

In the Matter Of:

10x GENOMICS vs

NANOSTRING TECHNOLOGIES

PAUL SPELLMAN

August 05, 2024



1 IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

2
3 BEFORE THE PATENT TRIAL AND APPEAL BOARD

4
5 10x GENOMICS, INC.

6 Petitioner,

7
8 v.

9 NANOSTRING TECHNOLOGIES, INC.

10 Patent Owner

11
12 Case No. IPR2023-01298

13 U.S. Patent No. 11,377,689
14

15
16 VIDEOTAPED DEPOSITION OF

17
18 PAUL THOMAS SPELLMAN, PH.D.

19
20 Monday, August 5, 2024

21
22
23 Reported by:

24 SUSAN ASHE, CER

25 Job No.: 950862

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2	9:09 a.m. Eastern Daylight Time	2	THE WITNESS
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7	Videotaped deposition of PAUL THOMAS	7	
8	SPELLMAN, Ph.D., taken on behalf of the Patent	8	EXHIBITS
9	Owner, beginning at 9:09 a.m., on Monday, August 5,	9	Exhibit No. Marked
10	2024, at the law offices of Sterne Kessler Goldstein	10	Exhibit 2050 Plaintiffs' Consolidated
11	& Fox, 1101 K-Street, Northwest, Washington, D.C.,	11	Brief (1) in Opposition to
12	before Susan Ashe, CER, and a Notary Public for the	12	Nanostring Technologies,
13	District of Columbia.	13	Inc.'s Summary Judgment and
14		14	Daubert Brief and (2) Reply
15		15	in Support of Plaintiffs'
16		16	Motion for Summary Judgment
17		17	of No Invalidity for No
18		18	Indefiniteness and Daubert
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20		20	Opinions of Michael Lasinski 89
21		21	Exhibit 2051 Patent No. 11,008,607 102
22		22	Exhibit 2052 Patent Application
23		23	Publication
24		24	No. US 2016/0194701 111
25		25	

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1	APPEARANCE OF COUNSEL:	1	PREVIOUSLY MARKED EXHIBITS
2	On behalf of the Petitioner and the Witness:	2	Exhibit No. Introduced
3	STERNE KESSLER GOLDSTEIN & FOX	3	Exhibit 1001 U.S. Patent 11,377,689 65
4	BY: PRATIBHA KHANDURI, PH.D., ESQ.	4	Exhibit 1002 Declaration of
5	BY: ROBERT GREENE STERNE, ESQ.	5	Paul T. Spellman, Ph.D. 10
6	BY: GABY L. LONGSWORTH, PH.D., ESQ.	6	Exhibit 1003 Curriculum Vitae of
7	BY: DAVID H. HOLMAN, PH.D., ESQ.	7	Paul T. Spellman, Ph.D.
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15		15	
16	On behalf of the Patent Owner:	16	
17	WEIL GOTSHAL & MANGES LLP	17	
18	BY: EDWARD R. REINES, ESQ.	18	
19	201 Redwood Shores Parkway, Suite 400	19	
20	Redwood City, California 94065	20	(REPORTER'S NOTE: All quotations from exhibits are
21	(650) 802-3000	21	reflected in the manner in which they were read into
22	edward.reines@weil.com	22	the record and do not necessarily denote an exact
23		23	quote from the document.)
24	ALSO PRESENT:	24	
25	Jonathan Perry, Videographer	25	

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1 MONDAY, APRIL 5, 2024; 2 9:09 A.M. EASTERN DAYLIGHT TIME 3 --000-- 4 VIDEOGRAPHER: We are now on the 5 record. My name is Jonathan Perry. I am 6 a videographer retained by Lexitas. 7 This is a video deposition for 8 the United States Patent and Trademark 9 Office before the Patent Trial and Appeal 10 Board, Case No. IPR2023-01298. 11 The date is August 5, 2024. The 12 time is 9:09 a.m. 13 We are at the offices of Sterne 14 Kessler, 1101 K Street, Northwest, in 15 Washington, DC. 16 And this is being taken in the 17 matter of 10x Genomics, Incorporated 18 versus Nanostring Technologies, 19 Incorporated. 20 The name of the Witness is Paul 21 Spellman, Ph.D. 22 And would counsel present please 23 introduce themselves and state whom they 24 represent. 25 MR. REINES: Ed Reines, on	1 A. Paul Thomas Spellman, 10807 Rochester 2 Avenue, Los Angeles, California 90024. 3 Q. When did you receive the assignment in 4 this matter? 5 A. A little over a year ago, is my 6 recollection. 7 Q. Other than this proceeding, do you work 8 with Sterne Kessler on other matters? 9 A. Yes, I have done at least one other case 10 with them -- I think, two. 11 Q. And what were those other cases? 12 A. One was TwinStrand versus Guardant, and 13 the other is -- I'm blanking on. 14 Q. Have you performed any work in relation to 15 10x before this matter? 16 A. I don't believe so. 17 Q. Other than the TwinStrand-Guardant case 18 that you're thinking about, are there any other 19 matters where you've served as a litigation expert? 20 A. Yes. 21 Q. Can you please describe those. 22 A. There have been several of them. 23 The first case I did was Foundation versus 24 Caris, which was an IPR. 25 I've also done Natera -- sorry, Natera
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1 behalf of the Patent Owner. 2 MS. KHANDURI: This is Pratibha 3 Khanduri, of Sterne Kessler, representing 4 10x, the Petitioner. 5 MR. HOLMAN: David Holman, from 6 Sterne Kessler Goldstein & Fox, on behalf 7 of 10x. 8 MS. LONGSWORTH: Gaby 9 Longworth, of Sterne Kessler Goldstein & 10 Fox, on behalf of 10x. 11 MS. KHANDURI: And we also have 12 Robert Sterne -- Robert Greene Sterne, of 13 Sterne Kessler, representing 10x. 14 VIDEOGRAPHER: The court 15 reporter is Susan Ashe, also with Lexitas. 16 Would you please swear in the 17 witness. 18 Whereupon, 19 PAUL T. SPELLMAN, PH.D. 20 having been first duly sworn, was examined 21 and testified as follows: 22 EXAMINATION 23 BY MR. REINES: 24 Q. Please state your name and address for the 25 record.	1 versus Guardant, where I represented Natera. 2 And I've done Ravgen versus LabCorp, where 3 I represented LabCorp. 4 I believe I've done a couple others. I'm 5 currently involved in one with Illumina. 6 Q. And what's the Illumina matter? 7 A. I can't recall at the moment. 8 Q. Is it current? 9 A. Yes. 10 Q. And you don't remember who's on the other 11 side? 12 A. I don't remember at the moment. 13 Q. And you're working for Illumina in that 14 one? 15 A. Yes. 16 Q. Are all of those IPRs, or are some of 17 those district court? 18 A. Two of them were district court. 19 Q. Which two? 20 A. Natera/Guardant and Ravgen versus LabCorp. 21 Q. On the Ravgen v. LabCorp, did you testify 22 at trial? 23 A. I did. 24 Q. On behalf of... 25 A. LabCorp.

