Exhibit 1013 was previously marked 10 for identification by the Certified 11 Shorthand Reporter.) 12 BY MR. SCHWARTZ: 13 Q. This is the same Tsien patent application that 14 you refer to in your declaration, correct? 15 A. It appears to be. 16 Q. Please direct your attention to pages 20 17 through 23 of Tsien. And there's pages 20 through 23, 18 and there's a section entitled Blocking Groups and 19 Methods for Incorporation. 20 Do you see that section? 21 A. I do. 22 Q. In this section Tsien addresses criteria for 23 the selection of 3-O [sic] capping groups to block the 24 3'-OH group of a nucleotide for incorporation by a 25 polymerase for SBS, correct?</p>	<p style="text-align: right;">Page 132</p> <p>1 A. I'm sorry. Did you say that he discusses 2 three blocking groups? 3 Q. 3'-O capping groups. 4 A. 3'-O capping, yes. 5 Q. To block the 3'-OH group of a nucleotide for 6 incorporation by a polymerase for SBS. That's what he 7 discloses here, correct? 8 A. Yes. 9 Q. And in this -- in this section, Tsien never 10 expressly states that the 3'-O capping group needs to be 11 small, correct? 12 A. I don't think -- I don't think Tsien ever 13 evoked small. 14 Q. And nowhere in this section does Tsien mention 15 the use of allyl ethers to cap the 3'-OH of the 16 nucleotide, correct? 17 A. I would have to check that -- I would have to 18 read this because Tsien talks about -- Tsien teaches 19 O-allyl ethers as blocking groups. So if he doesn't, I 20 would have to read this section to see if it's not in 21 here in particular. 22 Q. No. I'm asking in this particular section. 23 So he never mentions in this section anything about 24 allyl ethers? 25 A. So again, in the section "Blocking Groups and</p>


<p align="right">Page 133</p> <p>1 Methods for Incorporation", right?</p> <p>2 I'm going to take a second to read them.</p> <p>3 Q. Uh-huh.</p> <p>4 A. I'm just skimming the end of it.</p> <p>5 He does not appear. So where he goes through</p> <p>6 this litany of different ones, he says:</p> <p>7 "The most common 3'-hydroxyl</p> <p>8 blocking groups are esters and</p> <p>9 ethers. Other blocking</p> <p>10 modifications" then he goes on</p> <p>11 for this very long list.</p> <p>12 And I assume that what he was baking into</p> <p>13 "other ethers" were the allyl ethers, because that's --</p> <p>14 they are ethers, and they are discussed in --</p> <p>15 specifically called out in other parts of this same</p> <p>16 application. So I would assume that's where they're</p> <p>17 embedded, but he does -- you're correct, he does not</p> <p>18 call out at any spot then in this section.</p> <p>19 Q. Nowhere in this section does Tsien disclose an</p> <p>20 allyl group CH²-CH double bond CH² containing three</p> <p>21 carbons and five hydrogens to cap the 3'-OH of the</p> <p>22 nucleotide, correct?</p> <p>23 A. I did not see it in this section.</p> <p>24 Q. All right. And I want to just quickly look at</p> <p>25 pages 23 to 25.</p>	<p align="right">Page 134</p> <p>1 MR. SCHWARTZ: How much time?</p> <p>2 THE VIDEOGRAPHER: Two.</p> <p>3 BY MR. SCHWARTZ:</p> <p>4 Q. And in this section, Tsien addresses the</p> <p>5 criteria for the selection of the 3'-O capping group to</p> <p>6 block the 3'-OH group of the nucleotide for</p> <p>7 incorporation for -- by polymerase for SBS, correct?</p> <p>8 A. It's labeled deblocking methods. I mean, if</p> <p>9 you want me to read -- I mean, it's been -- I've read a</p> <p>10 lot of these. Do you want me to -- I would like to read</p> <p>11 it quickly.</p> <p>12 Q. While you're reading it, I guess I'll just</p> <p>13 pose my question, since we're running out of time. And</p> <p>14 nowhere in this section does Tsien expressly disclose</p> <p>15 the specific allyl group CH₂-CH double bond CH₂</p> <p>16 containing three carbon atoms and five hydrogen atoms to</p> <p>17 cap the 3'-OH of the nucleotide, correct?</p> <p>18 A. He includes the allyl ethers. And the one</p> <p>19 that you just described is the parent allyl ether, and</p> <p>20 that would have been the first one anyone would have</p> <p>21 thought of. But no, he does not expressly say "the</p> <p>22 parent allyl ether compound."</p> <p>23 Q. Okay.</p> <p>24 MR. SCHWARTZ: I have no further questions for</p> <p>25 this part of the deposition. Thank you.</p>
<p align="right">Page 135</p> <p>1 EXAMINATION</p> <p>2 BY MR. ZIMMERMAN:</p> <p>3 Q. Dr. Romesberg, I have just a few questions for</p> <p>4 you. If you could pull up the Ju '985 patent,</p> <p>5 Exhibit 1075.</p> <p>6 A. Not the '985?</p> <p>7 Q. I'm sorry. The '985. It's Exhibit 1075.</p> <p>8 A. Yes. Yes, I have it.</p> <p>9 Q. And we'll wait for them to get the copy.</p> <p>10 MR. SCHWARTZ: Okay.</p> <p>11 BY MR. ZIMMERMAN:</p> <p>12 Q. And to save you the headache of later</p> <p>13 questions, did we have any discussions at the break</p> <p>14 regarding the substance of your testimony?</p> <p>15 A. We did not.</p> <p>16 Q. And did we have any discussions at any of the</p> <p>17 breaks about questions I might ask you in today's</p> <p>18 deposition?</p> <p>19 A. We did not.</p> <p>20 Q. Okay. Looking at the Ju '985 patent,</p> <p>21 Exhibit 1075, if you could turn to Column 21, lines 57</p> <p>22 to approximately 64.</p> <p>23 A. Starting with "It is a routine"?</p> <p>24 Q. Yes. You'll see that there's reference to</p> <p>25 "10,000 bases can be identified after each cycle ..."</p>	<p align="right">Page 136</p> <p>1 Do you see that?</p> <p>2 A. It does -- that is what it says.</p> <p>3 Q. Okay. Does this suggest that the method of Ju</p> <p>4 can sequence 10,000 base pairs?</p> <p>5 A. It says:</p> <p>6 "Thus, in the DNA sequencing</p> <p>7 system disclosed herein, more than</p> <p>8 10,000 base cycles can be identified</p> <p>9 after -- more than 10,000 bases can</p> <p>10 be identified after each cycle, and</p> <p>11 after 100 cycles, a million base</p> <p>12 pairs will be generated from one</p> <p>13 sequencing chip."</p> <p>14 Q. Okay. Is there any data in Tsien showing</p> <p>15 sequencing of a million base pairs?</p> <p>16 A. No.</p> <p>17 Q. I'm sorry. Is there any data in the Ju</p> <p>18 patent, Exhibit 1075, showing the sequencing of a</p> <p>19 million base pairs?</p> <p>20 A. That would still be no.</p> <p>21 Q. Okay. Is there any data in the Ju patent,</p> <p>22 Exhibit 1075, showing 10,000 base pairs?</p> <p>23 A. No.</p> <p>24 Q. Is there any data in the Ju patent showing</p> <p>25 sequencing of a hundred base pairs?</p>

<p align="right">Page 137</p> <p>1 A. No, there is not.</p> <p>2 Q. Is there any data in the Ju patent,</p> <p>3 Exhibit 1075, showing 25 base pairs being sequenced?</p> <p>4 A. No, there is not.</p> <p>5 Q. Is there any actual sequencing data at all in</p> <p>6 the Ju patent, Exhibit 1075?</p> <p>7 A. I believe not.</p> <p>8 Q. Okay. Now, if you could turn to Claim 1,</p> <p>9 which starts on paragraph -- I'm sorry -- Column 34 of</p> <p>10 the Ju patent, Exhibit 1075. You'll see it recites, "A</p> <p>11 method for sequencing a nucleic acid" and then</p> <p>12 continues.</p> <p>13 A. Yes, I see that.</p> <p>14 Q. Okay. In all of Claim 1 does it refer to</p> <p>15 sequencing by synthesis?</p> <p>16 A. No, it would appear not to. I believe it just</p> <p>17 talks about the incorporation of one of these nucleotide</p> <p>18 of analogs.</p> <p>19 Q. Okay. And does Claim 1 expressly state that</p> <p>20 you have to sequence 25 to 30 base pairs?</p> <p>21 A. No.</p> <p>22 Q. Does Claim 1 of the '985 patent put any</p> <p>23 limitation on the number of base pairs that must be</p> <p>24 sequenced?</p> <p>25 A. There is no limitation, high or low.</p>	<p align="right">Page 138</p> <p>1 Q. If you do one base, does that qualify under</p> <p>2 Claim 1 of the '985 patent?</p> <p>3 A. I -- as I read it, yes.</p> <p>4 Q. Now, there was some discussion earlier and</p> <p>5 reference back to a prior deposition where you indicated</p> <p>6 or appeared to indicate that SBS wouldn't be useful for</p> <p>7 sequencing one nucleotide, correct?</p> <p>8 A. I don't recall that exact testimony.</p> <p>9 Sequencing -- sequencing a single nucleotide, if you're</p> <p>10 using a polymerase and you're incorporating a</p> <p>11 fluorophore, that is sequencing by synthesis, and that</p> <p>12 could be of interest.</p> <p>13 I think what I was trying to discuss then was,</p> <p>14 as we talked about earlier, was sequencing like a human</p> <p>15 genome, in which case you would need much longer</p> <p>16 sequences. But that's because you have to place them</p> <p>17 in -- you have to construct the genome from fragments,</p> <p>18 and you need enough overlap to be able to do that.</p> <p>19 There are certainly applications where one</p> <p>20 would want a smaller number of sequence information.</p> <p>21 Q. Are -- are there any real world practical</p> <p>22 applications where sequencing three base pairs is of</p> <p>23 value or use?</p> <p>24 A. No, absolutely. In the end, what most people</p> <p>25 care about is amino acid sequence in a protein, because</p>
<p align="right">Page 139</p> <p>1 lots of cancer states are caused by proteins with</p> <p>2 changes at the amino acid level. That's the only spot</p> <p>3 where differences are actually made and felt in nature</p> <p>4 to the cell.</p> <p>5 And nucleotide -- amino acids are coated in</p> <p>6 triplets of nucleotides. So three nucleotides</p> <p>7 correspond to one amino acid. So to identify what an</p> <p>8 amino acid is, you need three nucleotides. So -- and</p> <p>9 this is just off the top of my head, but it would seem</p> <p>10 very common and very reasonable to want a primer to lay</p> <p>11 down before a codon, read what the codon is. That would</p> <p>12 require three nucleotides. And then you would know the</p> <p>13 amino acid.</p> <p>14 So that what I imagine, off the top of my</p> <p>15 head, would be the most useful.</p> <p>16 MR. ZIMMERMAN: If you'll give me one quick</p> <p>17 second.</p> <p>18 I have no further questions for Dr. Romesberg.</p> <p>19 But I do want to make an objection on the</p> <p>20 record to Exhibits 2102, 2103, and 2104 as outside the</p> <p>21 scope and because they are not prior art, just to make</p> <p>22 sure that that's preserved.</p> <p>23 I also want to make clear for the record that</p> <p>24 this deposition is solely for the purposes of</p> <p>25 IPR2018-00797. And we will object to its use in any of</p>	<p align="right">Page 140</p> <p>1 the other four IPR proceedings.</p> <p>2 MR. SCHWARTZ: Okay. Can you give us a</p> <p>3 break --</p> <p>4 MR. ZIMMERMAN: Sure.</p> <p>5 MR. SCHWARTZ: -- for just a few minutes?</p> <p>6 THE VIDEOGRAPHER: Going off the record at</p> <p>7 4:30 p.m.</p> <p>8 (Recess taken from 4:30 p.m. to</p> <p>9 4:35 p.m.)</p> <p>10 THE VIDEOGRAPHER: We are back on the record</p> <p>11 at 4:35 p.m.</p> <p>12 BY MR. SCHWARTZ:</p> <p>13 Q. Dr. Romesberg, just one last question about</p> <p>14 the Claim 1 of the '985 patent that we just looked at.</p> <p>15 A. Yes. I have it.</p> <p>16 Q. Claim 1 is "A method for sequencing a nucleic</p> <p>17 acid," correct?</p> <p>18 A. That is what it says, yes.</p> <p>19 Q. A nucleic acid is a polymer of nucleotides; is</p> <p>20 that correct?</p> <p>21 A. A nucleic acid is a polymer of nucleotides</p> <p>22 made up of individual nucleotides, that's correct.</p> <p>23 MR. SCHWARTZ: I have no further questions.</p> <p>24 MR. ZIMMERMAN: I have no further questions</p> <p>25 either.</p>

Page 141

1 THE VIDEOGRAPHER: This concludes the
2 video-recorded deposition of Dr. Floyd Romesberg, Ph.D.
3 Going off the record at 4:36 p.m.
4 (Deposition concludes at 4:36 p.m.)
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Page 142

1 STATE OF CALIFORNIA)
2)
3 COUNTY OF SAN DIEGO)
4
5 I, Linda E. Marquette, a Certified Shorthand
6 Reporter, do hereby certify:
7 That prior to being examined, the witness in the
8 foregoing proceedings was by me duly sworn to testify to
9 the truth, the whole truth, and nothing but the truth;
10 That said proceedings were taken before me at the
11 time and place therein set forth and were taken down by
12 me in shorthand and thereafter transcribed into
13 typewriting under my direction and supervision;
14 I further certify that I am neither counsel for,
15 nor related to, any party to said proceedings, nor in
16 anywise interested in the outcome thereof.
17 Further, that if the foregoing pertains to
18 the original transcript of a deposition in a federal
19 case, before completion of the proceedings, review of
20 the transcript [X] was [] was not requested.
21 In witness whereof, I have hereunto subscribed my
22 name.
23 Dated: October 15, 2018
24 
25 Linda E. Marquette
RPR, CLR, CSR No. 11874,

Page 143

1 DECLARATION UNDER PENALTY OF PERJURY
2 Case Name: Illumina, Inc. vs. The Trustees of Columbia
3 University in the City of New York
4 Date of Deposition: 10/09/2018
5 Job No.: 10048075
6
7 I, FLOYD ROMESBERG, PH.D., hereby certify
8 that I have read the transcript of my deposition and that
9 this transcript accurately states the testimony given by me,
10 with the changes or corrections, if any, as noted on an errata
11 sheet or errata sheets.
12 Executed this _____ day of
13 _____, 2018, at _____.
14
15 _____
16 FLOYD ROMESBERG, PH.D.
17 NOTARIZATION (If Required)
18 State of _____
19 County of _____
20 Subscribed and sworn to (or affirmed) before me on
21 this _____ day of _____, 20____,
22 by _____, proved to me on the
23 basis of satisfactory evidence to be the person
24 who appeared before me.
25 Signature: _____ (Seal)

Page 144

1 DEPOSITION ERRATA SHEET
2 Case Name: Illumina, Inc. vs. The Trustees of Columbia
3 University in the City of New York
4 Name of Witness: Floyd Romesberg, Ph.D.
5 Date of Deposition: 10/09/2018
6 Job No.: 10048075
7 Reason Codes: 1. To clarify the record.
8 2. To conform to the facts.
9 3. To correct transcription errors.
10 Page _____ Line _____ Reason _____
11 From _____ to _____
12 Page _____ Line _____ Reason _____
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16 Page _____ Line _____ Reason _____
17 From _____ to _____
18 Page _____ Line _____ Reason _____
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24 Page _____ Line _____ Reason _____
25 From _____ to _____

Floyd Romesberg, Ph.D.