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1 Q. ...LabCorp? 2 In any of these matters, have you 3 represented the patent owner? 4 A. Yes. 5 Q. Which matter? 6 A. Natera versus Guardant. 7 Q. So Natera versus Guardant is district 8 court and also IPR? 9 A. No; it was just the district court case. 10 Q. Okay. I see. I'm sorry. 11 A. No worries. 12 Q. In an IPR, have you ever represented a 13 patent owner? 14 A. I don't think I have. 15 (Whereupon, Exhibit 1002, previously 16 marked, was presented to the witness.) 17 Q. I'd like to show you what's been 18 identified as Exhibit 1002, which is your 19 declaration in this matter. 20 A. Thank you. 21 Q. How much time did you expend on preparing 22 your opinions set forth in this declaration, 23 including preparation of the declaration itself? 24 A. I don't recall. 25 Q. What is your best estimate?	1 in that laboratory? 2 A. My laboratory? No. 3 Q. Have you ever used a spatial analysis 4 tool? 5 MS. KHANDURI: Objection; form. 6 A. I'm not sure I can answer that. 7 Q. And why do you say that? 8 A. Can you clarify what you mean by "used"? 9 Q. Operate, run an experiment on, personally. 10 A. Personally, no. 11 Q. Have you designed any spatial analysis 12 experiments? 13 A. I believe I have. 14 Q. And in what context? 15 A. In a series of conversations with graduate 16 students and other members of my laboratory. 17 Some members of my laboratory have been 18 interested in using spatial multiplexed analysis. 19 Q. Have they done that in your lab? 20 A. My laboratory does not own any of the 21 equipment necessary. 22 So I don't think -- I don't think so, 23 given the way you're asking the question. 24 Q. What would be the situation in which you'd 25 be helping a grad student design an experiment when
Page 11	Page 13
1 A. Somewhere around 50 hours -- perhaps more, 2 maybe a bit less. 3 Q. Prior to your involvement in this matter, 4 were you familiar with the So-456 reference, whether 5 it be in the form of the world application or in 6 some other published form? 7 A. Not by that name. 8 Q. How about by any other name? 9 A. Which reference? 10 Q. "So-456." 11 A. Oh. No, I had not read it. And I.... 12 Q. And prior to your involvement in this 13 matter, had you read this Stahl 2016 reference? 14 A. I may have. 15 Q. Do you know one way or the other? 16 A. I don't know for certain. 17 Q. Do you have a belief, sitting here now? 18 A. That I had read it closely, unlikely. 19 That I had seen it, possibly. 20 Q. Had you read the Chell disclosure before 21 your involvement in this matter? 22 A. No. 23 Q. Do you currently have a laboratory? 24 A. Yes. 25 Q. Do you have any spatial analysis products	1 your laboratory doesn't have the tools to perform 2 such an experiment? 3 A. Many of the technologies of this scale are 4 fairly expensive and not owned by individual 5 laboratories. They're in shared resources for 6 institutions. 7 And so, my current institution has many 8 such platforms that are available for faculty to 9 use. 10 My previous institution pioneered 11 developing many such technologies for spatial 12 detection. 13 And that would be one example of where I 14 might have designed an experiment, although it might 15 not have happened in my lab. 16 Q. Have any of your graduate students 17 published on any spatial analysis they performed 18 while in your lab? 19 A. I'm not sure. 20 Q. Are you aware of any that you can identify 21 now? 22 A. It would depend quite heavily on how you 23 define "spatial analysis." 24 Q. How do you define "spatial analysis"? 25 A. Detection of things in an image, for

Page 14 1 example, that represents the physical space. 2 Q. Three-dimensional space? 3 A. Not necessarily. 4 Q. You're currently at UCLA. 5 Is that correct? 6 A. That is correct. 7 Q. And what's the name of the Core lab -- 8 what you're calling the "shared resources" for 9 performing genomic analysis? 10 A. I don't understand the question. 11 Q. Yes. My understanding from you is that, 12 for expensive equipment in your current university, 13 there's a centered -- central place where shared 14 resources are contained so that labs can use such 15 equipment as needed. 16 Is that accurate? 17 A. Yes; more than one. 18 Q. What are the names of those shared 19 resources? 20 A. There is a neurogenomics shared resource, 21 for example. 22 The cancer center to which I am a member 23 has a high throughput genomics shared resource. 24 There are others. 25 Q. What equipment does the neurogenomics have	Page 16 1 available on campus. 2 I don't know if it's in the Neurogenomics 3 Core specifically. 4 Q. Bruker equipment? 5 A. I don't know about Bruker. 6 Q. Has your lab ever used 10x, Nanostring, or 7 Bruker spatial analysis products for the work that 8 you do? 9 A. If you hand me my CV, I can check some 10 references specifically. 11 (Whereupon, Exhibit 1003, previously 12 marked, was presented to the witness.) 13 Q. Let me show you what's been marked for 14 identification as Exhibit 1003. 15 A. If it is published, I believe 164, Eksi-SE 16 has spatial imaging in it. 17 There's another paper that's published 18 since this CV was submitted from Eksi that, also, 19 she may be the senior author on that one. 20 Q. What's the number? 21 A. No. 164 in my CV. 22 I believe that has spatial imaging in it. 23 Q. Do you know what type of spatial analysis 24 was performed? 25 A. I believe in that case it is multiplex
Page 15 1 for spatial analysis? 2 A. I can't tell you off the top of my head 3 what they have, for certain. 4 Q. Well, my questions aren't going to require 5 for certain. So if you have a reasonable basis, 6 please provide responses -- or I'm capable of 7 cycling through. It'll just be easier, I think. 8 In terms of the neurogenomics center, 9 there are 10x products there, to your knowledge? 10 A. Specifically 10x, I'm not certain. 11 Q. Do you have a belief, one way or the 12 other? 13 A. I believe there are 10x instruments at 14 UCLA. 15 Q. My question was confined to the 16 neurogenomics center. 17 A. I couldn't tell you exactly what's in the 18 Neurogenomics Core. 19 Q. I'm not asking for exactly. 20 My question is: Sitting here now, do you 21 have reason to believe there's 10x equipment at the 22 neurogenomics lab? 23 A. Neither one way or the 'nother. 24 Q. How about Nanostring equipment? 25 A. I know there's Nanostring equipment	Page 17 1 serial staining with antibodies for protein imaging. 2 Q. Do you know whether that includes 10x, 3 Nanostring, or Bruker products? 4 A. I believe it is self-developed technology 5 in this case. That's my recollection. 6 Q. Do you know what kind of probes are used 7 in that spatial analysis? 8 A. Primarily, antibodies. 9 Q. Other than that work that Eksi did, is 10 there any other spatial analysis that's been 11 performed in your lab, either at UCLA or before 12 that? 13 A. Quite a lot. 14 No. 169, Heskett, Michael, was a Ph.D. 15 student in my laboratory working on epigenetic 16 control of chromosome biology. 17 Q. And do you know if he used any 10x, 18 Nanostring, or Bruker spatial analysis products? 19 A. The primary imaging was done by my 20 collaborator, Matt Thayer. 21 I don't believe so. Again, I think it was 22 primarily home-developed technology. 23 Q. Has any of the work in your career 24 involved either 10x, Nanostring, or Bruker spatial 25 analysis products?

Page 18 1 A. I don't believe that anything that's 2 currently published has. 3 Q. Do you have future publications that 4 you're anticipating as possible using 10x, 5 Nanostring, or Bruker products? 6 A. Yes, I think so. 7 Q. Please describe that. 8 A. I can't give you an exact definition. 9 Papers in the future are not ready to be discussed. 10 Q. Who are you working with? 11 A. People in my laboratory, collaborators at 12 OHSU, collaborators at other institutions. 13 Q. And which spatial analysis products are 14 you using for that, in terms of commercial products? 15 A. I don't know that they're specifically 16 commercial. 17 Like I said, we do a lot of this in 18 home-developed technology. 19 Q. Have your labs that you've worked in ever 20 used -- performed any experiments involving 21 commercial products for spatial analysis? 22 A. "Commercial" is a very broad term. 23 You mean specifically the products at suit 24 in this case? 25 Q. Well, I was referring to not home	Page 20 1 amount of spatial technology being developed, 2 implemented, and utilized. 3 And so, it gets a little fuzzy between my 4 exact laboratory and the bounds of my professional 5 responsibility. 6 Q. Prior to this case, did you ever have any 7 direct involvement with 10x spatial technology? 8 A. I don't believe so. 9 Q. Prior to your involvement in this case, 10 have you had any direct involvement with the 11 Nanostring spatial technology? 12 A. Define "direct." 13 Q. To what extent do you have something that 14 you might call "direct"? 15 A. My colleague, Gordon Mills, had used the 16 Nanostring technology extensively at MD Anderson. 17 And when he moved to OHSU approximately 18 five to six years ago, they worked to -- along with 19 my -- the director of the center I was codirector 20 for, they purchased a Nanostring instrument. 21 Q. Which instrument? 22 A. The -- I think, the first generation one, 23 but I'm not certain. 24 Q. Do you know what the name of it is? 25 A. I don't pay attention to the names of
Page 19 1 developed, if that's easier. 2 A. Very hard question to answer. 3 There is a constant interplay of doing 4 stuff at the cutting edge when it's not yet 5 commercial and then migrating toward commercial 6 implementations when they're available. 7 Q. And does that preclude you from answering 8 the question? 9 A. What was the question again? 10 Q. In your labs, have you ever worked with 11 commercial spatial analysis tools? 12 A. I couldn't be certain one way or another 13 if any of my collaborators or students or staff have 14 done anything in that space exactly. 15 Q. Do you have any reason to believe that 16 they've done it, removing the limitations of certain 17 and exact? 18 A. At my prior institution, my role was 19 somewhat broader than a regular faculty member. I 20 was the codirector of an entire center. 21 The center had 150 members, approximately. 22 And as a scientific leader in that center, I was 23 responsible for directing a substantial fraction of 24 the scientific portfolio. 25 So in that role, there was an enormous	Page 21 1 commercial products. 2 Q. Did you have an understanding, while you 3 were at OHSU, how the Nanostring spatial system 4 worked? 5 A. Yes. 6 Q. This was after Gordon Mills came from 7 MD-Anderson over to OHSU? 8 A. I have collaborated with Gordon for nearly 9 20 years, and I believe my conversations with Gordon 10 about the Nanostring product preceded his movement 11 to OHSU, but I couldn't be certain about that. 12 Q. And when you said there was a lot of 13 innovation in the area of spatial at OHSU, what you 14 what were you referring to there? 15 A. When I was recruited to OHSU in 2011, it 16 was with my colleague Joe Gray. 17 Joe Gray is a pioneering innovator in 18 the -- in many fields of biotechnology, one of which 19 was a series of experiments around spatial imaging, 20 spatial technology, spatial detection. 21 And his intent was to develop a spatial 22 systems biomedicine program, of which I was one of 23 the founding members. 24 So in that sense, Dr. Gray's scientific 25 leadership hired roughly 20 faculty to start a

Page 22 1 center in spatial systems biomedicine, of which I 2 was a member and had extensive conversations for 3 nearly 15 years with those faculty. 4 Q. And what 15-year period are you talking 5 about? 6 A. Roughly -- sorry, starting prior to 2011, 7 going until Dr. Gray retired in 2022 -- so, at OHSU 8 was roughly a decade. 9 That effort was picked up and carried on 10 in the center that I was a codirector of with 11 Dr. Esener. 12 Q. And did Dr. Gray -- was there any.... 13 Well, let me ask: Was there a spatial 14 systems biomedicine program developed at Oregon? 15 A. I believe so, yes. I think that's what 16 the title of the center was. 17 Q. And you were involved with that? 18 A. Yes, I was a member of that center. 19 Q. And were there particular tools developed 20 at that center for spatial analysis? 21 A. Yes. 22 Q. Did you have any name for that technology? 23 A. I'm not fixated on names. I'm fixated on 24 utility. 25 So the exact nomenclature that someone may	Page 24 1 that platform. 2 Other examples, Dr. Andrew Adey, who is a 3 member of CEDAR and a member of the Department of 4 Genetics, of which I was also a member in, was a 5 postdoc in Jay Shendure's lab. 6 In Dr. Shendure's lab, Dr. Adey invented a 7 whole series of tagmentation-based protocols for 8 single-cell analysis. 9 Those protocols, while not directly 10 spatial in nature, were individual cells. 11 But with Dr. Emek Demir, we spent a 12 considerable amount of time considering how to 13 project single-cell data into multiomics spatial 14 space using more conventional imaging-based 15 technologies. 16 Q. Try to be more responsive to my question. 17 My question was just the names of the 18 technology, not the biographies of individuals or 19 that kind of thing. 20 Did the super-resolution microscopy 21 technology involve ligation of probes? 22 A. I don't believe so. 23 Q. Did you ever have any involvement, 24 professionally, with Joe Beechem? 25 A. I don't recognize the name -- I mean, I
Page 23 1 have called something is not so important to me. I 2 care more about its capabilities. 3 Q. Right, yeah. No; I wasn't asking you 4 about what your preferences were, your fixations. 5 My question was just: Do you know what 6 the name of the technology is at the center that 7 you're working at for spatial? 8 A. Dr. Gray had instituted a very broad 9 endeavor. He had hired faculty like Xiaolin Nan, 10 who was a postdoc with Steve Chu, Nobel Prize 11 winning member in all sorts of fields of physics. 12 Xiaolin came previously from Sunney Xie's 13 lab at Harvard and worked on super-resolution 14 microscopy in that context. 15 Xiaolin -- I was a mentor to Xiaolin after 16 Dr. Gray retired and served both in the early 17 detection program and in -- as the interim chair for 18 the Computational Biology Program. I mentored a 19 number of faculty, including Xiaolin, on the 20 application of their technologies. 21 So Xiaolin's super-resolution multicolored 22 detection platform certainly would qualify as a 23 spatial multianalyte detection system. 24 They endeavored both on protein, 25 initially, and then later using oligonucleotides in	Page 25 1 recognize the name from the patents. I don't 2 believe so, but you'll find that many of the papers 3 I'm an author on have thousands of authors. 4 So to say with certainty that he's not on 5 any of those, I can't be certain. 6 Q. Yeah. I wasn't asking for certainty. 7 To the best of your knowledge, you can't 8 recall or identify any instance where you had an 9 interaction with Professor -- with Joe Beechem -- 10 A. That's correct. 11 Q. -- professionally? 12 In your consulting work, have you given 13 opinions on the subject of patentable subject 14 matter? 15 A. I believe so. 16 Q. Have you given opinions on the subject of 17 enablement? 18 A. I believe so. 19 Q. And have you given opinions on the subject 20 of written description, prior to this instance? 21 A. I believe so. 22 Q. With respect to patent eligibility, 23 enablement, and written description, have you ever 24 given such opinions in any of the Patent Office 25 proceedings that you've been involved with?