<div>1 DEPOSITION ERRATA SHEET</div> <div>2 Page _____ Line _____ Reason _____</div> <div>3 From _____ to _____</div> <div>4 Page _____ Line _____ Reason _____</div> <div>5 From _____ to _____</div> <div>6 Page _____ Line _____ Reason _____</div> <div>7 From _____ to _____</div> <div>8 Page _____ Line _____ Reason _____</div> <div>9 From _____ to _____</div> <div>10 Page _____ Line _____ Reason _____</div> <div>11 From _____ to _____</div> <div>12 Page _____ Line _____ Reason _____</div> <div>13 From _____ to _____</div> <div>14 Page _____ Line _____ Reason _____</div> <div>15 From _____ to _____</div> <div>16 Page _____ Line _____ Reason _____</div> <div>17 From _____ to _____</div> <div>18 Page _____ Line _____ Reason _____</div> <div>19 From _____ to _____</div> <div>20 Page _____ Line _____ Reason _____</div> <div>21 From _____ to _____</div> <div>22 _____ Subject to the above changes, I certify that the transcript is true and correct</div> <div>23 _____ No changes have been made. I certify that the transcript is true and correct.</div> <div>24</div> <div>25 _____ FLOYD ROMESBERG, PH.D.</div>	

Exhibits	PREVIOUSLY MARK ED EXHIBIT 2080 4:10 11:9,11	(3) 22:17 (4) 22:22	100 25:7 87:2 88:2,10 99:25 136:11
ALL COMBINED	EXHIBIT 2095 4:14 21:10,11 40:18 42:13 45:18 46:15	0	1001 13:10
PREVIOUSLY MARK ED EXHIBIT 1001 6:19 13:10	EXHIBIT 2096 5:23 114:19	0.19 53:11	1013 131:7,9
PREVIOUSLY MARK ED EXHIBIT 1013 6:15 131:7,9	EXHIBIT 2097 5:3 61:11,12,18	0.23 52:13 60:8	1014 123:18
PREVIOUSLY MARK ED EXHIBIT 1014 123:18	EXHIBIT 2098 5:10 77:1,5 78:8	0.39 53:9	1015 120:11
PREVIOUSLY MARK ED EXHIBIT 1015 6:21 120:11	EXHIBIT 2099 5:15 84:15,16	0.735 87:8	1023 79:10,14
PREVIOUSLY MARK ED EXHIBIT 1023 5:13 79:10,14	EXHIBIT 2100 5:17 92:5	0.85100 30:2	1036 49:6,8 50:12,13 71:4
PREVIOUSLY MARK ED EXHIBIT 1036 4:18 49:6,8 50:12,13 71:4	EXHIBIT 2101 6:3 126:1	0.9530 28:23	1075 10:23 11:1 41:4 97:24 113:22 135:5, 7,21 136:18,22 137:3,6,10
PREVIOUSLY MARK ED EXHIBIT 1075 4:8 10:23 11:1 41:4 97:24 113:22 135:5, 7,21 136:18,22 137:3,6,10	EXHIBIT 2102 4:22 49:15,19 50:14 51:3	0.956 87:8	1078 10:15 48:22 118:17,18,22,23
PREVIOUSLY MARK ED EXHIBIT 1078 6:18 118:17,18	EXHIBIT 2103 5:19 98:5,6,13,18 101:20 103:7	026 11:20 13:3,4,10 14:8 15:4	108 119:10
PREVIOUSLY MARK ED EXHIBIT 2007 4:12 18:14,16 28:1,3 34:8 39:6,20 41:19, 23 45:7 46:9	EXHIBIT 2104 5:21 99:15 100:3,6,12 101:19	079 19:20 20:21 21:4, 24 23:7,17 29:16 40:11,14,17 41:1,5, 14 42:1,12 43:2,7,9, 21 44:1 45:12,17 46:2,5,10,14,17 47:1,5,17	11 12:7,14 15:18 35:9 46:12 47:6,10,11,18
PREVIOUSLY MARK ED EXHIBIT 2035 4:16 26:2,3 35:23	EXHIBIT 2105 5:7 72:12,13	1	11th 94:11
PREVIOUSLY MARK ED EXHIBIT 2054 5:5 65:22,23	EXHIBIT 2106 6:7 127:20	1 20:22 21:6 27:2,3 61:19 75:11 92:11, 15,16 93:13 95:21 96:8 113:24 117:15 118:9 126:14,24,25 127:4 128:13 137:8, 14,19,22 138:2 140:14,16	12 24:10 113:3 130:12,13
	EXHIBIT 2107 6:11 129:3	10 18:20 19:11,12 24:23 31:7 33:12 42:2,7,14,18 43:3 45:24 46:11,16,18 47:2,14 105:12 130:13	12065 62:6
	\$	10,000 10:15 25:6 48:22 135:25 136:4, 8,9,22	12069 62:23
	(12790 7:14
	(1) 22:6		12:31 7:2,6
	(2) 22:11		13 27:25 28:6 29:10, 16 35:9 41:9 45:13, 14,15,18 46:3,12 47:6,11,12,18 128:13
			130 118:25 119:1,3
			131 119:15,17,19,24
			1319 129:9,11,14,15
			132 120:3
			14 34:12,13 38:25 39:8,22 47:10 65:11
			14:18:33 65:11
			15 38:16 53:9 56:3
			16 23:2,17 40:15,20,

23 53:8 56:3,5		206 115:9,10	137:3,20
17 52:16,24 53:2	2	2080 11:9,11	25th 50:9
54:3,5 55:4,6,9,11,		2095 21:10,11,19	26 20:22 21:6
19,23 56:3,5,10,16	2 24:23 35:24 37:3	40:18 42:13 43:8	2680 126:11
57:6,8 58:24 59:1,4	42:1,7,14,18,20 43:3	44:1 45:18 46:15	2681 126:25
60:11	50:20,21 51:7 62:7,	2096 114:18,19	28 19:23,25 21:1
183 119:19	8,12,16,20 63:4,9,	2097 61:11,12,18	29 22:2,3 23:13 40:9,
18th 99:2,10	24,25 64:5 65:6	2098 77:1,5,7 78:8	10,12,13
19 31:7 33:12 46:11,	72:19 84:25 85:14	2099 84:15,16	2:56 91:17,18
16,18 47:2	96:7 107:24 108:1,		
1982 126:10 127:6	17,20 113:11	20a 129:23 130:1,9,	
1985 72:20	2(A) 123:24	10,12,17	3
1994 67:18,20 68:2,9	2,4 63:1	20b 130:13	3 23:2,17 40:14,20,23
69:6,19 70:4 80:17	20 41:7 105:12	20c 130:13	61:19 119:11,14,21
84:9,12 85:25 86:9,	131:16,17	21 20:22 21:6 23:2,17	128:10,13
11,12 87:16,19,20	2000 50:9 64:13	25:10 28:23 29:10,	3' 47:23 68:11,21
89:21 90:2,9,14,22	71:24 74:20 75:6	16 35:9 40:14,19	112:4,5 125:1,20
93:3,6,7,9 94:22	78:7,25 79:3,4 82:10	41:9 42:2,9 43:6,7,9,	3'-hydroxyl 133:7
109:1 125:15,16,19	83:5 88:6,15,20	16,18,22 45:12,15,	3'-O 132:3,4,10 134:5
1995 44:2 77:12 78:8	89:11 94:11,14,15	18,23,24 46:3,12	3'-o-allyl 108:5,14
1996 128:8	97:6,13,16 104:13	47:6,14,18 85:15	109:2,8 111:1
1998 49:1,7 50:11,19,	106:9 113:8 124:5,	135:21	113:13
21 51:8,25 59:21	11,16,21 125:5	2100 92:4,5	3'-OH 22:10,18 28:13
61:22 62:1 63:23,25	2003 78:25 79:2	2101 125:23 126:1	30:7 35:5 48:1
64:13 66:4 67:24	2005 104:13 105:14	2102 49:15,19 50:14	131:24 132:5,15
68:12 70:4,12,14	110:25	51:3 139:20	133:21 134:6,17
71:4,7,20,25	2005-2000 109:5	2103 98:5,6,13,18	3-O 131:23
1999 61:21,22 62:1,6,	2005-2006 104:14	101:20 103:7 139:20	30 23:21 24:21 25:1,
11,12,15,23 63:11	105:4 106:6 108:11	2104 99:15,20 100:3,	14 26:18,22 27:4,7,
64:4,8,14 65:6 79:13	2006 98:15 99:2,10	6,12 101:19 139:20	10,19,21 28:11,20
82:11 84:10 89:9,12	100:10 108:12 109:5	2105 72:12,13	36:11 37:14,25 38:6,
19th 114:8	111:1	2106 127:20,24	16 110:17 137:20
1:28 44:22,23	2007 18:14,16 28:1,3	2107 129:2,3	300 7:18
1:31 44:24 45:1	34:8 39:6,20 41:19,	2185 50:19	31 42:21,24,25 46:23
1:37 48:11,12	23 45:7 46:9	22 20:22 21:5	32 24:11,13 25:23
1:55 48:13,15	2014 18:24 19:3	22% 30:2	41:18,22,24,25 42:5
1a 128:11	26:13	220 52:13 60:4,8	33 27:25 28:6 29:19
1K 113:1,5	2018 7:1,5	23 131:17 133:25	45:6,9,11
1R21HG003977-01	202 60:13	25 24:23 36:11 37:14,	338 123:23
98:12	2035 26:2,3 35:23	25 38:6,18 42:2,7,	34 30:13,14 32:5
	2054 65:22,23	14,18 43:3 133:25	

34:7,11 46:8,9 53:10 113:23 137:9	54 52:19,25 53:1 54:2 56:4	29:10,16 45:13,14, 15,18 46:3 47:14 51:25 59:21 115:12	ability 87:9 89:2 112:24
35 110:17	57 93:13 135:21	83 64:6,10,12,16,18, 23,24 65:2,4	able 36:9 37:12 69:18 106:15 112:11,14 138:18
36 114:1,2	5A 21:16	87 26:10	absolutely 138:24
363 66:7	5th 19:3	88 27:1	abstract 103:9,10 107:23
37 11:15 15:1 86:15	<hr/>	<hr/>	ac 22:7,12
38 12:4 15:17 80:5, 11,14,16	6	9	accepted 109:22,23, 25 112:5
3:17 91:19,21	6 51:19 63:1,5 77:13, 14,17,24 114:3	9 7:1,5 60:25 63:6,16 119:25 120:5,15,16, 19,22 121:12,19,25 122:2,14	accomplished 83:2
3:57 123:11,12	6,013,445 92:10	9,868,985 10:18,24 11:6 41:2	account 29:2
3rd 100:10	6,664,079 19:16,20 21:9	92101 7:18	accumulation 96:10, 12 97:17
<hr/>	60 43:16,18	92130 7:15	accurate 30:23 33:4
4	600 7:17	95 28:19 29:2 87:5 88:21	acetates 126:16
4 20:22 21:5 31:7 33:12 46:11,15,18, 22 47:2 63:4 129:20, 23	61 95:23	952 79:18	Acetonides 77:11
40 56:4 92:11,16	63 25:10 42:2,9 43:6, 7,9,11,22	956 80:19	Acetoxy 126:8
400 53:8	64 43:16,19 135:22	96 60:21 61:1 64:16, 19,20,22 65:12	acetylenic 124:2
41 42:23 46:23	65 41:8 51:5,6,10 52:7,13 53:16 54:11 55:1,9 56:9,17 57:6 59:3,20 60:4,8	96% 60:13	achieve 28:10 83:3
42 51:4	66 51:23 53:16 54:11 59:20 60:13,21	98 62:3,5	acid 11:7,25 12:23 14:3 15:11 16:16 17:19 18:4 75:1 76:19 137:11 138:25 139:2,7,8,13 140:17, 19,21
43 80:5,11,14	67 25:10 42:2,9 43:6, 7,10,11,22	98.5 29:25	acidic 74:17,21 75:8, 12 122:22,23
441 72:22	<hr/>	985 41:3,5,7,14 42:17,19 43:4,15,23 44:3 45:22,24 46:4, 6,21 47:3,13,19,24 97:22 98:1 113:22 118:10 119:12 135:4,6,7,20 137:22 138:2 140:14	acids 139:5
46 42:21,23,24	7	99 35:23 62:5	action 65:17
49 48:24,25 49:2	7 51:7,11 59:20 67:1, 18	<hr/>	actual 101:3 137:5
4:09 123:13,15	75 87:6 88:22	A	add 122:23
4:1 60:12	77 52:3,5 54:23 55:1 56:8 59:23,25 60:5	<hr/>	added 53:10 58:14
4:30 140:7,8	7719 128:9	<hr/>	addition 10:3 14:14 80:6 85:16,19 87:3 88:4 97:8
4:35 140:9,11	<hr/>	<hr/>	additional 80:9 97:11
4:36 7:2 141:3,4	8	aa 22:7,12	addresses 131:22 134:4
<hr/>	8 11:16 14:23 15:1		
5			
5 20:23 21:6 26:11,14 39:21,22 45:23			
5,547,839 120:12			
5,858,671 84:25			

addressing 38:22	126:20	analyses 80:2	138:19,22
adenine 115:16	alkylamines 123:6	analysis 31:2 33:7	applies 56:22
administered 8:14	alleged 26:18	and/or 29:6	appreciate 111:13
admit 111:21	allow 22:19 30:17	aniline 122:25	approach 86:21 87:2, 23,25 88:10
advances 103:20	31:19 32:22 117:22	annealed 22:24	approaches 92:13, 22,25 95:5 96:3
advantages 112:12	allyl 51:24 52:6 60:20	announced 106:19, 22	104:3,10,11,15
affiliation 50:18	62:8,11,15 63:9,25	answer 9:6 11:21	105:23 106:6 107:10
70:15 91:2	64:6,8,14 65:5,6	12:3,19 15:6,15,24	approximately 9:16
affirm 8:10	70:23 71:3 72:1,18,	16:14,18 17:17	135:22
affordable 110:21	23 73:1,8,9,25 76:1,	26:20 27:4 34:6	Aptus 7:17 8:9
afternoon 8:19,20	9 77:18,19 78:10	68:15 79:6 111:10,	aqueous 71:6,12 72:2
ag 22:7,12	90:11 126:9,15	25 112:2,8 115:19,	aromatic 122:25
agency 113:11	127:1,2,3,4,6,7,15	23 116:6,21 118:7	array 80:3
aggressive 71:9	128:6,11,14,17,18	122:16	art 19:13 20:4 23:24
ago 33:23 34:3 54:19	129:12,16 130:2,7,9,	answered 16:20	24:19 25:12 30:4
101:25 113:3 128:2	11,18,21,24 132:15,	55:21 56:1 58:2 59:7	34:20 35:10 57:22
agree 12:16 15:21	24 133:13,20	69:8 107:15 111:6,7,	68:13 71:10 82:16,
17:10 19:5 26:16	134:15,18,19,22	17,24 113:17	22 139:21
65:15 67:7 79:3	Allylic 77:11 128:10	answering 14:13	article 70:25 100:19
106:5 125:10 130:14	alpha 61:19 78:2,3,15	16:11 17:2 36:23	102:8,9,14,20
agreed 14:10 17:12	Alpha-oxy 128:7	111:19	artist 71:24
Ah 98:16	alternative 92:13,19, 21	anybody 9:22	Asanas 7:16
ahead 12:4 15:17	ambiguous 56:25	apologize 100:1	asked 14:7 15:17
111:25	57:17 58:5,7,10,18	Appeal 7:12	16:19 17:15,21
Aim 107:24 108:1,17,	amine 68:11 121:17	appear 51:22 52:8,11	44:11 46:6 55:20,25
20,21 113:11	122:25 123:3 124:9	100:14 128:16 133:5	58:1 59:6 69:7 85:7
Aims 108:16	amines 123:6	137:16	107:14 111:7,16
al 44:2	amino 138:25 139:2, 5,7,8,13	appeared 138:6	113:16 114:7
Albrecht 92:10,20	amount 57:12 68:10	appears 21:17 50:8	asking 9:6 14:19
93:7,17 94:1,4,10,	90:16,23	76:11 80:18 87:14	16:23 17:24,25 19:1
14,15,21 96:1,9	amounts 69:19,23	89:18 127:8 131:15	41:13 53:22 76:12
97:7,13,15	analog 86:25 87:12	applicant 103:11	106:3 109:4 111:3,
alcohol 73:11 74:7,22	88:9 89:14 90:10	application 33:1	22 112:4,9 117:17,
75:9 76:14	109:22	93:20 95:1,16 96:20	19 132:22
alcohols 61:21 78:11, 18	analogs 49:25 85:24	97:2 107:4 110:11	assignee 91:8
aldehyde 78:5,16	86:5,8 106:11 110:6,	112:7 131:8,13	associated 29:3
alkaline 75:13	20 112:15 127:16	133:16	association 31:4
alkoxy 78:2,3,4	137:18	applications 30:22	33:10
	analogues 22:7,11	31:24 33:2 110:14, 22 112:14 117:25	

<p>assume 50:17 58:4 133:12,16</p> <p>atoms 127:11,12 128:19,24 130:13,22 134:16</p> <p>ATP 69:23</p> <p>attach 102:25 114:11 116:1 124:9,13</p> <p>attached 115:17 117:11 121:24 122:1,3,6 124:1 125:17</p> <p>attachment 121:13, 14</p> <p>attacks 76:3</p> <p>attention 11:16 12:7 19:23 22:2 23:20 24:11,12 39:10 46:22 48:24 50:20 51:4 52:22 62:7,24 63:24 66:5 79:19 80:20,25 103:9 119:23 123:24 126:12,24 128:10 129:10,22 131:16</p> <p>attorney 7:21 45:4</p> <p>attorneys 9:4,8,12, 20,23 48:18 91:25</p> <p>author 50:13,14 61:23</p> <p>authors 61:25 62:1,3 66:7,19,22 67:20,24 68:12 69:13,17 70:3, 11,14 74:4 79:24 80:8,11 81:5 82:1,3 83:25 84:8 126:12, 22 130:2,8,20</p> <p>automated 96:6</p> <p>availability 22:6</p> <p>avoid 114:16</p> <p>award 99:1,2,5,10</p>	<p>awarded 98:15</p> <p>aware 70:18,21</p> <hr/> <p style="text-align: center;">B</p> <hr/> <p>back 14:18,22,23 22:1 23:6 34:7 35:21 38:4,20,25 40:9 44:18,25 46:21 47:13 48:14,21 50:11 51:2 63:23 64:4 91:20 95:21 97:22 103:7 118:15 119:15 123:14 138:5 140:10</p> <p>baking 133:12</p> <p>base 24:21 25:2,8,15, 16 26:19 28:11 80:6, 9 85:16,19 87:3 88:4 92:24 95:4 115:17 116:5,14 117:5,10, 11 120:20 121:13, 14,18,25 122:1,4,7, 12,23,24 123:1,25 124:1,14 125:18 136:4,8,11,15,19,22, 25 137:3,20,23 138:1,22</p> <p>base-by-base 92:24 93:18 94:3,25 95:4, 10,11,14,15,24 96:2, 21 97:2</p> <p>based 66:3,8,17 71:15 72:4 96:16</p> <p>bases 25:6 28:20 30:1 67:3 135:25 136:9</p> <p>basic 112:17</p> <p>basically 41:11 42:16</p> <p>BASS 80:7,10 81:11, 24 82:4,8,13 83:8</p> <p>Bear 8:4</p>	<p>Bearing 126:6</p> <p>beginning 31:16 105:14</p> <p>begins 7:7 24:12 93:14 95:23 100:16</p> <p>behalf 7:8 8:4</p> <p>believe 16:3,21 17:16,17,18,22 19:7 25:20,21 29:13 30:11 33:15,23 35:19 47:22 51:12 53:20 60:15 65:14 68:1 78:14 82:8 88:24 90:7 101:21, 24 109:14 110:12 137:7,16</p> <p>believed 110:11,25</p> <p>benzoquinone 126:19</p> <p>Benzyl 128:6</p> <p>beta 63:5 78:4,16 126:20</p> <p>better 105:22 110:14 130:16</p> <p>beyond 28:22</p> <p>Bieg 72:19,21,22 73:5,7 74:11,15,20 75:7</p> <p>big 105:18 106:20,21</p> <p>Bill 8:3 9:10</p> <p>binder 118:20</p> <p>Birch 8:6</p> <p>bit 51:12 71:9 76:12 95:16 107:23</p> <p>block 131:23 132:5 134:6</p> <p>blocking 125:20 131:18 132:2,19,25 133:8,9</p> <p>blows 123:2</p>	<p>board 7:12 105:22</p> <p>bond 75:25 122:6 133:20 134:15</p> <p>bonds 116:10 117:1</p> <p>bottom 50:7 52:22,25 53:1 119:3,24,25</p> <p>box 67:7,10 115:19, 22</p> <p>boxes 67:6</p> <p>boy 69:2</p> <p>bps 24:21</p> <p>break 44:14,15 45:3 48:8,17 91:14 92:1 123:8 135:13 140:3</p> <p>breaks 135:17</p> <p>briefly 102:2</p> <p>brighter 110:21</p> <p>Broadway 7:17</p> <p>brought 128:1</p> <p>building 61:5</p> <p>built-in 122:4</p> <hr/> <p style="text-align: center;">C</p> <hr/> <p>California 7:1,14,18</p> <p>call 80:6,9 113:1 133:18</p> <p>called 47:22 68:7 73:14 82:5,7 115:18, 19,22 133:15</p> <p>calling 41:3 120:23</p> <p>calls 114:11 116:1</p> <p>Camino 7:14</p> <p>cancer 139:1</p> <p>cap 132:15 133:21 134:17</p> <p>capable 35:14</p> <p>capped 90:3,11 109:2 111:1,5</p>
---	---	--	---

capping 22:9,17 28:13 30:8 35:6 131:23 132:3,4,10 134:5	121:22 125:10 127:16 138:19	chip 136:13	82:18 83:13,25 84:1 98:23 105:15 113:6 139:23
caption 65:3	Certified 11:2,12 18:17 21:12 26:4 49:9,16 61:13 65:24 72:14 77:2 79:15 84:17 92:6 98:7 99:16 114:20 126:2 127:21 129:4 131:10	chip' 25:9	clearly 16:13 27:17, 19 116:10 117:2
carbamate 121:14,17 122:5,14,21 123:4		chloride 49:4 50:23 52:14 53:10,17 54:8, 12 55:3,12,16,18,24 56:6,9,16 57:12,13 59:12 60:9 62:13,16 64:1,9 71:5,12 75:14 77:21 78:10 126:17, 18	cleavable 114:5,9,10 115:24 116:12 117:3,10,14,15 118:10,11 119:5 122:9 124:5,8,10,13
carbohydrates 72:18, 25	cetera 12:1 15:13 16:6,24	chromatography 60:12	cleavage 22:24 30:7 72:18 73:3 74:1 75:17 76:10 117:24 118:10
carbon 76:3 127:11, 12 128:7,19,23 130:12,18,22 134:16	CH2 134:15	CH² 133:20	cleave 74:22 75:8
Carbonates 77:11	CH2-CH 134:15	CH²-CH 133:20	cleaved 74:17 75:12 123:7
carbons 127:16 133:21	challenge 119:21	citation 85:25 87:16 93:3	cleaving 118:2
carbonyl 74:22 75:9, 18 76:8,11	challenging 105:18	citations 95:14	clip 118:20
care 138:25	change 69:25 79:6 110:15 116:20	cite 21:1 23:1,16 29:9,15 31:6 33:11 35:7 50:25 70:10 80:11,13 94:24 95:2	CO2 123:2
carefully 52:10 53:24 58:22 75:4 83:18	changes 110:15 139:2	cited 85:5 86:11 87:19 93:6	coaching 111:13,14, 15
carries 84:15	characterization 34:14	cites 27:6,7 94:21 95:3	coated 139:5
carry 99:19	cheaper 110:20	citing 67:1	code 82:18
case 7:12 48:19 52:11 90:8 97:23 101:21 108:25 114:24 118:16,17 128:16 138:15	check 132:17	City 7:10 8:1	codon 139:11
case 7:12 48:19 52:11 90:8 97:23 101:21 108:25 114:24 118:16,17 128:16 138:15	checking 71:22	Cl2 72:19	coffee 91:24
catalyst 58:13 77:20 126:19	chelates 75:25	claim 113:24,25 114:2,3 117:15 118:9 137:8,14,19, 22 138:2 140:14,16	collaborate 105:8
Catalysts 126:8	chemical 22:9 49:24 114:5 116:10 117:1, 14,23 118:11 119:5 124:13 125:7	claims 113:23 119:12	collaborator 101:22
cause 28:21	chemically 114:4 117:14 118:11 119:5 122:9 124:12	clarification 64:11 73:15 121:16	colleague 7:24
caused 139:1	chemist 58:12	clarified 110:24	Columbia 7:10,23 100:7
cell 139:4	chemistries 93:22 94:17 97:9	clarify 14:19 37:25 104:20 105:1	column 20:22 21:5,6 23:2,17 24:23 25:10 29:10,16 31:7 33:12 35:9 40:12,14,19 41:7,9 42:1,2,7,9,14, 18,20 43:3,6,7,8,9, 16,18,22 45:12,18, 23,24 46:3,11,12,15, 18,22 47:2,6,14,18 60:11 84:25 85:14
Cella 7:25	chemistry 64:15	clear 16:8 38:3 39:4 71:18 81:2,7,21	
certain 88:2 99:4,25 112:12	chemists 57:14		
certainly 12:8,12 17:8 20:18 25:20 68:21 75:2 82:7 89:5 99:8 103:1 105:19 110:1 116:18,25 117:12	Chemoenzymatic 61:19		
	chief 70:19		

92:11,15,16 93:13 95:21 96:7 113:23, 25 114:1,2 129:10 135:21 137:9 com- 127:10 Combinatorial 79:12 come 100:1 105:15 112:13 coming 112:23 113:9 comma 44:3 commercialization 105:19 commercialize 105:10 commercialized 106:16 common 68:18 130:23 133:7 139:10 communicating 56:19 compare 41:16 compatible 71:13 118:12 122:10,15 complete 46:20 58:16 77:10 93:24 94:18 97:10 complex 61:20 73:13 75:21 78:20 component 117:9 compound 51:5,6,7, 10,11,19,21,22,23, 25 52:7,13,24 53:2, 16 54:3,4,11 55:1,6 56:3,5,9,17 57:5,6 58:24 59:1,3,19,20 60:4,6,8,21 63:6,15 74:23 75:9 77:17 84:3 130:12 134:22 compounds 126:25 127:11 128:13 129:23 130:1,10,17,	24 concentrations 56:11 concludes 141:1,4 conclusion 82:17 83:16,22 94:22 conclusions 68:13 80:22 81:1 82:25 83:6 conclusory 15:18 concurrently 82:6 condition 57:16 122:15 conditions 35:12 56:20 57:15 58:13 59:11,17 71:7 72:1, 2,3 74:17,21 75:8,12 117:16,22 118:12 124:6 confirm 80:16 confused 100:6 confusing 116:23 connected 116:5 consecutive 86:22 consider 121:2 consideration 34:22 considered 34:25 39:13 40:1 consistent 116:18 construct 138:17 contain 127:11 128:18 containing 22:9 130:21 133:20 134:16 contains 77:24 130:12,13 contaminating 68:11 69:20,23 70:1,8,10 90:16,24	contend 108:24 119:11 Content 19:13 context 36:22 118:7,9 continue 41:8 63:16 66:21,22 108:6 110:19,20 continued 117:23 continues 137:12 continuing 102:8 convenience 21:23 conveniently 73:1 conventional 103:21 conversations 48:18 conversion 74:6,7 convert 125:6 converts 73:9,10 copper 126:17 copy 21:18 84:20,21 135:9 corner 89:7 94:10 115:10 correct 10:9,12 11:7, 8,20,21 12:18,19,20, 24 14:5 15:5,7,23,25 16:1,18 19:8,10 20:12,13,16,23 21:6, 7,16 23:3,5,15,18 24:8 25:18 26:24 27:23 29:12,17 30:10 31:9 33:14,19, 20 35:18 36:20 37:23 38:23 40:7 41:5,15 42:3,10 43:4,23 46:4,12,13 47:3,19 48:5,6 49:4, 7 50:15,24 51:8,20 52:1,7,17 53:18 54:13 55:4,7,11,24 56:17 57:4,8,21 58:24 59:2,5,21,22	60:17,18,19,22 61:23 62:1,9,10,13, 17,22 63:7,10,21 64:2,3,7,21 65:7 66:19 67:18,19 68:14 69:6,20 70:8, 9,12,16 71:7 73:5,6, 11,12 74:23 75:9,18 77:18,21,24 78:2,5, 11,18 80:8,12 82:1, 2,5,14 83:25 84:9 86:1,9,13 87:21,25 88:10,23,25 89:4,9, 10,15,21 90:3,11,12, 16 91:3 93:8 94:2,5, 19,22 95:12 97:13, 20 98:2,15,20,21 99:11 100:12 101:5, 20,23,24 102:6,17 104:8,9,11,18 107:13 108:8,9,14 114:13,24 116:5,15 117:10,16,24 118:13,14 119:13,21 120:13,17,20,21,23 121:15,20,25 122:2, 7,10 123:21 124:2,3, 6,8,14,15,18,19,23 125:8 126:22 127:1, 7,12 128:11,14,20 130:2,18,22 131:14, 25 132:7,11,16 133:17,22 134:7,17 138:7 140:17,20,22 correctly 32:1 81:18 correspond 139:7 corresponding 126:20 cost 103:18,22 106:14,25 107:18 costs 107:2 110:19 counsel 7:19 115:8 count 130:15
---	--	--	--