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1 MS. KHANDURI: Objection; form. 2 A. Patent Office, meaning IPRs? 3 Q. IPRs, PGRs, those kind of things, yes. 4 A. I don't know what a "PGR" is. 5 Q. You've never heard of a "PGR," is that 6 right? 7 A. I may have heard of it. I don't know what 8 it is. 9 Q. Have you ever given a patent eligibility 10 opinion in the context of an IPR? 11 MS. KHANDURI: Objection; form, 12 foundation. 13 A. Outside of this case, I'm not certain. 14 Q. How about enablement? 15 A. I'm not certain in an IPR. 16 Q. Do you have a belief, one way or the 17 other? 18 A. I'm not prepared to answer that at this 19 moment. I don't know. 20 Q. Do you know whether you've ever given an 21 opinion on written description prior to this IPR in 22 the context of an IPR? 23 A. I have not reviewed all the IPRs I've 24 issued, and I can't recall. 25 Q. Have you given an enablement or written	1 will caution you to not divulge the 2 substance of communications with counsel. 3 Subject to that instruction, you 4 can answer the question. 5 A. I don't know how to answer the question, 6 given the objection. 7 Q. Okay. Did you locate the So-456 8 publication in the course of your prior art search 9 for this matter? 10 A. I don't believe so. 11 Q. And how much time did you expend searching 12 for prior art? 13 A. I don't know. 14 Q. Was it more or less than 10 hours? 15 A. I don't know. 16 Q. More or less than 20 hours? 17 A. I don't know. 18 Q. More or less than 50 hours? 19 A. Less than 50 hours. 20 Q. More or less than one hour? 21 A. Nearly certain, more than an hour. 22 Q. Can you be more specific than between one 23 and 50 hours, in terms of an estimate of how much 24 time you expended prior art searching in this 25 matter?
Page 27	Page 29
1 description opinion in any of your litigation 2 consulting, other than in the Ravgen/LabCorp matter? 3 A. I think I have. 4 Q. And where? 5 A. I think I did in Natera versus Guardant. 6 Q. How did you identify the So-456 reference 7 for your Ground 1? 8 A. I don't understand the question. 9 Q. Prior to your involvement in this matter, 10 you hadn't heard of or read the So-456 reference, is 11 that right? 12 A. That's correct. 13 Q. Yet you relied on that for your Ground 1, 14 is that right? 15 A. That's correct. 16 Q. And also your Ground 2? 17 A. That's correct. 18 Q. How did the So-456 publication come to 19 your attention? 20 A. After being retained in this case, 21 discussing with attorneys for 10x, we reviewed prior 22 art that might be relevant. 23 Q. Did you discover the So-456 reference, or 24 was that provided to you by counsel? 25 MS. KHANDURI: Dr. Spellman, I	1 A. Prior art searching occurred over a fairly 2 long period of time and did not -- and was 3 iterative. I could not tell you how long I spent. 4 Q. Right. I understand that. 5 We've established that you believe that 6 you've spent more than an hour and less than 50 7 hours, and I'm asking if you can narrow your 8 estimate to something tighter than a one-to-50-hour 9 range. 10 If you could stay quantitative, I'd 11 appreciate it. 12 A. Probably between five and 10 hours. 13 Q. Did you discover the Stahl reference in 14 your prior art searching? 15 A. I'm not certain. 16 Q. Do you have a belief, one way or the 17 other, sitting here now? 18 A. I probably did not. 19 Q. Did you discover the Chell reference in 20 the course of your prior art searching? 21 A. No. 22 Q. Is it your general belief that your -- the 23 prior art references you relied on came from 24 counsel? 25 I'm not asking you for the communications

Page 30 1 associated with that, just in terms of the source. 2 A. Likely. 3 Q. Now, you understand of the four grounds 4 that you identified, the Patent Office rejected -- 5 or the panel of the Board rejected three of them as 6 not establishing a preponderance of evidence that 7 there's a likely invalidity? 8 MS. KHANDURI: Objection; form, 9 foundation. 10 A. I haven't looked at what the "PTB" 11 returned. 12 Q. Did you review the PTAB institution 13 decision at all? 14 A. I don't believe so. 15 Q. Do you have any idea what the PTAB said or 16 did in its institution decision? 17 A. Not particularly. 18 Q. After you prepared your declaration, did 19 you review the petition that the declaration was 20 supporting? 21 A. I don't believe I did. 22 Q. Have you ever reviewed the petition 23 submitted in this matter? 24 A. I'm not certain. 25 Q. Do you have a belief, one way or the	Page 32 1 matter after you submitted the declaration and 2 before deposition preparation? 3 A. I have an extremely busy set of jobs. I 4 moved. 5 No, I don't. 6 Q. Can you identify any tasks you performed 7 associated with this case, after you submitted your 8 declaration in support of the petition and before 9 deposition preparation? 10 A. I'm not certain. 11 Q. Can you identify anything at all that you 12 think there's -- reasonably likely occurred? 13 A. Communication with counsel. 14 Q. Anything else? 15 A. Nothing I billed for. 16 Q. Anything else you can identify, whether or 17 not you billed for it? 18 A. I routinely think about things that I call 19 "unreimbursed time," things where I happen to think 20 about things. 21 So there's a constant process. And some 22 days, I wake up and think about things. I don't 23 keep track of it since I'm not billing for it. 24 Q. When did you begin preparation for this 25 deposition?
Page 31 1 other? 2 A. No. 3 Q. Did you review the patent owner's 4 preliminary response to the petition? 5 A. I don't believe so. 6 Q. After you prepared your declaration and 7 signed it, how much time did you expend in this 8 matter, up to the deposition preparation process? 9 A. Very little. 10 Q. More or less than three hours? 11 A. I don't know. 12 Q. More or less than five hours? 13 A. I don't know. 14 Q. More or less than 10 hours? 15 A. Unlikely, it was more than 10 hours. 16 Q. More or less than one hour? 17 A. Could have been more than one hour. I 18 don't know. 19 Q. It could have been less than one hour? 20 A. I don't know. 21 Q. You don't know whether it could have been 22 less than one hour? 23 A. That's correct. 24 Q. Do you have a belief, one way or the 25 other, as to whether you spent any time on this	Page 33 1 A. Starting roughly three weeks ago, I think. 2 Q. How much time did you spend between the 3 beginning of that preparation period and now, 4 preparing for the deposition? 5 A. Roughly, 30 or 40 hours. 6 Q. Did you meet with counsel in preparation 7 for your deposition? 8 A. Yes. 9 Q. How long were those meetings? 10 A. 25 hours, perhaps. 11 Q. What documents did you review to prepare 12 for your deposition? 13 A. Many of those that have been introduced in 14 this case. Others that may have been relevant. I 15 don't -- I can't give you a full list. 16 Q. Did you review your declaration? 17 A. Yes. 18 Q. Did you review the documents upon which 19 your declaration relied? 20 A. Yes. 21 Q. Can you identify any other documents? 22 A. Papers I had written. Papers that were 23 germane in the field. 24 Q. And what papers did you consider to be 25 germane in the field that you didn't rely on in your