couple 10:5 73:22	5,16 40:10,13,24	65:5,6 70:24 71:3	67:6 71:21 73:13
court 7:17 8:8,9	41:19,22,25 45:6,11	72:1 73:8 74:5 76:10	78:21 102:22
64:11 73:15 78:24	46:9,10 48:21,23	87:1,13 88:9 89:14	110:14,23 133:6
121:16	49:3 86:13 87:21	90:10 108:7 128:6	difficult 68:15 96:17
covalent 122:6	93:8 108:24,25	describe 16:7 120:25	97:18
criteria 117:17,19	109:16 118:15,17	127:14,15	difficulties 96:19,25
131:22 134:5	119:10,16 120:4,13,	described 14:8 52:15	Diols 77:12
cup 91:24	17 123:20 131:14	55:3,11,18,23 56:10	direct 23:20 121:14
current 28:2	decrease 28:22	59:4 60:10 66:16	126:11,24 131:16
cycle 25:7 28:16,18	deduced 66:13	127:17 134:19	directly 82:19 116:4
29:4 35:1 40:2 86:25	define 53:23 106:10	describes 54:7 56:4	117:11 121:24
87:4,12 88:9,21	definition 70:2 94:6	58:11 59:10	122:1,6
89:13 90:9 112:12	125:2	description 103:10,	disclose 124:12
135:25 136:10	definitive 102:19	14,16	125:17 133:19
cycle,' 35:7	demonstrate 90:9	design 34:22	134:14
cycles 25:7 87:8	demonstrated 87:14	Designed 79:11	disclosed 25:5 136:7
88:23 136:8,11	89:15 109:20 112:18	desired 25:13 29:25	discloses 53:15
Cyclic 77:11	demonstration 89:24	despite 68:9 69:19	54:10 128:13 132:7
	90:1,6	76:9	discover 109:6
	denoted 117:15	details 52:6,23 53:2,	discuss 45:4 138:13
D	denying 113:10,14	3,6	discussed 133:14
damage 125:7	deoxynucleotide	detectable 28:22	discusses 132:1
dash 47:23 73:16	104:6,18 105:5	detecting 66:9	discussing 24:14,18
data 136:14,17,21,24	107:12	detection 22:20,23	44:3 109:12
137:2,5	dependence 55:15	30:25 33:5 67:3	discussion 138:4
date 7:5 89:8 94:11	depending 38:14	determination 20:8	discussions 135:13,
99:1,11	depends 106:10	93:23 94:17 97:9	16
datp 68:11 69:20	depicted 120:5	develop 35:13	disease 31:4 33:9
70:1,8,10 90:16,24	deponent 8:11	developed 81:11,24	disparaging 27:20
ddntp 125:6	deposition 7:7 8:22	82:14 83:8	distinct 85:22
ddntps 124:17,19,22	9:5,12,17,24 10:2,8	developing 103:18	DMF 77:25
de 38:2	11:10 13:25 26:1	development 30:18	DNA 20:8 22:14,22,25
deblocking 134:8	35:22 45:4 92:1	31:20 32:23 103:25	25:4 30:20,24 31:18,
dec 28:2 34:9 39:15,	114:8,23 134:25	104:2	22 32:7,14,21,24
19 109:12	135:18 138:5 139:24	dideoxy 124:19	33:4 34:14 38:15
decade 66:14	141:2,4	Diego 7:1,14,18	71:13 79:12 85:16,
declaration 10:12,16,	deprotected 51:25	difference 47:21 48:4	19 87:11 88:4 89:3
20 18:15 21:16 22:1	deprotection 33:24	differences 72:9	92:22 104:5,17
23:15,21 24:10 28:1,	52:6 53:16 54:11	139:3	105:25 106:7,8
4 30:13 34:7 39:1,2,	60:20 62:8,12,15	different 27:13 43:25	107:11,12 109:3
	63:9,25 64:6,8,14,15		110:5 117:23 118:1,

2 136:6	121:23	employing 96:14	ethers 72:18,23 73:8
dntp 125:6	drew 120:17	ended 63:15	74:13,16 75:1,11
dntps 12:1,24 14:4	drive 110:19	ends 16:5,6,24 63:6	76:18 78:10,11,18
15:13 16:16 17:20	duly 8:14	entire 91:6	126:9,15 127:1,2,3,
18:5 104:7 105:25	dye 102:11,16 103:4	entitled 10:16 19:12,	4,6,7,15 128:7,11,
106:8 108:4,14		15 49:23 50:4 61:8,	14,18 129:12,16
113:13		18 66:2 72:17 77:10	130:2,7,9,11,18,21,
document 31:11 44:7	E	79:11 80:22 98:11	24 132:15,19,24
49:13,23 54:15,17	earlier 75:16 138:4,14	100:7,23 103:9	133:9,13,14 134:18
57:10 61:7,17 67:5,9	early 82:9	119:4 126:5 128:4,	eventually 107:20
68:17 81:14,16	easier 19:19 118:6	10 129:11 131:18	Evidence 128:7
84:15 86:3 88:2 92:3	easy 120:10	entry 62:25	evoked 132:13
98:11 100:7 125:22	echoing 34:1	environment 71:21	evolve 108:2,12
126:5 128:3	edited 57:1 116:17	environments 71:13	113:12
documents 10:7 61:5	efficiency 28:17 29:1,	enyl 73:9,10 74:6,7,	evolving 98:19
doing 41:12 125:11	24 30:7 87:2,5	21 75:1,7,19,25	100:23 112:10
dollars 112:25	88:10,22 107:19	76:18,20,21 78:11,	exact 33:22 138:8
double 75:25 108:6	109:11 110:23 112:3	18	exactly 14:6 25:19
133:20 134:15	efficient 33:25 69:11	enzymatic 49:24 96:3	71:8 74:25 75:22
doubt 68:23 69:13,15	109:10,13 110:10	enzyme 81:9,22	94:7 111:5
102:23	efficiently 22:13	82:12 83:7 111:4	EXAMINATION 8:17
Dower 119:12 120:8,	68:22 108:3,13	equation 77:17	135:1
12,15,16,19 121:13,	109:3,7 110:5,8	equivalents 59:13	examined 8:15
19,25	111:2,5 112:6	errors 28:20 116:16,	example 28:16 36:8
Dr 8:1,19 45:3 48:17	113:12	19,20	37:11 73:14 106:11
70:15,18 91:23	efforts 96:22 97:4	established 59:19	112:10
101:22 104:22	eight 127:12	esters 126:9 133:8	examples 11:23 15:9
110:25 111:19	either 140:25	estimation 109:19	16:23
123:17 135:3 139:18	EI 7:14	et 12:1 15:13 16:6,24	excuse 96:10 98:10
140:13 141:2	electrophoresis 80:4	44:2	exhibit 10:15,22,23
draw 11:15 12:7	element 113:24	et al 19:16 21:9 44:2	11:1,9,11 13:10
19:23 22:2 24:11	eliminate 76:4	61:21 66:3 67:1	18:14,16 21:10,11
39:10 46:22 48:24	eliminates 122:12	77:12 78:8 79:12	26:2,3 28:1,3 34:8
50:20 51:4 52:22	123:2	86:9,11 92:10 93:3,6	35:23 39:6,20 40:18
62:7,24 63:24 66:5	embedded 133:17	126:10 128:8	41:4,19,23 42:13
68:13 75:22 79:18	Emphasis 99:3	ether 49:3 50:22	45:7,18 46:9,15
80:20,25 103:8	emphasize 33:21	70:23 73:9,10 74:6,	48:22 49:6,8,15,19
119:23 120:5 122:19	34:4 68:25 69:14	7,21 75:7,11,20	50:4,12,13,14 51:3
123:24 128:9	emphasizing 33:24	76:1,20,21 77:18,19	61:11,12,18 65:21,
129:10,22		134:19,22	22,23 71:4 72:12,13
drawing 18:22			77:1,5 78:8 79:10,14
drawn 77:16 115:15			84:15,16 92:4,5

97:24 98:5,6,13,18 99:14,15,19 100:3,4, 6,12 101:5,19,20 103:7,14 113:22 114:17,18,19 118:17,18 120:11 123:18 125:14 126:1 127:19,20 129:3 131:5,7,9 135:5,7,21 136:18,22 137:3,6, 10	fact 27:9 32:9 61:25 68:9 69:19,25 70:5,7 98:25 106:21 factually 69:24 70:9 failed 125:4 fair 90:21 faithfully 22:13 familiar 17:1 95:6 far 87:15 103:2 fashion 52:15 55:3, 11,13,18 56:10,17, 23 58:9,11 59:4 60:10 fast 30:23 33:3,18,21 34:16 35:13 fast' 34:15 faster 69:15 feasible 103:24 feel 12:8 felt 139:3 fidelity 30:19 31:21 32:24 fields 30:25 33:5 figure 65:3 119:25 120:5,15,16,19,22 121:12,19,25 122:2, 14 123:24 find 38:24 58:16 111:4 finger 52:20 113:25 119:9 firm 8:1 first 8:14 12:11 19:24 31:14 48:24 50:13 61:23 63:4 66:6 72:21 73:9 74:6,11 77:13,20,23 79:20 96:8 100:16 111:12 126:12 134:20 Fitzpatrick 7:25	five 39:10,22,24 84:8 133:21 134:16 flawed 68:2 Floyd 7:8 8:13 10:16 100:11 141:2 fluorescent 66:24 67:13 85:23 96:15 97:19 98:2 102:11, 16,24 103:4 fluorescently 66:17 85:20 124:17,22 fluorinenal 122:3 fluorophore 108:4,13 109:8 113:13 116:13 117:4,9,11 121:5,8 122:3 138:11 fluorophores 102:25 Fmoc 120:22 121:3, 10,13,14,24 122:1,2, 3,4,11,14,20,21 FMOCS 123:5 focus 113:24 focused 25:22 125:20 focusing 73:24 follow 93:2 followed 73:10 74:6 75:12 following 12:13 29:19 34:12 follows 8:15 footnote 77:13,14,17, 21,24 forensics 31:3 33:9 form 17:5 50:4 121:17 123:4 forms 122:20 forward 19:19 21:23 112:23 forward-looking 83:17,22	found 43:3,22 46:3,5 47:2,18 four 22:4,6,11 23:12 24:1,12 33:23 34:2 53:12,18 54:9,13,18 55:7,24 56:2,7,16 57:7,20,24 59:1,15 61:25 62:3,5 63:18 64:7,9,12 65:7 85:24 107:15 114:24 127:11 140:1 fourth 50:3 fragments 138:17 frame 104:14 105:5 106:6 108:11 109:6 frankly 107:20 free 12:8 front 10:14,15,23 11:9 13:8,12 18:14 20:18 21:8 25:25 41:1,4,20 49:6,14 51:1 61:7,17 65:21 72:11 76:22 77:9 79:9 84:13,14,24 86:5,7 89:6 91:6 92:3,9 94:9 98:10,11 100:3,4 120:8,9,11 123:17 125:21 126:5 128:3 129:1 131:6 full 63:4 79:20 96:8 Function 126:7 fund 106:3 107:3 fundamental 22:5 23:12 24:1 86:16,20 87:24 funded 98:24 99:3,4, 7,13,21,22,24 101:8, 14 108:12 funding 112:9 further 96:4 107:23 134:24 139:18 140:23,24
<hr/>			
F			
<hr/>			
face 91:1,5 facilitate 80:1 facility 101:1			

future 72:6 83:2	99:11,22	good 8:19,20 44:13 48:7 91:13	122:20
<hr/>	Glycosides 61:20	grand 106:18	Harper 7:25
G	go 8:22 14:18,22,23 22:1 23:6 24:10 27:25 30:13 35:21 38:25 39:8 40:9,17 41:2,18 42:12,19 43:6 45:6,17 46:8, 14,21 47:5,13 48:21 50:11 51:2 58:15 62:6 63:23 68:22 72:21 93:13 95:21 97:22 100:1,15 103:7 111:25 113:23 118:15 119:15 123:23	grant 98:13,18,23 99:8 100:21 101:15, 18,19,23 102:6 104:15 108:10,19,22 110:2 111:4 112:25	head 139:9,15
Gal(nac) 61:19	goal 26:19,21 27:5,17 83:3 108:21 110:2 113:6,8	granting 113:11	headache 135:12
Garrett 7:24	goals 108:10,18 111:3	grants 100:1	heading 128:15 129:11,17
gel 80:3	goes 14:9 95:9 133:5, 10	great 103:17	heat 112:12
gene 31:2 33:7	going 10:14,22 11:9 12:4 19:19 21:8,23 25:25 34:7 35:21 36:10,17 37:13,20 40:21 41:11 44:16, 21 48:10 49:6,13 64:4 65:21 68:22 70:22,23 72:11 75:2 76:22 84:13 91:14, 16 92:3,4 96:7 97:25 98:4 99:14,19 102:3 105:15 106:21 107:3,4 111:14 113:21 114:18 116:9 117:1,19,25 118:19 120:8 123:10,17 125:13,21,22 127:18,24 129:1,2,9 131:5 133:2 140:6 141:3	greater 28:18 29:24	Helicos 100:7,25
general 75:1 95:14 117:18		ground 8:21 119:11, 14,20	help 105:10 110:3 112:9,16
generally 104:4,16 105:24 106:7 107:10		group 22:10,17 28:14 30:8 35:6 48:1 73:1, 4,25 74:2 76:8,9,11 79:21,25 95:13 100:25 109:21,23 125:1 127:15 128:17 130:24 131:24 132:5,10 133:20 134:5,6,15	hesitant 118:4
Generate 128:4		groups 66:15 72:25 108:5,14 112:5 113:14 125:20 131:18,23 132:2,3, 19,25 133:8	hexanes/etoac 60:12
generated 25:8 136:12		growing 22:22	hey 82:18
Generation 100:8 128:7		guess 13:17 51:17 65:9 94:7 99:6 104:20 134:12	high 22:18 30:19 31:21 32:24 137:25
generic 99:5		<hr/>	high-throughput 30:19 31:21 32:24 33:18 34:5,19
generically 121:7		H	high-throughput' 34:17 35:15
genetic 31:4 33:9			higher 29:2
genome 30:22 31:24 33:3 38:1,10,17,22 98:14,19 100:9,22, 24 102:8,14,18 103:23 105:17 106:13,14,18 107:3 109:5 112:23 113:1, 5 138:15,17			highlight 68:19
genomes 38:7 103:19 105:16 110:4 112:24			hindered 76:3
genus 127:7			history 99:22
getting 20:24,25 76:13 110:18			hold 39:16
Gibbs 66:16			Homoallyl 126:9
give 8:24 9:1 18:21 62:18 76:16 100:5 109:6,20 111:4 139:16 140:2			honest 99:7
given 18:22 55:8,9			hope 76:13
gives 27:16 59:11			hour 36:12 37:15 48:8 91:14
			hours 9:18 10:5 53:12,18,20 54:9,13, 18 55:7,24 56:2,7, 12,16 57:8,21,25 59:1,15 63:18 64:7, 9,12 65:7
			human 38:17 98:14 100:22 105:16 106:13,14 109:4 138:14