Page 34 1 declaration? 2 A. I can't recall exactly. 3 Q. Can you identify anything at all? 4 A. Specifically? No. 5 Q. How about generally? 6 A. Papers in the space of spatial detections. 7 Papers in the space of things I've worked on. 8 Q. In the course of your review of papers 9 that you consider germane to your opinions in this 10 case, other than those you relied on did you find 11 any prior art that you consider to be better than 12 that upon which you relied? 13 MS. KHANDURI: Objection; form. 14 A. I don't believe so. 15 MR. REINES: Why don't we just 16 take a short break and -- 17 THE WITNESS: Sure. 18 MR. REINES: -- resume in a bit. 19 Thank you very much. 20 VIDEOGRAPHER: Off the record at 21 9:52. 22 (Whereupon, a recess was taken.) 23 VIDEOGRAPHER: On the record at 24 10:03. 25 BY MR. REINES:	Page 36 1 doing so, we reviewed competing technologies from 2 other vendors. 3 And in those conversations, particularly 4 with concerns about novel inventive ideas, we may 5 have gone over how the competitor platforms worked 6 in the space -- you know, as part of a conversation. 7 Q. When was this analysis of competing 8 spatial technologies that you performed in 9 connection with your responsibilities at the center? 10 A. It would have been from 2019 until 2023, 11 when I left. 12 Q. What technologies were considered as part 13 of that analysis? 14 A. The conversations I had with junior 15 scientists were not led by me. They were led by my 16 colleagues. 17 And they would -- we would have 18 conversations about the technologies in the space 19 and where there were inventive openings available. 20 Q. Can you identify any technology that you 21 addressed in those discussions? 22 A. My recollection is that it was 23 technologies like Stahl, so -- and Chell. 24 But whether they were specifically 25 discussed, I don't recall.
Page 35 1 Q. Do you know whether the Nanostring 2 products work according to the technology described 3 in the '689 patent? 4 MS. KHANDURI: Objection; form. 5 A. I don't believe I've rendered an opinion 6 on that. 7 Q. Do you have a belief, sitting here now, 8 one way or the other? 9 A. No. 10 Q. But you do believe that the 10x spatial 11 products work according to the Chell disclosure, is 12 that right? 13 MS. KHANDURI: Objection; form, 14 scope. 15 A. My recollection is the Chell disclosure 16 mirrors the 10x implementation very closely. 17 Q. And before this matter, did you know how 18 the 10x implementation worked? 19 A. I may have at one time. I may have 20 forgotten the details. 21 Q. Do you have a belief, one way or the 22 other, as to whether you know? 23 A. As part of my responsibilities running the 24 early detection center, I met with junior scientists 25 who were developing spatial technologies. And in	Page 37 1 Q. Do you remember anything, any type of 2 particular technology, that was considered when you 3 were evaluating the competing spatial technologies 4 in this 2019 to 2023 time period? 5 A. We were specifically concerned around 6 implementations on how analytes being detected were 7 going to be spatially encoded. 8 So I'm pretty sure the colleagues that I 9 had were looking at all the patents and technologies 10 that were issued and trying to find openings for the 11 center. 12 Q. Did the center identify any openings? 13 A. My recollection is that they did. 14 Q. What were they? 15 A. I can't tell you that. 16 Q. Why not? 17 A. That's protected under IP. 18 Q. We have a protective order here. I think 19 we can... 20 MS. KHANDURI: Objection -- 21 Q. ...go ahead. 22 MS. KHANDURI: -- scope. 23 A. I'm not comfortable telling you about 24 technology that I don't own. 25 Q. Even with the protective order here, you

Page 38 1 refuse to answer about the spatial technologies that 2 are being worked on in your center? 3 A. If counsel instructs me to answer, I will 4 answer. 5 MS. KHANDURI: We don't -- we do 6 not have a protective order, I think. 7 So I would instruct the witness 8 to not answer. 9 Q. All right. In terms of the.... 10 Do you remember any conversations 11 involving Nanostring technology when you were 12 discussing competing spatial technologies from 2019 13 to 2023 with colleagues at the center? 14 A. They were not our primary concern. 15 Q. When you say "not the primary concern," 16 was there any discussion about that? 17 A. As I've testified, we had extensive 18 conversations with Gordon Mills and -- around the 19 use of Nanostring and hit the assays he was using 20 and had, I believe, agreed to purchase one as part 21 of the center. 22 But the Nanostring technology was not what 23 we were concerned about. 24 Q. And why do you say that? 25 A. We did not feel that the technology, as	Page 40 1 A. I have read the entire '689 patent and the 2 claims, yes. 3 Q. And what was your reaction regarding the 4 quality of the technology disclosed there for the 5 purposes of spatial analysis? 6 A. I don't understand the question. 7 Q. Yes. You reviewed the '689 patent, 8 correct? 9 A. Yes. 10 Q. And that's about spatial technology, 11 right? 12 A. Yes. 13 Q. And you consider yourself an expert in the 14 area of spatial technology. Is that true? 15 A. Broadly speaking, yes. 16 Q. When you say "broadly speaking," what do 17 you mean by that? 18 A. My expertise is larger than just spatial 19 technology. But, yes. 20 Q. Spatial technology is one of the areas 21 where you're holding yourself out as being an 22 expert, or not? 23 Well, let me take you back and not 24 presume. 25 Do you consider yourself to be an expert
Page 39 1 described, was one that would impinge on where we 2 thought we wanted to go. 3 Q. At any point in time, did you develop 4 opinions as to the efficacy of the Nanostring 5 spatial technology? 6 A. No. 7 Q. Do you recall any colleagues addressing 8 anything about the quality of the Nanostring spatial 9 products? 10 A. Yes. 11 Q. And what do you recall in that regard? 12 A. Dr. Mills liked it. Other colleagues I 13 have liked the technology. 14 Q. And what did Dr. Mills say to you about 15 what he liked of the Nanostring spatial technology? 16 A. I'm not sure I could quote you exactly. 17 My general impression was that he 18 appreciated the ability to measure mRNAs and 19 proteins simultaneously. 20 Q. Anything else? 21 A. No. 22 Q. Did Dr. Mills express any opinions to you 23 regarding the 10x spatial technology? 24 A. No. 25 Q. Did you review the '689 patent closely?	Page 41 1 in the area of spatial technology? 2 A. I would say I'm an expert in the field of 3 genomic technologies, very broadly, including 4 spatial technology, implementations of genomics. 5 Q. And in terms of just being an expert in 6 the area of spatial, why would you not -- why would 7 you -- why do you keep putting it in the context of 8 the overall broader field? 9 A. I have expertise that is broader than just 10 spatial technology. 11 Q. Right. As it relates just specifically to 12 spatial technology, do you believe that you're a 13 scientific expert in that area? 14 A. Within the field of genomics spatial 15 technology, yes. 16 Q. And after reviewing the '689 patent, did 17 you have any belief as to how efficacious that 18 technology is? 19 MS. KHANDURI: Objection; form. 20 A. Scientists don't normally judge the 21 quality of science by patents. 22 So reading a patent alone would not 23 generally make a scientist believe that something 24 was amazing or not. 25 Q. Were you able to reach any qualitative