<p>hundred 25:16 30:1 136:25</p> <p>hurdles 97:11</p> <p>hybridization 11:25 12:23 14:3 15:12 16:16 17:19 18:4</p> <p>hydrogen 134:16</p> <p>hydrogens 133:21</p> <p>hydrolysis 75:13</p> <p>hydrolyzed 75:20</p> <p>hydroxy 72:25</p> <p>hydroxyl 125:1</p> <p>Hypervalent 128:4</p> <p>hyphen 47:23</p> <hr/> <p style="text-align: center;">I</p> <hr/> <p>i.e 28:23 30:2</p> <p>Id 24:22 25:9</p> <p>idea 91:4</p> <p>ideas 105:10</p> <p>identical 41:14,17 43:24 44:4,10,12 47:20 48:2</p> <p>identification 11:2,12 18:17 21:12 26:4 31:3 33:8 49:9,16 61:13 65:24 72:14 77:2 79:15 84:17 92:6 98:7 99:16 114:20 126:2 127:21 129:4 131:10</p> <p>identified 25:6 135:25 136:8,10</p> <p>identify 7:19 139:7</p> <p>Illumina 7:9 8:4,6 70:20 107:20</p> <p>imagine 125:11 139:14</p> <p>impact 72:9</p>	<p>implicit 59:16</p> <p>implies 56:21</p> <p>important 34:22</p> <p>improved 100:8 105:2</p> <p>improvements 105:3</p> <p>inability 104:4,17 105:24 106:7 107:11</p> <p>incentive 103:17 106:20</p> <p>incentives 106:21</p> <p>include 105:23</p> <p>included 16:12 58:23 95:13 107:10 128:17</p> <p>includes 95:12 127:7 134:18</p> <p>including 66:15 70:5 95:7 104:11,15,16 105:4 106:6</p> <p>inconvenient 96:18</p> <p>incorporate 108:3,13 109:7 113:12</p> <p>incorporated 22:14 69:15 109:3 111:2 124:25</p> <p>incorporates 111:5</p> <p>incorporating 138:10</p> <p>incorporation 22:19 29:7 66:10,23 67:21 69:5 70:5 87:1,13 88:9 89:14,25 90:2, 7,10 131:19,24 132:6 133:1 134:7 137:17</p> <p>incorrect 53:21</p> <p>increase 35:3 40:4</p> <p>increasing 107:19 110:18,23</p> <p>independent 18:13</p> <p>indicate 55:17 70:15</p>	<p>138:6</p> <p>indicated 138:5</p> <p>indicates 98:18</p> <p>indication 91:1</p> <p>individual 140:22</p> <p>industry 105:8</p> <p>inefficiencies 29:3,5</p> <p>inefficient 93:22 94:16 97:8</p> <p>inevitably 61:2</p> <p>information 93:10 98:12 99:24 103:8 115:2 138:20</p> <p>inherent 86:21</p> <p>Institute 98:15 100:22 109:5</p> <p>instrumentation 96:5</p> <p>intended 24:5</p> <p>intending 69:13</p> <p>Inter 10:17</p> <p>interest 87:7 88:23 138:12</p> <p>interested 105:11</p> <p>internal 76:2 126:6</p> <p>interpret 58:6</p> <p>interpretation 57:6 96:16 97:17</p> <p>interpretations 69:18</p> <p>interpreted 58:7</p> <p>introducing 95:3</p> <p>introductory 95:20</p> <p>inven- 11:5</p> <p>invention 11:5 20:7</p> <p>inventor 91:8</p> <p>involve 17:9 18:6</p> <p>involved 17:6 105:9</p> <p>Iodanes 128:4</p>	<p>Iodine-centered 128:5</p> <p>IPR 10:7,12 48:22 140:1</p> <p>IPR2013-00128 11:10</p> <p>IPR2013-00517 18:15 26:1 28:4 35:22</p> <p>IPR2018-00797 7:12 10:9 48:23 108:25 118:16 139:25</p> <p>IPRS 114:24</p> <p>isolated 64:19,20,23, 25</p> <p>isomerization 72:17 73:2 74:1 75:17,18, 19 76:10</p> <p>isomerize 75:3</p> <p>isomerizes 76:1</p> <p>issue 94:11 97:23</p> <p>issued 89:8,12 94:16 97:13</p> <p>issues 97:15</p> <p>item 65:17</p> <p>iterative 86:21</p> <p>iteratively 66:13</p> <p>IX 119:11,14</p> <p>IX.A.9 119:4,20</p> <hr/> <p style="text-align: center;">J</p> <hr/> <p>January 50:9 89:9,12 94:11,15 97:13,16</p> <p>John 7:24</p> <p>Jones 66:16 84:25 85:18 86:8,12,19 87:20,23 88:6,7,13, 14,18,20 89:1,4,7, 11,12,17,20 90:13 91:2</p> <p>Ju 19:16 20:6 21:9</p>
---	---	---	--

23:1 24:19,25 25:3 26:21 27:5 28:25 29:9 30:15 31:6,17 32:6,20 33:11 34:1 35:8 36:14,15 37:17, 18 65:13 101:22 135:4,20 136:3,17, 21,24 137:2,6,10 Ju's 20:6,14,16 22:4 23:12,25 24:4 25:3, 13 28:13 29:25 30:5 34:14,23 35:1,6,15 39:14 40:2 65:12 100:25	19,24 72:5 <hr/> L <hr/> lab 70:15 91:3,10 label 22:8 85:23 114:10 115:25 120:23,25 121:2,6, 10 124:13 labeled 22:8 66:18 85:20 102:11,15 103:3 115:1 123:25 124:17,22 129:23 130:10 134:8 labeling 12:1,24 14:3 15:12 16:16 17:20 18:5 102:24 labels 96:15 97:19 98:2 124:1 125:17 labile 73:3 74:2 law 82:23 lay 139:10 leaves 51:10 57:17 123:3 leaving 32:13 led 34:19 left 12:9 77:17 79:19 80:20 86:4 98:17 102:9 legal 68:16 82:24 legend 62:20 length 25:13 27:10 28:11,19 30:1 36:7 37:10 lengths 27:22 36:5,11 37:8,14 110:18 let's 14:18 42:13 62:4 76:7 107:22 114:15 118:9 level 66:23 69:4 95:20 139:2	levels 67:21 Library 50:4 ligands 58:14 Likewise 29:22 limit 87:9 89:2 limitation 27:8,10,12 86:20 87:24 119:4 137:23,25 limited 104:4,16,21 105:1,24 106:2,7,10, 25 107:11,18 limits 28:22 Linda 8:8 line 11:16 12:7,14 14:23 15:1,18 23:2 26:11,14 27:2,3 34:13 35:24 37:3 39:22 41:8,9 42:18 43:18 60:3,5 65:11 80:25 85:15 86:15 92:11,16 93:13 95:23 96:8 114:3 115:12 lines 20:22 21:5,6 23:17 24:12,23 25:10,22 29:10,16 31:7 33:12 35:9 39:10,22,24 40:14, 20,23 42:2,7,9,14, 21,23 43:3,6,7,9,16, 22 45:13,18,23 46:3, 11,12,16,18,23 47:2, 6,14,18 48:25 81:1 86:15 93:3 119:24 135:21 link 114:10 115:25 linkage 121:15 122:14 linker 114:5 117:14 118:2,11 121:5,7 122:4 124:2,5,7,13 linker.' 119:6	linkers 102:25 list 16:4 23:13 61:23 93:10 133:11 listed 12:17 14:11 15:22 16:4 17:11 64:9 108:17,20 lists 11:18 15:3 95:5 litany 133:6 literally 107:15 literature 71:16 little 51:12 58:18 68:15 71:9 107:23 116:7,23,24 117:7 118:4 122:20 Livenote 65:10 located 7:14,17 83:21 long 27:18 59:18 101:25 110:18 133:11 longer 26:21,22 27:14,19 38:13 47:23 138:15 look 14:23 19:25 26:10,14 27:2 35:24 38:4,20 41:8 42:20 43:15,16 45:18,22, 23 46:15,21 47:5,14 49:22 51:12,18,23 53:24 54:20 62:18, 20 67:17 74:10 82:17 85:14 86:15 89:7 92:11 94:10 97:24 98:17 107:22, 24 113:22 114:15 129:19 133:24 looked 54:22 97:7 140:14 looking 42:13 54:1,2 62:21 64:5 77:14,16 84:14 135:20 loosely 130:23
<hr/> K <hr/> Kang 77:12 78:8,9 keep 32:13 41:19 51:1 52:20 113:25 119:9 120:9 ketone 76:21 78:2,16 ketones 126:9,21 kind 78:19 106:20 113:6 knew 106:23 113:9 Knobbe 7:13 8:3 know 13:14 14:11 18:23 38:9,11 40:22 41:10 42:15,22 43:12,17 45:19,25 46:19,24 47:9,15 53:3 58:6 67:5 70:17 73:12 75:22 82:6 90:4 93:10 102:20, 21 105:21 115:4 116:22 125:13 130:25 139:12 knowing 69:11 knowledge 69:9 known 28:25 29:23 57:23 58:3 71:11,17,			

loss 61:2 lot 61:5 100:1 102:22 134:10 lots 36:3,4 37:6,7 139:1 low 66:25 67:21 69:5, 10 70:6 103:18 137:25 Luman 8:5 <hr/> M <hr/> making 107:19 manipulations 96:4 manuscript 51:16 53:21 Marcus 8:5 9:10 mark 13:12,13,18 26:8 61:3 98:4 99:14 114:16 125:14 127:19 marked 11:1,11 13:11 18:16 21:10,11,18, 19,20 26:2,3,6 35:22 40:18 49:8,15,19 61:10,12,18 65:22, 23 72:12,13 77:1,4,6 79:14 84:16,20,21 92:4,5 97:23 98:5,6 99:15 114:19 118:16 123:18 125:22 126:1 127:20,24 129:2,3 131:7,9 marking 49:20 114:18 Marquette 8:8 Martens 7:13 8:4 material 36:15 37:18 matter 7:9,23 16:25 17:15 38:5 109:16 mean 19:5 33:22	47:25 48:2 53:24 57:24 58:5,21 71:18 72:8 75:2,20,24 78:19 82:9,24 83:17 84:5 104:19 106:11 110:9 116:6,22 134:8,9 meaning 106:2 means 13:15 56:24 57:7 58:9 103:13 105:1 115:3 126:7 meant 69:10 78:20 79:3 104:20 107:17 114:8 130:25 measurements 96:16 mechanism 73:19,21 75:3 78:21 mechanisms 73:21 75:21 78:20,21 meet 9:4,11,19 meeting 9:14,19 10:3 102:2 memory 10:6 23:7 Menchen 8:2 mention 132:14 mentioned 9:23 122:5,21 mentions 132:23 meritorious 110:12 met 8:22 9:9 methanol 53:9,17 54:8,12 56:6,11 57:13 59:12 62:13, 17 64:1,9,12 71:5 method 11:6 20:9,16 24:4,20 25:1,3,14 27:7,21 30:6 35:4,16 40:5 66:2 87:10 88:8,17 89:2 97:25 136:3 137:11 140:16 methodologies	103:25 methods 22:4 23:12, 25 24:19 71:11 86:22 103:21 104:2 105:4 131:19 133:1 134:8 Metzker 66:25 67:18 68:9 69:6,18,22,25 70:4,11 80:17 84:9, 10 85:25 86:9,11,12 87:16,19,20 89:21 90:2,6,9,14,22 91:3, 10 93:3,6,7,9 94:22, 24 95:2,7,12,13 106:11 109:1,19 111:2 119:13 125:15,16,19 Metzker's 67:20 68:2 70:15 90:15 mg 52:13 53:8,10 60:4,8,13 Michael 70:11 91:3, 10 middle 42:8 74:11 129:23 mild 117:22 122:12, 23,24 million 25:8 136:11, 15,19 Min-u-script 115:3 mind 13:18 38:18 mine 26:6 67:6 minute 12:25 54:19 62:18 minutes 128:1 131:3 140:5 mischaracterize 54:16 81:15 mischaracterizes 31:10 44:6 54:14 57:9 67:5 78:12 81:13 86:2 89:16	misread 31:12,13 missing 76:8 125:1 misspeak 75:4 mistake 65:10 mixture 53:11 56:20 59:14 ml 53:9 Mm-hmm 39:23 mmol 52:13 53:9,11 60:8 modifications 81:3,8, 21 82:12 83:6 133:10 modified 69:3 71:6 104:6,18 105:5,25 106:8 107:12 109:22 110:6 modifying 72:3 moiety 22:9 molar 59:13 molecular 96:13 moment 33:22 36:24 money 109:6 111:4 Monica 62:4 monitor 58:15 mor- 122:24 morning 10:5 motivated 109:1 multiple 80:2 115:4,7 128:23 Murnane 7:24 mutants 83:19 <hr/> N <hr/> name 7:16 50:16,17 94:3 99:5 names 9:8 62:2,3
---	--	--	---

narrower 95:16	novo 38:2	53:16 54:11 102:3	19:11,21,22 21:8,21,
Nate 8:5 9:10	nuclear 116:14 117:5	109:21,23 112:4,5	24,25 22:1 23:11
National 98:14	nucleic 11:7,24 12:23	132:19	27:1 31:16 37:1,2
100:21 109:4	14:3 15:11 16:15	O-allyls 112:18 113:7	38:25 40:9 41:1,18
natural 68:23 69:1,12	17:19 18:4 137:11	O-mom 77:18	42:12,19 43:15 44:4
102:12,16 103:4	140:16,19,21	O-o-allyl 49:3	46:8,14 47:21 48:4,
110:1	nucleobase 117:5	O-octyl 51:13	17 49:13 50:11 51:1,
nature 139:3	nucleophile 76:3	oath 8:14	23 53:5,15 54:10
nearly 28:14 30:6	nucleoside 81:23	object 67:4 111:15	55:6 57:3 59:1,19,23
neat 69:2	82:13 83:7 102:24	139:25	61:3,15 63:23 64:22
necessarily 125:13	Nucleosides 79:11	objection 16:19	65:2 67:12,17 69:17
need 12:9,12 13:5	nucleotide 20:7 22:7,	31:10 44:6 54:14	70:25 72:11 73:24
22:12,18 33:24 38:6,	11,20 24:22 27:22	55:20,25 57:9 58:1	74:4 76:22 79:9
7,18 44:15 85:8,11	31:1 33:6 38:8,9	59:6 69:7 78:12	80:19 83:4 84:13,22
97:24 125:14 130:5	66:9 68:22,23 81:9	81:13 84:3 86:2	85:4 86:7 91:12 94:9
138:15,18 139:8	86:5,7 89:24 90:1,3,	89:16 107:14 111:7,	95:21 99:9,14
needed 30:24 33:5,24	6,11 105:12 109:2	16 113:16 139:19	101:10 103:3 105:23
105:3 106:2	111:1,5 115:16	OBN 77:18	107:9,22 113:20
needs 132:10	120:20 121:25	obvious 119:12	115:2 117:6,8
Neighboring 126:7	124:14 125:8 131:24	obviously 23:8 82:9	118:25 121:24
never 36:5,8 37:8,11	132:5,16 133:22	occur 117:23	125:21 127:10,18
38:8 67:6 102:4	134:6,17 137:17	occurs 60:21 73:8	128:17 129:1
132:9,23	138:7,9 139:5	74:5 87:5 88:21	130:12,20 131:1
new 7:10 8:1 79:9	nucleotides 11:19	Ochiai 128:8	134:23 135:10,20
92:3,4 103:25 104:1,	15:4 26:23 27:5,8	October 7:1,5 64:13	136:3,14,21 137:8,
3,10,15 105:23	29:8 38:7,12,16	71:24 82:10 88:15	14,19 140:2
106:6 107:10 109:6	66:18,24 67:21	100:10 124:4,11,16,	Olefins 126:6
news 100:9 102:8,14	86:23,25 88:8,16	21 125:5	Oligosaccharide
NI 113:10	93:24 94:18 97:10,	octyl 51:15,19 63:1,4	49:24
NIH 106:3,18,22,24	19 98:1 102:3,10,15	odd 58:18	Olsen 8:4
107:3,4 111:3	103:3 109:8 110:17	Office 7:11	One's 73:14
nine 128:19	112:5 123:25 124:2,	officer 70:19	ones 95:20 133:6
nitrobenzyl 90:3,8	17 125:17 139:6,8,	offices 7:13	open 42:19 61:5
note 33:17	12 140:19,21,22	oh 13:1,10 19:10 21:2	opens 88:3
noted 27:12	number 13:16 77:6	26:8,12 32:12 47:23	operation 93:25
notice 99:1,2,5,10	99:19 127:16 137:23	53:23 54:4 60:5	94:18 97:10
notion 106:17	138:20	100:4	opinion 12:22 14:2
novel 98:19 100:23	numerous 93:21	okay 9:4,11,22 10:11,	16:15 17:4,23 18:3,
101:2		22 12:15 13:21,22	11 20:14,20 21:3
	O	14:18 15:20 18:1	23:5,8,11,16 24:7
	O-allyl 50:22 51:7		25:17 29:12,14,15

37:22 40:7 50:22 71:3 104:13 opposed 118:7 125:1 optimism 109:20 optimization 110:22 optimize 106:4 optimized 105:20 optimizing 105:2 order 28:10 38:14,15 86:23 88:7,13,15 ordinary 20:1,4 23:23 24:24 25:11 26:17 28:12,24 29:22 30:3 34:20,24 35:10 39:12,25 57:19,22 71:10 78:7,25 79:1 82:10,16,21 83:5 88:14 output 97:18 outside 9:19 139:20 overall 35:3 40:4 overlap 138:18 oxidation 77:11 78:14 126:6,15 128:6,11 oxidized 78:10 oxygen 122:22 126:7, 17 ozonolysis 75:12	28:5,6 34:12,13 35:23 38:25 39:8,21, 22 48:24,25 49:2,23 50:3,4,7,19 51:4 52:3,5,12,19,23,25 53:1 54:2,23 55:1 56:4,8 59:23,25 60:5 62:6,8,23,24 66:6,7 72:21 74:11 77:14 79:18,19 80:15,19, 21 89:6 91:6 94:9 100:16 115:4,9 118:25 119:3,9,10, 15,19,24,25 120:3,4 121:1 123:23 126:11,25 128:9 129:9,11 pages 115:4,7 131:16,17 133:25 pair 26:19 pairs 24:21 25:2,8,15, 16 28:11 136:4,12, 15,19,22,25 137:3, 20,23 138:22 Palcic 62:4 palladium 49:4 50:23 52:14 53:10,17 54:8, 12 55:3,12,16,18,23 56:5,9,16 57:12,13 59:12 60:9 62:12,16 64:1,9 70:24 71:5,12 75:25 76:2 77:21 78:9,21 126:8,16,18 Panel 99:4 paper 49:1,7 50:12, 20,22 51:1,17,18 56:12 59:21 61:3,18 62:3,5,16,19 63:11, 24 64:5,8 65:1 66:2, 6 67:18,25 68:4,10, 13,17 69:6,17,19,21 71:20,25 72:12,17 73:24,25 74:4,5,8 75:5,6 76:22 77:9,14	79:10 80:17,20 82:11 83:11,15,19 84:9,10,11 86:11,12 87:19,20 89:21 90:14 93:6,7,11 125:19 127:6 128:14 129:1,7 130:3,21 papers 61:22 73:20 94:21 paragraph 19:23,24, 25 20:25 21:1,2 22:2,3 23:13,21 24:11,13 25:23 27:25 28:6 29:19 30:13,14 32:5 34:7, 11 40:9,10,13 41:18, 22,24,25 42:5,8 45:6,9,11 46:8,9 66:6 79:20 85:15 88:3 93:14 100:15 119:19 126:12 129:17 137:9 parallel 80:2 96:22 97:3 parens 55:2 parent 134:19,22 part 16:5 17:7 18:12 95:1 107:1 114:10 115:24,25 116:11 117:2,3 119:19 124:7,8,9,10 134:25 Partes 10:17 partici- 112:15 participating 112:23 particular 16:4 20:9 79:20 115:16 132:21,22 particularly 96:14 97:18 partner 8:5 parts 18:7 46:6 133:15	pass 60:13 patent 7:11,12 10:18, 23 11:6,20 13:3,4,8 14:8,14,20 15:5 16:4,7,12,22 17:1,16 19:16,20,21 20:15, 16,18,21 21:5,9,15, 24 23:1,7,17 29:9,16 31:6 33:11 35:8 36:15 37:18 40:11, 14,17 41:1,2,3,5,8, 14 42:1,12,17,19 43:2,4,9,15,21,23 44:1,3 45:12,17,22, 23,24 46:2,4,5,10, 14,21 47:1,3,5,13, 17,19,24 84:24 89:7, 8,13 90:17 91:2,5 92:9 94:11,16,20 97:7,13,22,23 98:1 101:8,14 113:22 118:10 120:12 131:8,13 135:4,20 136:18,21,24 137:2, 6,10,22 138:2 140:14 patents 41:19 118:5 pending 7:10 people 73:19,20 105:11,13,15 106:14,15,23 110:16 112:7,14 130:23,24 138:24 peptide 123:5 percent 28:19 29:2, 25 60:21 61:1 64:6, 10,12,16,18,19,20, 22,23,24 65:2,4,12 87:2,5,6 88:2,10,21, 22 99:25 perform 112:6,15,21 period 44:2 permanent 124:22
<hr/> P <hr/>			
p.m. 7:2,6 44:22,23, 24 45:1 48:11,12,13, 15 91:17,18,19,21 123:11,12,13,15 140:7,8,9,11 141:3,4 page 10:19,20 11:15 12:4 14:25 15:1,17 18:20 19:11,12 24:10 26:10 27:1,25			

permanganate 75:14	59:23 60:1 62:6,7,23	95:22	primary 123:6
permit 28:19 67:3	63:23 66:5 72:21	portions 20:21 21:4	primer 139:10
Peroxyiodane 128:11	74:10 77:13 79:18	44:9 97:6	primer-directed
person 25:11 26:17	80:15,19,20,25	POSA 64:13 73:7	66:11
30:3 34:20 35:10	84:25 85:14 86:15	74:20 83:14 88:6,20	principle 106:12
57:19,22 71:10 75:5,	92:10,11 93:13	89:3,11 94:14 97:6	prior 19:13 24:19
6 78:7,25 79:1	95:21 100:15 103:7,	109:1,20 124:4,11,	68:13 138:5 139:21
82:10,16,21 83:5	8 113:23,24 114:1,2	16,21 125:5	probably 23:10 38:3
88:14	115:9 118:15,25	pose 134:13	94:7 120:24
perspective 68:6	119:2,9,15,23 120:3,	position 83:21	Prober 119:12
Petition 10:17	15 123:23,24	possible 35:2 40:3	123:19,20,23
Ph.d 52:5	126:11,24 128:9	125:6	124:12,15
Ph.d. 7:8 8:13 10:16	129:10,22 131:16	practical 138:21	Prober's 123:25
51:3,6,24 53:15	point 38:8 95:19	practice 28:25 97:12	124:1,17,22
54:10 141:2	106:17 107:2	precede 73:23	problems 56:18
pharmacogenetic	pointed 65:9 78:23	preceding 80:13	93:21 94:16 96:4
33:1	96:23	predict 72:6	procedure 125:7
pharmacogenetics	polymer 140:19,21	prefer 8:25	proceed 35:2 40:3
30:21 31:23 33:2	polymerase 20:8	preferably 25:15	proceedings 140:1
phasing 28:20	22:14,15 29:6 36:3	premarked 49:22	proceeds 53:18
place 9:14 55:7 65:7	37:6 66:11 81:8,22	126:8 129:11,16	54:13
118:11 138:16	82:12 83:7,19 85:21	prepare 10:1	process 61:2
placement 38:19	105:9,20 109:4,9	prepared 10:11	processes 22:24
places 38:12	112:11 131:25 132:6	preparing 9:17	processing 96:6
plaintiff 7:9	134:7 138:10	presence 90:15,23	produce 74:22 75:8
platform 112:18	polymerases 98:19	present 7:19 48:22	76:4
please 7:19 10:19	100:8,23 101:2	56:21	produced 74:21 75:8
11:15 12:5,7,10	102:13,17 103:1,5	preserved 139:22	78:1
18:1,20 19:11,23,24	104:5,17 105:25	president 70:19	produces 76:5,7,14
22:2 23:20 24:10,11	106:8 107:11 108:2,	pretty 95:6	product 78:4 87:7
25:24 26:10,14 27:1,	12 109:7 110:3,13	prevent 93:23 94:17	88:23
2,25 28:6 30:13	112:6,19,21 113:12	97:9	production 78:15
35:23 37:2 38:25	polymorphism 30:21	prevented 118:3	products 78:1,10
39:3,8 40:9,17,20	31:23 32:25	previous 114:24	program 106:22
41:2,7,8,16,18	polymorphisms 31:1	previously 11:1,11	progress 83:2 107:2,
42:12,14,19,20 43:6,	33:6	18:16 26:3 49:8,21	19
12,15,16 45:6,17,19,	polynucleotide 11:24	84:19 131:7,9	project 98:12 99:11,
22,23,24 46:8,14,21,	12:22 14:2 15:10	promising 104:1	22,23,24 103:8
23 47:5,8,13,14	16:15 17:4,6,8,18		
48:21,23,24 49:22	18:3		
50:3,11,19,20 51:1,	poor 102:12,16 103:4		
4,18 52:3,19,22	portion 29:19 44:11		
	90:19,20,21,25		

promote 68:18	purify 58:17	30:6 49:4 50:23	reactions 36:4 37:7
prone 125:10	purpose 24:6	71:17,25	73:13,19,23 105:11
prop-1-enyl 73:4	purposes 139:24	quench 58:17	read 12:5,8,13,25
74:2,12,16 75:11	pushing 112:22	question 11:18,22	13:24 25:13 27:4,9,
propargylamine	put 10:14,22 11:9	12:11,15 13:22 14:1,	15,18,22 28:9,10,19
124:3,8	13:7,11,16 21:8	16 15:2,8,18,19	29:20,21 30:1 31:16
properties 101:2	25:25 34:16,18 49:6,	16:5,9,25 17:24,25	32:1,15,17,19 34:11,
propine 75:11	13 57:1 58:18,20	18:1 25:23 26:16	12 36:1,4,7,10,21,24
proposal 98:13	61:17 65:21 68:6	37:2,22 38:22 41:11	37:7,10,13 38:9
101:9,14 104:15	72:11 76:22 77:9	62:14 67:14 68:16	40:21,25 41:9 42:14,
108:10 110:12	84:13 92:3,9 100:3	70:3 71:2 74:24 75:6	18,21 43:1,12,16,20
protected 51:7 68:11,	113:20,21 120:8	78:24 109:11 111:7,	44:9,12 45:19,21,25
21 109:8,21 125:2	123:17 125:21	17,20,22,25 112:2	46:1,7,18,23 47:8,15
protecting 108:5,14	127:18 129:1 131:5	115:14,21 116:3	52:10 55:2 57:11
109:23 112:4,5	137:22	118:7 125:15 130:16	58:22 62:19,25
113:14	putting 10:15 18:14	134:13 140:13	63:14,15,16 64:13
protection 72:24	61:7 79:9 84:14,24	questions 17:2 70:23	65:1 67:25 68:4,5
123:5	98:10,11 100:4	85:7 121:9 134:24	69:2,9,11,12 74:25
protein 96:10,12	120:11 126:5 128:3	135:3,13,17 139:18	75:16 78:13 81:6,17,
97:17 138:25	131:6	140:23,24	19 82:15,19,22
proteins 139:1	pyridine 123:1	quick 123:8 139:16	83:14,15,18 85:1
protocols 66:17 67:2	Pyrophosphate 66:3	quickly 35:2 40:3	89:17 90:19,21,25
proton 122:22	pyroseq- 110:7	133:24 134:11	91:6,7 95:22 96:11
provide 95:17	pyrosequencing	quote 31:14	110:18 117:7 127:8,
provided 16:14 52:24	24:19 27:6,20 110:7	quoted 100:12	13 128:15 129:7
103:11		quotes 34:16,18	130:3,4,5 132:18,20
provides 11:22 15:9	Q	R	133:2 134:9,10
16:23 52:5 121:10	Qian 49:1,7,25 50:8,	Radicals 128:5,8	138:3 139:11
providing 27:21	11,12,14,19,21 51:3,	ran 102:5	reader 20:14 83:24
publications 10:7	8,25 52:9,12,17	rapid 35:11	readily 74:16 75:11
published 61:21 66:4	53:7,13,15 54:10,23	ratio 28:21	reading 26:20 36:14
69:22 72:20 77:12	57:5 60:3,18,20	reaching 94:22	37:17 56:21 57:4,19
79:13 84:9 93:11	61:21,22,23,25 62:1,	reaction 22:16 50:24	62:2 63:16 67:10
100:9 126:10 128:8	6,11,12,15,23 63:23,	55:6,8,9 56:20 57:5	73:7 74:11,20 75:5,6
pull 135:4	25 64:4,5,13,14 65:6	58:12,15,16 59:10,	78:8 82:11 83:5
pure 83:14	71:4,7,24 72:5	18 62:8 63:9,20,25	88:2,6,13,14,20
purification 60:11	Qian's 51:6,24 52:3,	65:5 71:12,19 75:13	89:4,11,22 90:17
61:1	5,19 59:20,21,23	77:16,20,23 78:1	94:14 97:6 134:12
purified 60:25	64:15 65:6 72:1	121:12 122:18 128:1	reads 11:17 26:15
	qualify 138:1		27:3,14 35:25 36:13
	quantitative 28:15		37:16 78:25 83:1
			94:20 100:19 102:9
			103:16 108:1 114:3
			115:13