Page 42 1 conclusions about the spatial technology disclosed 2 in the '689 patent? 3 MS. KHANDURI: Objection; form. 4 A. I'm not sure I understand the question 5 again. 6 The specification describes the 7 capabilities of Nanostring. It describes them 8 clearly. 9 I don't know what else you want me to say. 10 Q. Sitting here now, do you believe that the 11 spatial technology described in the '689 patent 12 works for its intended purpose? 13 MS. KHANDURI: Objection; form. 14 A. The specification included with the '689 15 patent, irrespective of the claims of the '689 16 patent, to the best of my knowledge works. 17 Q. Were you able to reach any conclusions as 18 to how the technology disclosed in the Chell 19 reference works relative to that in the '689 patent, 20 in terms of how effective it is for spatial 21 analysis? 22 MS. KHANDURI: Objection; form. 23 A. I'm not prepared to render an opinion on 24 that. 25 Q. And why is that?	Page 44 1 Q. The Chell reference is in anticipation. 2 How come you included that after the 3 Grounds 2 and 3, which were obviousness 4 combinations? 5 MS. KHANDURI: Dr. Spellman, 6 same caution. 7 A. Logically, it stands on its own, as it 8 requires that the specification for the '689 be 9 shown to not provide written support for the 10 underlying methods of '689. And therefore, it has a 11 different priority date. 12 Q. And how come you didn't include the Chell 13 ground in front of the So-456-related grounds? 14 MS. KHANDURI: Objection; form. 15 Dr. Spellman, same caution. 16 A. I believe they are logically provided. 17 Q. Yeah. My question wasn't whether it was 18 logical. My question: What is the logic? 19 MS. KHANDURI: Objection; form. 20 Dr. Spellman, same caution. 21 A. I think they're logically arranged. I 22 don't know how else to explain it to you. 23 Q. You included the So-456 grounds in front 24 of the Chell ground. 25 And my question to you is: Can you
Page 43 1 A. I have not done a deep technical 2 comparison of the two platforms to assess which one 3 is a better quality. 4 Q. Did you order the grounds in your 5 declaration according to the strength of each 6 position? 7 A. No, I don't believe so. 8 Q. What was the basis for your ranking of the 9 different grounds, 1 through 4? 10 A. Organizationally, I discussed with counsel 11 how to structure the declaration and, in developing 12 the declaration, ordered them in a seemingly logical 13 manner. 14 Q. Why did you put the So-456 reference ahead 15 of the Stahl -- excuse me -- ahead of the Chell 16 ground? 17 MS. KHANDURI: Dr. Spellman, I 18 will caution you to not divulge the 19 substance of communications with counsel. 20 Subject to that instruction, you 21 can answer the question. 22 A. I believe it would be because we wanted 23 to -- I wanted to declare that due anticipation and 24 then obviousness and then combinations of 25 obviousness.	Page 45 1 identify anything at all, any reason at all, why you 2 would have used that order? 3 A. I already identified a reason. 4 Q. I'm sorry. What was that? 5 A. I told you that the '689 patent priority 6 application doesn't provide written support for the 7 claim methods and therefore has a different priority 8 date. And so, we put -- I put that one as a last 9 ground. 10 Q. I'd like to direct you to Page 7 of your 11 declaration. 12 Let me know when you have that, please. 13 A. Yes. 14 Q. And here, you reference the person of 15 ordinary skill in the art. 16 Do you see that? 17 A. Yes. 18 Q. And your view of the person of ordinary 19 skill in the art in this space is that they think 20 along conventional wisdom in the art. 21 Is that right? 22 A. That is what I understand. 23 Q. And do you agree with that? 24 A. I believe it's a matter of law. 25 Q. For purposes of your opinions in this

Page 46 1 case, the person of ordinary skill in the art was 2 presumed to follow the conventional wisdom. 3 Is that right? 4 A. I don't understand the question. 5 Q. In the analyses you performed in your 6 report, you used the viewpoint of a person of 7 ordinary skill in the art. 8 Is that right? 9 A. Yes. 10 Q. And in understanding the characteristics 11 of a person of ordinary skill in the art for 12 purposes of this proceeding, you presume that they 13 think along the lines of the conventional wisdom in 14 the art. 15 Is that right? 16 A. Yes. 17 Q. The person of ordinary skill in the art in 18 this field would have a strong understanding of 19 genomics' approaches, such as spatial detection of a 20 target analyte in a tissue section? 21 A. Yes. 22 Q. For the person skilled in the art with a 23 strong understanding of the technology of spatial 24 detection of target analyses -- including, for 25 example, mRNA and DNA -- what would be the basic	Page 48 1 oligonucleotide binding, hybridization, microarray 2 experience as a foundational approach previously -- 3 all host of molecular biology approaches of that 4 flavor. 5 Q. You're saying those would be within the 6 competency of a person of ordinary skill in the art 7 in this field? 8 A. Yes, I believe so. 9 Q. And would that include tagging with 10 barcodes and using ligation for specificity? 11 MS. KHANDURI: Objection; form. 12 A. Yes, I think so. 13 Q. Would a person of ordinary skill in the 14 art, as you looked at it, be familiar with tagging 15 and ligation and barcoding techniques, both on and 16 off an analyte? 17 MS. KHANDURI: Objection; form. 18 A. The foundational molecular biology would 19 fall under the genetic and genomic approaches 20 component of what I've described. 21 Q. Is that a yes or a qualification? 22 A. Can you repeat the question? 23 Q. Sure. Would a person of ordinary skill in 24 the art, at the relevant time, have basic competency 25 with tagging and -- tagging, ligation, and barcoding
Page 47 1 competencies? 2 MS. KHANDURI: Objection; form. 3 A. The field of spatial detection of target 4 analytes -- specifically, mRNAs or DNAs -- is a -- 5 would historically have involved microscopy, 6 pathological imaging, tissue sectioning, and related 7 technologies. 8 And the intersection with genomic 9 approaches would have required broad-scale 10 understanding of the genome as a whole, the 11 structure of the genome. 12 And then, spatial detection of that would 13 add a whole other set of competencies. 14 And further, the multiplex components of 15 the data would require substantial experience in 16 image processing, image segmentation, image 17 analysis, multianalyte interpretation, multiplex 18 measurements. 19 It's extensive space. 20 Q. You're not saying a person of ordinary 21 skill in the art with their basic competencies would 22 understand, for purposes, spatial analysis, 23 ligation, and tagging with barcodes? 24 A. The genomic components of that would 25 require high-throughput DNA sequencing,	Page 49 1 techniques, both on and off of the analyte? 2 MS. KHANDURI: Objection; form, 3 foundation. 4 A. You're using rather specific language in 5 that phrasing. 6 I think a person of ordinary skill in the 7 art would be familiar with ligation as a broad 8 concept, extremely broad, and how and when it can be 9 utilized effectively. 10 Q. And how about barcoding? 11 A. That would fall under genomic approaches, 12 yes. 13 Q. So, same answer? 14 A. Yes. 15 Q. And then, how about tagging with 16 identifiers? 17 A. In the context of barcodes or unique 18 molecular identifiers, yes, that was a foundational 19 technology in the space and fall under the genomic 20 approaches component. 21 Q. And if you turn to Paragraph 36, please. 22 A. Paragraph 36? 23 Q. Yes; on Page 11. 24 A. Yes. 25 Q. And you understand that, if we get to

Page 50 1 this, that for anticipation that the elements of the 2 claim must be disclosed in a single prior art 3 reference arranged as they're arranged in the claim? 4 A. Yes. 5 Q. And insofar as you're relying on 6 inherency, inherency requires that something -- that 7 a feature be necessarily present? 8 A. Yes. 9 Q. And did you offer any inherency opinions 10 in this matter? 11 A. I believe so. 12 Q. And can you show me what claim requirement 13 you believe is inherently disclosed in the So-456 14 reference? 15 A. You'd like me to go through the 16 declaration and find all the examples of inherency? 17 Q. Yes, please. 18 Maybe we could start one by one. 19 A. Sure. 20 (Witness reading.) 21 A. So in the section of Figure 9, the release 22 of the 950 ligation product is inherent in the 23 amplification step of -- 24 Q. Just orient me. I'm sorry to do that -- 25 A. I'm on Page 71, 72.	Page 52 1 the target nucleic acid 2 molecules. 3 Q. I'm sorry, I may not be following you. 4 A. Paragraph 134. 5 Q. Oh, 134. 6 A. The last sentence: 7 The amplicons generated by 8 isothermal amplification are 9 free from (i.e., not bound to) 10 the target nucleic acid 11 molecules. 12 Q. All right. And what are you saying next 13 is an inherency opinion of yours? 14 (Witness reading.) 15 A. So in Paragraph 149 on the second part of 16 that paragraph on Page 79, I discuss the extension 17 reaction and I identify that the configuration of 18 the assay, as described with the 950 molecule bound 19 to the capture probe on the surface at -- between 20 hybridization of positions 935 and 960, that the 21 extension is inherently in both direction unless 22 it's chosen not to be. 23 The So-456 is fairly clear that that 24 happens, and the So-456 specifically says that both 25 extension products can be used for downstream
Page 51 1 Q. Thank you. 2 A. Let me know when you're ready. 3 Q. Yes, I'm ready. 4 A. The amplification of DNA is 5 semi-conservative, which means that when you have a 6 duplex DNA molecule, you separate the two strands 7 and replicate them, if possible, independently. 8 In this case, the structure of the 9 molecule means that only the ligated oligos will 10 replicate in this case. 11 And the release from the parent strand of 12 the ligated molecule 950 is inherent in the 13 amplification step, for example. 14 Also, in -- 15 Q. Oh, before we move on -- 16 A. Yeah. 17 Q. -- in terms of the -- that release that 18 you're saying is inherent, have you set forth an 19 opinion on that in your declaration? 20 MS. KHANDURI: Objection; form. 21 A. At the end of Paragraph 135 [sic], I state 22 that: 23 The amplicons generated by 24 isothermal amplification are 25 free from (i.e., not bound to)	Page 53 1 library preparation. 2 So it's an inherent argument about how DNA 3 polymerases work. 4 Q. And a person skilled in the art would know 5 how to limit the extension reaction so it proceeds 6 in only one direction? 7 A. Yes. 8 Q. Does So-456 state anywhere that the 9 extension reaction should proceed in both 10 directions? Does it teach that? 11 A. I missed a "should" or "shouldn't." 12 Q. Does So-456 teach that it is...that the 13 experiment should be designed so that the extension 14 reaction proceeds in both directions, as compared to 15 just one? 16 MS. KHANDURI: Objection; form. 17 A. You'll see in Paragraph 1- -- I've got a 18 citation to Paragraph 173 of So, that So-456 19 confirms that both extension products -- and the 20 quote is "both extension products can be used for 21 downstream library generation." 22 Q. This says: 23 When the captured DNA 24 molecule is used as a primary, 25 the spatial region is copied.

Page 54 1 That's not true, insofar as there's a 2 blocked or modified nucleotide? 3 MS. KHANDURI: Objection; form, 4 foundation. 5 A. I didn't understand the question. 6 Q. Yes. If there is a blocked nucleotide, 7 then the spatial address region 130 won't 8 necessarily be copied, right? 9 MS. KHANDURI: Objection; form. 10 A. A POSA would know how to configure this 11 assay to alter its chemistries to allow extension at 12 960 or extension of 935, exclusively. So confirms 13 that, in this configuration, both extension happens. 14 MS. KHANDURI: Counsel, can we 15 take a break? 16 MR. REINES: Sure. 17 MS. KHANDURI: Thanks -- for 18 like one minute, I just want to -- 19 VIDEOGRAPHER: Off the record at 20 10:41. 21 (Whereupon, a recess was taken.) 22 VIDEOGRAPHER: On the record at 23 10:48. 24 BY MR. REINES: 25 Q. Did you, in your declaration, identify	Page 56 1 MS. KHANDURI: Objection; form. 2 A. There are conditions in which you don't 3 want something to happen. 4 In this particular assay, I can't identify 5 any advantages. 6 Q. Is that an issue you considered as part of 7 formulating your opinions in your declaration? 8 A. In the context of So's instruction, both 9 extension products can be used for downstream 10 library generation. 11 A POSA, from my perspective, would read 12 that and understand that the 95- -- extended 950 13 molecule was available. 14 Q. My question was: Did you consider what 15 the benefits would be for using blocking or modified 16 basis instead of permitting bidirectional extension? 17 MR. REINES: Objection; form, 18 foundation. 19 Q. When you formulated your opinions 20 regarding the cell reference. 21 A. My understanding is that a POSA would take 22 the So reference and apply its teachings as written 23 and modify them as necessary. 24 But in this case, they don't need to be 25 modified. And I don't know why a POSA would examine
Page 55 1 where you were offering inherency opinions and where 2 you weren't? 3 MS. KHANDURI: Objection; form. 4 A. I'm not sure how to answer that. 5 I don't know the legal basis of how to 6 communicate that. 7 Q. When you were offering an inherency 8 opinion in support of the grounds in your 9 declaration, did you use the word "inherency"? 10 A. I do not see it either in the section on 11 release of the 950 molecule nor in the section on 12 the bidirectional extension. 13 Q. Why would a person of ordinary skill in 14 the art want to use a modified nucleotide to block 15 bidirectional extension? 16 MS. KHANDURI: Objection; 17 foundation, form. 18 A. I actually think that So is telling the 19 POSA that they shouldn't. 20 Q. Leaving out what they're saying, what 21 would be the advantages of doing that -- in terms 22 of, if you were talking to a graduate student or 23 something like that? 24 What would be the advantages of having 25 unidirectional?	Page 57 1 this description and not follow So's teachings. 2 Q. I'd like you to turn to your Table 1. 3 A. What page is that on? 4 Q. I'm just getting that myself. 5 (Pause.) 6 Q. It's on Page 21. This is in Paragraph 58. 7 A. Yes. 8 Q. And with respect to -- well, what was your 9 purpose in preparing Table 1? 10 Let me start with that. 11 A. Sorry. I couldn't hear. 12 Q. What was your purpose in preparing 13 Table 1? 14 A. The '689 patent uses oligonucleotides 15 extensively and, in doing so, has different names 16 for different classes of oligonucleotides. 17 I constructed Table 1 to help communicate 18 the features of different classes of 19 oligonucleotides in the '689 patent. 20 Q. Now, you used the parenthetical phrase 21 "excluding the claims." 22 Do you see that? 23 A. Yes. 24 Q. And can you explain why you excluded the 25 claims in your classification of the probes in the