reagents 56:20	reducing 107:18	reinitiate 118:1,2	114:21 121:16 126:3
real 7:14 138:21	reductions 103:22	related 18:7	127:22 129:5 131:11
Real-time 66:3	reexamine 94:23	relates 11:6 98:13	reporting 7:17 8:9
really 44:15 85:7	refer 19:20 20:20	102:6 119:11,20	60:20
reason 8:23 9:1 38:6	21:24 40:11,13,24	relating 48:18 92:1	reports 56:12 60:25
53:20 56:13 58:4	41:13 42:1,7,8 46:10	relationship 10:9	62:11,15 64:6 65:2,3
118:3	57:15,16 69:5 77:13	91:9	represent 7:20,23
reasonable 139:10	80:5 104:10 119:25	relative 109:11,12,17	represented 114:9
reasonably 33:25	130:23 131:14	112:3	represents 108:21
112:19	137:14	Release 50:4	114:4 117:9 119:5
reasons 109:10	reference 44:1 67:1,	relengths 110:4	120:19
reassemble 38:7	17,18 80:11,14,16	relied 68:12	require 103:24
reassembly 38:2	93:10 95:10,17	relies 95:11	139:12
rec- 112:14	120:9,13 123:19,20	rely 49:1 50:21	required 35:12 37:25
recall 71:8 85:3 88:1	135:24 138:5	123:19,20	71:21 81:10,24
89:22 90:17 100:13	references 80:5,15	remain 22:24	82:13 83:8 103:23
125:16 138:8	95:18	remember 34:3 98:24	109:18
received 95:1,16	referred 20:10 21:4,	101:25 102:19	requirement 26:19
99:2,10	15 45:12 94:4 101:5,	109:13 114:12,14	118:5
recess 44:23 48:12	18 127:1 128:14	remembered 68:8	requirements 22:5
91:18 123:12 140:8	130:1,7,11,21	removable 85:23	23:12 24:2,3 71:14
recites 137:10	referring 16:3,25	removal 28:17 29:1,6,	requires 28:25 30:6
recognition 103:1	17:14 51:3 54:4	23 35:5,11	96:3
105:20	84:11 87:23,25	removed 22:18 28:14	reread 13:24
recognitions 110:23	89:23 90:5,7 95:2	49:3 50:23 73:2 74:1	rereading 10:6
recognize 112:15	refers 56:19 57:12	renders 96:15 97:17	research 98:14
recognized 112:19,	86:9 89:21 90:13	repeat 13:22 37:2	100:22 109:5,6
20 113:7	99:24 121:7 127:6	42:4 62:14	researchers 66:14
recollection 99:23	refined 87:4	repeated 38:13	resequencing 30:24
101:7,13,16	reflect 107:5	repeating 111:17	33:4
record 7:4 12:6 32:8	refresh 23:7 101:7,13	report 53:19 72:5	respectfully 104:22
33:17 39:5 44:21,25	refresher 13:2	reported 68:9 69:22	response 113:1,4
48:10,14 63:17	refreshing 10:6	71:4,7,20	restart 124:24 125:2
91:16,20 123:10,14	regarding 25:3	reporter 8:8 11:3,13	restrictions 36:18
139:20,23 140:6,10	135:14	18:18 21:13 26:5	37:21
141:3	regenerate 123:3	49:10,17 61:14	result 75:18
recovered 61:1	Regioselection 77:10	64:11 65:25 72:15	results 60:21 70:7
recovery 61:2	Regioselective 126:6	73:15 77:3 78:24	75:19 121:13
reduce 102:25 106:24	regioselectively	79:16 84:18 92:7	rethink 16:9 25:19
107:1	126:21	96:13 98:8 99:17	

Reverse 77:10	samples 80:3	schemes 93:19 94:25	48:5 63:14 80:22
reversible 85:21	San 7:1,14,18	95:10,11,15 96:21	81:1 82:25 83:16
reversibly 108:3,13 113:13	Sanger-based 92:13, 22	97:3	103:9 107:23 119:4, 11,14,20 129:19
review 10:17 85:11	satisfied 24:3	Schena 44:2	131:18,20,22 132:9, 14,20,22,23,25
right 17:10 38:20	save 114:16 135:12	Schwartz 7:22 8:18	133:18,19,23 134:4, 14
44:16,18 51:13,19	saying 32:8,10 56:23	11:4,14 13:23 17:3	see 11:18 12:2,11
53:13 54:2,23 55:10	57:4 70:1 71:8	18:19 21:14,20,22	13:4,8 15:3,14
60:7 62:24 63:2,3	83:10,11,14,25 84:1,	26:9 31:12,15 32:3,	19:13,17 20:1 24:15
64:4 65:18 67:22	4 88:4,14 91:5 98:24	4,12,15,16 39:6,7	26:13 38:4 40:15
71:1 74:8 76:13	103:2 112:20 117:13	44:8,15,19 45:2	42:11 45:13,16 50:1,
78:19 82:20 89:7	122:13	48:7,16 49:12,18	5,9 51:13,19 52:23,
94:1,10 95:8 101:6	says 14:20 27:17	54:16,21 55:22	24 53:2,6,25 54:19,
103:5,14 107:6	53:19 55:10,12 56:2,	57:18 58:8 59:8	20 58:3,4 62:4 63:2,
108:16,22 111:9	7,8,12,15 59:1,3,10,	61:16 65:9,20 66:1	8,13,17 74:13,18,25
115:10 118:21	13 63:17 65:8,11	67:7,11 69:16 72:16	75:10 76:7 79:22
119:14 120:16,18	74:9 75:10,16 83:13,	76:16,17 77:4,7,8	80:23 81:3 83:24
121:8 129:10 131:5	24 89:17 94:24 97:5,	78:17,23 79:8,17	85:16 86:17 87:17
133:1,24	14 98:22 99:1	81:15,19,20 84:7,21,	90:25 91:8,11 92:12,
Robert 7:22	100:19 103:6,10	23 85:13 86:4,6	14,16 93:4,15 94:6,
Romesberg 7:8 8:13,	116:23 133:6 136:2,	89:19 91:15,22 92:8	12 95:24 100:17
19 10:16 45:3 48:17	5 140:18	98:4,9 99:18 107:21	103:11 107:24 114:5
91:23 100:11,16,20	SBS 11:7 12:18,24	111:8,12,19,23	115:10,14,20 119:7
101:4 104:22 110:25	14:4 15:23 17:5,7,	113:19 114:22	120:1,6 129:13,19,
111:19 123:17 135:3	12,20 18:5,7,10,12,	118:24 123:8,16	20,24 131:20 132:20
139:18 140:13 141:2	13 20:16 22:4 23:12	126:4 127:23 129:6	133:23 135:24 136:1
Ronaghi 66:3 67:20,	82:5,7 87:25 88:8,	130:6 131:2,4,12	137:10,13
24 68:12 69:17 70:4,	16,21 89:15 94:4,16	134:1,3,24 135:10	seeing 85:3
12,14,18	97:12,18,25 102:6	140:2,5,12,23	seen 85:1,11 114:25
room 50:24 53:12,17	104:11,16 105:4,24	science 68:19 82:22	115:5,8
54:12 59:14 63:10,	106:7 107:10 109:2	102:19	selected 10:6
17,20 64:2 128:5	117:16 118:12	Scinto 7:25	selection 131:23
Rosenthal 66:15	122:10,15 124:6,23	scope 19:12 139:21	134:5
routine 135:23	131:25 132:6 134:7	Scripps' 100:8 101:1	selectively 125:11
rules 8:21	138:6	search 53:24	selectivity 105:21
run 54:18 72:6,10	scale 105:18	second 39:17 44:17	self-evident 129:8
running 134:13	scheme 50:20,21	49:23 61:9 66:5	semantic 116:7,24
Ryan 7:16	51:7 62:7,8,12,16,20	73:10 76:16 98:11	senior 70:19
	63:9,24,25 64:5 65:6	133:2 139:17	sentence 19:25
	71:3 80:10 81:12,25	second-to-last	24:12,13 31:14
	82:4,14 83:9 85:16,	100:15	55:16 56:7,8 74:12
	20 87:4 88:4 94:4	secret 102:10	
	121:12 129:20,23	section 19:12,15,24	
		21:16 40:21 46:23	
<hr/> S <hr/>			
SAGE 31:3 33:8			

80:13 81:2,17 82:15, 23 83:1,21 86:16 92:12 93:2 95:23 96:8 119:23 separate 17:24 56:6 116:12 117:3 September 114:8 sequence 20:7 24:21 25:1 38:14,19 66:12 86:22,24 87:10 88:7, 11,15 89:2 106:23 112:24 136:4 137:20 138:20,25 sequenced 106:13 137:3,24 sequences 87:11 89:3 105:12 138:16 sequences' 24:22 sequencing 11:6 14:9,12,14,21 16:10, 12,17 17:9 18:7,9 20:10,15 23:25 24:4 25:4,9,14 28:16 29:4 30:5,16,20,23 31:18, 22,25 32:7,14,21,25 33:3 34:15,23 35:1, 4,7,13,15 36:6,16 37:9,19 38:2,23 39:14 40:2,5 66:2 71:14 79:12 80:7,9 81:12,25 82:4,8,14 83:9 85:16,19 87:3 88:4,5 92:23,25 93:19,25 94:4,18,25 95:4,10,11,15,19 96:21,22 97:3,4,10 98:19 100:9 101:1,3 103:19,21,23 105:12,17 106:15 109:17,18,24 110:16,17,19 112:17,22,24 117:20 125:3 136:6,13,15, 18,25 137:5,11,15	138:7,9,11,14,22 140:16 Sequencing,' 100:24 Sequencing-by- synthesis 66:8 serial 31:2 33:7 settings 101:3 seven 127:12 131:3 severely 87:9 89:1 125:7 sheet 99:24 103:8 short 87:11 89:3 shortcomings 24:14, 18 Shorthand 11:3,13 18:18 21:13 26:5 49:10,17 61:14 65:25 72:15 77:3 79:16 84:18 92:7 98:8 99:17 114:21 126:3 127:22 129:5 131:11 shortly 113:5 show 14:6 showed 106:11 showing 78:13,15 105:11 136:14,18, 22,24 137:3 shown 66:25 126:14 129:23 shows 62:8 123:24 sic 30:2 32:21 36:8 37:11 49:22 73:16, 17 81:10 96:18 131:23 side 62:24 77:17 79:19 80:21 120:16 122:22 sign 18:25 signal-to-noise 28:21	signature 10:20 50:7 signed 19:3 50:8 significant 103:20 significantly 29:1 96:19 97:1 similar 96:25 simply 36:5 37:8 38:9 57:23 single 30:25 33:6 56:8 89:24 90:1,6 92:24 95:4 115:4 138:9 sir 23:9 sit 75:21 site 123:19 situ 64:25 six 9:18 80:25 87:8 88:23 127:11 size 38:15 127:12 skewed 70:7 skill 20:1,4 23:23 24:24 25:11 26:17 28:12,24 29:22 30:4 34:20,24 35:10 39:12,25 57:19,22 71:10 78:7,25 79:1 82:10,16,21 83:5 88:14 skilled 71:23 skimming 133:4 skip 12:4 15:17 96:7 slowed 96:20 97:1 small 68:10 69:19 72:8 90:16,23 132:11,13 smaller 138:20 SNP 11:25 12:23 14:3 15:12 16:16 17:19 18:4 SNPS 31:1 33:7	so-called 92:23 95:4 solely 139:24 solid 60:14 solution 53:8 54:7 59:11 75:14 128:6 solved 97:12,16 solvent 58:14 77:23 soon 106:14 sorry 10:15 13:11 20:24 26:12 32:17 39:15,16 42:4 54:4 56:3 60:5,6 61:9,15 62:14 63:4 92:15 100:5 101:12 121:9 129:14 132:1 135:7 136:17 137:9 sort 27:11 42:8 71:12 105:18 106:16 110:6,13 118:7 121:6 sorts 110:21 112:13 sounds 88:5 114:13 source 102:19 spark 101:16 speak 9:22 91:25 spec 95:22 spec- 21:1 Special 99:3 specific 14:11,16,21 107:24 108:1,16,17, 20,21 113:11 117:19 118:5 134:15 specifically 20:21 21:5 38:22 73:25 105:7 133:15 specification 20:15, 21 21:5 23:1 29:9 31:6 33:11 35:8 40:11,14 42:1 43:2, 4,21,23 45:12 46:2, 4,5,11 47:1,3,17,19
---	---	--	---

<p>97:7</p> <p>specifications 48:5</p> <p>speculate 83:6</p> <p>speculating 82:18 83:1,3,12</p> <p>speculation 83:14</p> <p>speculative 83:22</p> <p>speed 34:21 35:3 40:4</p> <p>spend 9:17</p> <p>spent 10:5</p> <p>spirit 116:11 117:2,12</p> <p>spoke 102:2</p> <p>spot 27:13 76:12 94:24 133:18 139:2</p> <p>spots 14:10</p> <p>spring 100:17,20</p> <p>stability 71:14</p> <p>stable 75:1</p> <p>standard 71:11</p> <p>start 42:13 60:6 63:3 99:11 113:23 116:8</p> <p>starting 7:20 11:16 15:1 26:11,14 27:2 35:24 37:3 46:15 60:3 115:12 120:4 135:23</p> <p>starts 12:14 19:25 24:13 63:1 74:12 79:20 81:2 85:15 86:16 92:12,14,17 103:10 116:25 137:9</p> <p>state 7:20 67:20 69:4 99:9 137:19</p> <p>stated 37:4 57:23</p> <p>statement 49:2 56:19 59:17 68:25 71:9 80:12 83:16,17,23 89:20 95:17</p>	<p>statements 69:21 70:4 73:18</p> <p>states 7:11 24:20 30:15 31:17 32:6,20 57:8 82:19 87:24 132:10 139:1</p> <p>stating 20:6 69:23</p> <p>step 34:25 35:6 39:13 40:1 44:20 64:5 73:9,10 125:3</p> <p>steps 29:4 73:8 74:6</p> <p>Steven 8:1</p> <p>stirred 53:11 54:8 56:7 59:14,18</p> <p>stop 111:15 116:8</p> <p>stops 117:1</p> <p>strand 22:22</p> <p>strike 25:23 40:12 101:12 127:4</p> <p>structure 115:15,18 120:5,17 122:7,9</p> <p>structures 123:25</p> <p>studies 11:25 12:23 14:3 15:12 16:16 17:19 18:4 31:5 33:10</p> <p>study 73:20</p> <p>subject 16:25 17:15 38:5 109:16</p> <p>subjects 70:22</p> <p>submitted 98:14 104:14 108:11</p> <p>subsequent 73:3 74:1 75:17</p> <p>substance 116:21 135:14</p> <p>substitute 127:2</p> <p>substituted 77:19 127:7 128:19,21</p> <p>substrates 102:12,16</p>	<p>103:4</p> <p>success 30:15 31:17 32:7,20 72:4 109:21</p> <p>successfully 97:11</p> <p>sufficiently 109:24</p> <p>Sugar 61:20</p> <p>suggest 128:16 136:3</p> <p>suggesting 83:4</p> <p>suggests 91:9</p> <p>suitable 117:16 124:6</p> <p>Suite 7:18</p> <p>superior 68:20</p> <p>superstrike 47:22</p> <p>supply 102:3</p> <p>support 10:17 20:20 21:3 23:16 29:15 49:1 50:22 80:12 89:20</p> <p>sur- 68:6</p> <p>sure 13:1,9,14,17 18:23 36:22,25 38:5 39:18 44:19 48:9 57:17 64:24 65:1 75:4 79:1 90:4 91:15 98:23 99:6,7 102:18 104:24 115:7 117:18,21 120:25 121:11 122:16 139:22 140:4</p> <p>surprise 127:9</p> <p>survive 22:23</p> <p>suspect 94:6</p> <p>swear 8:10</p> <p>switch 70:22</p> <p>Syntheses 79:11</p> <p>synthesis 11:24 12:23 14:2,9,13,15, 21 15:11 16:10,13, 15,17 17:5,6,7,8,19 18:4,8,9 20:11 23:25</p>	<p>24:4 30:17 31:19 32:14,22 36:6,17 37:9,20 38:2 49:24 61:19 71:15 82:9 88:5 95:20 108:6 109:17,18,24 112:17,22 117:20,23 118:1,2 124:24 125:2,3 137:15 138:11</p> <p>synthesize 104:5,17 105:25 106:8 107:12 110:4,5</p> <p>system 25:5 30:17, 20,24 31:19,22 32:14,22,25 33:4 34:15,23 35:13 126:19 136:7</p> <p>systems 96:13,17</p> <p>Szeja 72:19</p> <hr/> <p style="text-align: center;">T</p> <hr/> <p>T-r-o-a-s-t 73:17</p> <p>T-s-u-g-i 73:16</p> <p>table 126:14,24,25 127:4 128:10,13,15</p> <p>tag 22:17 29:5 114:11 115:17 116:2,4,8,13, 24,25 117:4</p> <p>tagged 108:4,13 109:8 113:13</p> <p>tainted 90:15,23</p> <p>take 9:14 12:25 36:24 44:17 48:8 56:10 67:17 85:11 102:18 118:11 122:11,13 123:8 130:4 133:2</p> <p>taken 7:8 44:23 48:12 91:18 123:12 140:8</p> <p>takes 65:6</p>
--	--	---	---

talked 38:1 102:23 138:14	Terminating 61:20	105:16,22 106:25 110:14	today 8:8,24 9:2,5,12 82:7 106:16
talking 18:24 58:13, 25 74:25 75:15,16 76:9 95:9 105:17 107:18 112:22 116:7,24 118:6	terminators 22:15 85:21 124:23	think 14:7,20 16:10 26:20 27:11,15 41:12 56:13 57:22 58:3 61:6 62:20 65:12 68:8 70:3 71:10 73:16,17 75:3, 20 76:7,11,13 82:16 89:17 95:2 98:16,25 99:3,5,12,21,25 102:1,2,4 104:20 105:14 106:25 112:25 113:4 118:5 121:6 125:9 132:12 138:13	today's 7:5 10:1,8 45:4 135:17
talks 27:14 58:12 132:18 137:17	tert-butylperoxy 128:4	thinking 36:16 37:19 75:22 85:9	told 57:1 113:10
taught 68:14 111:2	Tertiary 61:20	third 34:13 60:3,5	told 57:1 113:10
tautomerize 76:20	test 100:7 101:1	thought 32:15 125:12 134:21	top 34:11,13 62:7 63:2 80:21 89:7 94:10 98:17 115:10 120:4,15 121:12 139:9,14
teach 74:5,8	testified 8:15 14:5,6 85:5	thousand 112:25	Trademark 7:11
teaches 25:4 73:25 88:7 97:16,20 132:18	testify 13:7 16:21 71:18 104:23	three 25:22 61:25 62:4 119:24 128:18, 24 129:22 130:18,22 132:2 133:20 134:16 138:22 139:6,8,12	Trans-[pd(nh3)] 72:19
teaching 24:25 75:7	testifying 16:22 19:6	till 41:8	transcript 11:10,17 14:23,24 26:1,15 27:2,3 35:22,24 37:3,4 38:21 114:23 115:12
teachings 20:6 121:19	testimony 8:24 9:2 12:8,13,20 13:24,25 14:1 16:1 17:13,14, 16 18:22 26:12,24 27:23 36:19 37:23 38:4 57:3 71:23 114:9,12 116:15 117:8 135:14 138:8	time 7:5 8:22 9:13,16, 20 17:1 32:1 38:1,18 44:13 48:7 53:23,25 54:19 55:8,9,15 56:13,21,22,24 57:2, 16 58:4,15,19,20,23 65:11 73:20 84:14 85:11 91:13 101:25 103:22 104:14 105:4 106:6,23 108:11,19 109:5,6 113:3 123:6 130:4 131:2 134:1, 13	treat 122:11,14
technical 97:11,15	text 41:13,14 43:2,21 46:2 47:1,17 51:16 53:19 56:11 103:9, 13 107:23	times 9:11 107:15	treated 52:14 54:7 55:2,12,17 56:9,15 57:20 59:4 60:9
technique 14:21 68:18	thank 8:7 19:4 37:1 65:16 91:23 123:9 134:25	title 91:7 98:18 129:7	treatment 55:15 56:5 57:11 58:5,12 75:14
techniques 12:17,24 14:4 15:22 17:11 18:10	Thanks 85:12		Tri-o-benzyl 63:1,5
technologies 103:18	thermostable 112:11		Trial 7:12
technology 70:19	thesis 51:2,3,6,10,14, 15,23,24 52:3,5,19 53:15,22,23 54:2,10, 24 56:15 57:4,20 59:20,24		triphosphate 81:10, 23 82:13 83:8 104:7 110:1
tell 8:25 13:5 56:25 101:17 107:17 109:15	thick 118:19		triphosphates 69:1, 14 102:24 104:18 105:6,21 107:13
telling 82:21,25	thing 42:17 48:3 63:1, 15 68:1 82:24 95:18 121:22		triplets 139:6
temperature 50:24 53:12,17 54:12 57:14 59:14 63:10, 13,18,21 64:2 128:5	things 12:17 14:8,11, 14 15:22 16:7,12,17 17:11,20 18:5,6 57:14 85:8 102:23		trite 72:8
template 22:25			trouble 62:2
template-directed 87:12 89:14 90:10			true 68:21 69:24 70:2 106:9 110:1 113:2,4
temporary 72:24			Trustees 7:9
tend 102:25			truth 56:25
term 109:11 112:3			truthful 8:24 9:1
			try 32:3 68:19 107:4

111:10 112:2 trying 38:4 68:18,24 105:8 107:7 114:16 138:13 Tsien 95:7 131:8,13, 17,22 132:9,12,14, 18 133:19 134:4,14 136:14 Tsuji 126:10 127:6,25 Tsuji-trost 73:14,16 128:1 TUESDAY 7:1 turn 10:19 11:15 18:20 19:11 26:10 27:1 35:23 41:7 45:22 47:13 48:23 50:3,19 51:4 52:3,19 59:23 62:23 79:18 80:15,19 84:25 85:14 89:6 92:10 94:9 113:25 114:1,2 115:9 118:25 119:10 120:3,15 126:11 128:9 129:9 135:21 137:8 twice 59:7 two 38:11,12 48:24 53:20 56:12 73:8 74:5 78:1 90:2 106:11 134:2 two-hour 50:24 two-year 100:21 type 69:10 typical 83:20 typically 58:15 typo 60:15 typographical 116:16,19,20	19:16,20 21:8 41:2 84:24 92:9 120:12 Uh-huh 10:4 55:14 133:3 ultra 30:18 31:20 32:23 33:18 34:5,17, 18 35:14 underlined 32:9 33:18 underneath 19:15 understand 10:8 24:25 25:12 26:18 34:21 35:11 36:17, 22 37:20 41:12 47:25 48:2 57:20 67:12 71:23 75:7 82:8 116:3 120:10 understanding 114:7 115:22 understood 20:5,15 23:24 28:13 30:5 57:24 64:14 73:7 74:20 78:9 82:11 88:6,15,20 89:3,11 94:14 97:8 102:15 106:5 124:5,11,16, 21 125:5 undesirable 25:2 unfortunately 93:14, 18 94:25 95:15 unimaginable 113:8 unique 22:8 38:13,19 United 7:11 University 7:10,23 unmodified 69:14 110:6 unnatural 29:7 unprotected 68:23 unrelated 18:8 unsubstituted 128:20,21	unusual 127:14 use 64:19 65:12,13, 14 69:3,14 109:2 110:15 112:7 117:20 124:9,12 132:15 138:23 139:25 useful 36:6 37:9 138:6 139:15 uses 11:19 15:3 71:5 85:20 98:1 usually 75:24	W Wack 78:14 Wacker 77:10 78:14 wait 56:3 135:9 want 12:5 13:4,8,12 14:23 16:8 23:6 52:20 54:19 57:3 64:19 65:11,12,13 67:4 68:1 73:18 80:16 83:18 91:6 107:1 110:15,16,20 111:10 112:14 113:24 125:14 130:15 133:24 134:9,10 138:20 139:10,19,23 wanted 71:2 102:2 105:9 106:24 110:3 112:7 113:11 washing 22:23 wasn't 69:11 101:11 105:10 110:10 112:20 water 76:2,18 77:24, 25 78:9 way 14:10 17:17 43:25 57:6 63:3 68:7 75:24 80:1 123:7 124:25 127:25 we'll 114:15 116:6,23 135:9 we're 7:25 41:3 44:3 54:1,2 61:4 95:6 109:12 110:13 118:6 134:13 we've 59:19 91:14 102:23 weak 123:1 Web 100:9 102:8,14, 18
U		V	
U.S. 10:17,23 11:5		vacuum 118:8 vaguely 101:25 value 27:16 138:23 variants 73:13 varies 64:15,22 variety 73:22 116:16 various 11:23 15:9 66:16 126:15 vary 127:12 Vent 109:3 version 67:6 115:3 versus 47:23 viable 73:21 81:12,25 82:14 83:9 vice 70:19 video-recorded 7:7 141:2 videographer 7:4,16 8:7 44:21,25 48:10, 14 91:16,20 123:10, 14 131:3 134:2 140:6,10 141:1 virtually 99:4	

weights 59:13 Welch 79:12 80:20 82:11 went 8:21 21:4 weren't 106:15 112:20 West 7:17 whit 60:13 white 60:15 widely 72:23 widespread 93:20 95:1,16 wild 69:10 withdrawing 17:12 witness 8:5 13:21 26:6,8 44:17 65:17 79:7 85:12 118:21, 23 won 100:20 word 32:13 33:21 34:4 43:3,22 46:3,6 47:2,18 67:13 82:23 86:4,7,8 109:13 words 32:9 33:18 84:5,6,8 104:25 107:6,9,13,16,17 work 24:5 68:19 71:6 100:24 working 110:13 world 138:21 worry 13:19 wouldn't 38:9 71:24 138:6 write 20:3 22:3 23:22 24:17 28:8 29:20 30:14 34:13 39:11, 24 66:7,19,21,22 70:9 76:5 79:24 80:8 81:5 82:2,3 126:13, 22	writes 51:9 52:9,12, 17 53:7,13 60:3,18 72:22 73:5 74:15 85:18 86:8,19 88:18 89:1 92:20 93:17 96:1,9 writing 68:16,17 writings 85:6 written 12:21 16:2 19:7 20:17,19 23:4 26:25 27:24 29:13, 18 30:11 33:15 35:19 36:21 37:24 49:5 51:15,16 52:18 53:14 55:5 63:22 66:20 67:23 69:24 84:5,6,10,11 86:10 88:19,24 89:5 94:1 97:21 102:15 104:19 113:18 126:23 wrote 20:12,13 23:3 24:8 25:18,20 29:11 30:10 31:8 33:13,19, 23 35:18 40:6 84:8 99:8 102:20 103:13 104:8 106:1 108:8, 15 110:2	125:11 years 33:23 34:3 84:8 113:3 yep 51:20 78:3,6 102:7 108:9 yesterday 9:15,16 10:3 yield 22:19 28:15 29:25 49:4 50:23 56:5 60:22 64:6,19, 20,23,25 71:25 yields 71:16 York 7:10 8:1
<hr/>		
Z		
<hr/>		
Zachary 7:24 Zimmerman 8:3 13:19 16:19 21:18, 21 26:7 31:10,13 32:2,11,13 39:4 44:6,13,20 48:9 54:14 55:20,25 57:9 58:1 59:6 65:16,19 67:4,9 69:7 77:6 78:12 79:5 81:13,17 84:3,19,22 85:10 86:2 89:16 91:13 107:14 111:6,16,21, 24 113:16 118:19,22 130:4 135:2,11 139:16 140:4,24		
<hr/>		
ß		
<hr/>		
ß-alkoxy 126:8		