Page 58 1 '689 patent in Table 1? 2 A. The use of these terms in the claims is 3 different in the '689 patent than in the 4 specification. 5 So I focused this table specifically on 6 the use of these terms in the specification. 7 Q. Have you construed, as part of your work 8 in this case, the nucleic acid probes that are in 9 the claims? 10 A. What do you mean, "construed"? 11 Q. You're familiar with claim construction 12 principles from your prior work as a litigation 13 expert. Is that correct? 14 A. Reasonably. 15 Q. And have you construed the phrase "nucleic 16 acid probes" from the claims of the '689 patent? 17 A. You'll see an extensive analysis, starting 18 on Page 128, on the use of the various terms for the 19 various oligonucleotides in discussion, starting on 20 Page 128 and continuing on, I believe, to 21 Page 137 -- but perhaps it extends a little beyond 22 that -- extending all the way to -- actually, it 23 extends quite a bit beyond that. 24 I believe it goes all the way to Page 142. 25 Q. Great. My question was: Do you have a	Page 60 1 with you now, we describe how they're used in the 2 specification and contrast them to how they're used 3 in the claims. 4 Q. Is there anything you would consider to be 5 a claim construction? 6 And if so, can you state it. 7 MS. KHANDURI: Objection -- 8 well, form. 9 A. My declaration as a whole is my testimony. 10 If you have a specific question about a 11 specific component of it, I'm happy to answer it. 12 Q. I think I'm asking a fairly simple 13 question, and let me just ask it again. 14 Have you construed the term "nucleic acid 15 probe" in the claims of the '689 patent? 16 That, I think, submits to a yes or no. 17 A. Table 1 characterizes the properties of 18 the oligonucleotides and how they're utilized in the 19 specification. 20 And in this section, I show how they are 21 not utilized the same way in the '689 claims. 22 Q. Is that as responsive as you can be? 23 A. I believe so. 24 Q. Okay. So you can't answer my question 25 more directly, is that right?
Page 59 1 construction of the term "nucleic acid probe" as 2 that term is used in the claims of the '689 patent? 3 MS. KHANDURI: Objection; form. 4 Counsel, could you speak a 5 little bit louder. I'm having a hard 6 time. 7 (Witness reading.) 8 A. So I discuss in this section the use of 9 the terms in the specification and contrast it to 10 the use in the claims. 11 I'm not sure what you're asking beyond 12 that. 13 Q. Yeah, you're familiar with the concept of 14 forming a claim construction on claim language? 15 A. I believe so. 16 Q. And that's something you've done in most 17 of the cases in which you've testified as an expert? 18 A. I believe so. 19 Q. Did you do that with respect to "nucleic 20 acid probe" in the claims? 21 A. Yes. I think what's important in Table 1, 22 I describe the features of the oligonucleotides used 23 in the '689 specification and mapped them to how 24 they behave in the specification. 25 And in this section that I'm discussing	Page 61 1 A. I believe my declaration covers this 2 completely. 3 Q. Covers what completely? 4 A. The topic at hand. 5 Q. Yeah, my question wasn't whether your 6 deposition -- your declaration covers the topic at 7 hand completely. 8 My question was whether you performed 9 claim construction as it relates to the phrase 10 "nucleic acid probe" in the claims. 11 And you haven't been able to give me a 12 direct yes or no answer. 13 Is that something you think you can do? 14 A. I compared the use of the phrase -- and 15 the utility of the various oligonucleotides in the 16 claims to the specification and find that they do 17 not align. 18 Q. That wasn't my question. 19 My question was: Are you able to give a 20 yes or no answer as to whether or not you have 21 construed the phrase "nucleic acid probe" from the 22 claims of the '689 patent? 23 Can you give a yes or no answer to that? 24 MS. KHANDURI: Objection -- 25 objection; form.

Page 62 1 A. I believe my declaration covers the topic. 2 Q. Can you answer more directly my question, 3 which is whether you can provide a yes or no answer. 4 MS. KHANDURI: Objection; form. 5 A. I don't think I need to. 6 Q. Did you construe the claims of the '689 7 patent at all? 8 A. I considered all the components of the 9 '689 patent. 10 Q. You understand what a claim construction 11 is, is that right? 12 A. I'm not a lawyer. 13 Q. Do you understand what a "claim 14 construction" is? 15 A. Claims are given their ordinary and 16 customary meaning at -- by a POSA. They're viewed 17 in the patent specification and prosecution history. 18 I can read you the entire section. 19 Q. My question to you is: Do you understand 20 what a claim construction is, based on your surveys 21 as a litigation expert in more than a half dozen 22 different proceedings? 23 A. The entire complexities of all of what is 24 involved in claim construction, I am not a complete 25 expert at.	Page 64 1 A. Repeat the question, please. 2 Q. What are the words of your interpretation 3 of the term "nucleic acid probe" from the '689 4 patent claims? 5 MS. KHANDURI: Objection; form. 6 A. So the use of nucleic acid probes is a 7 very specific language in the specification. 8 It is much narrower than a POSA would 9 understand it to be broadly. 10 In the '689 specification, nucleic acid 11 probes are pairs of oligonucleotides that hybridize 12 to an identifier oligonucleotide, that identifier 13 oligonucleotide having been cleaved from the -- at 14 the spatial -- at the spatial -- at the spatial 15 restriction step. 16 And the nucleic acid probes are hybridized 17 to that released identifier oligonucleotide. 18 In the '689 patent claims, the thing named 19 "nucleic acid probe" is still a pair of 20 oligonucleotides. But they were never released 21 from -- sorry, they never hybridized -- my 22 apologies -- they do hybridize to the target 23 analyte. 24 I believe I've said that correctly. 25 Q. Would a person skilled in the art
Page 63 1 Q. Yeah, I didn't include any of those 2 extreme qualifiers, such as "entire complexities of 3 all." 4 I'm just asking: Do you have a general 5 understanding of what a "claim construction" is in 6 patent litigation? 7 A. Generally, yes. 8 Q. And you understand that's providing an 9 interpretation of claim language. Right? 10 A. Yes. 11 Q. Do you have an interpretation of the term 12 "nucleic acid probe" from the '689 claims in this 13 case? 14 That's a yes or no question, not what it 15 is -- but, do you or don't you? 16 A. I'm failing to understand how I haven't 17 answered that question by showing you how I've 18 mapped the '689 specification to the claims, and 19 showing where they do and do not align. 20 I believe that answers your question. 21 Q. What are the words of your interpretation 22 of the term "nucleic acid probe" from the '689 23 patent claims? 24 MS. KHANDURI: Objection; form. 25 (Witness reading.)	Page 65 1 understand that "collecting the nucleic acid probes, 2 or portions thereof" of Claim 1 of the '689 patent 3 can happen without cleaving? 4 MS. KHANDURI: Objection; form, 5 foundation. 6 A. In the specification or the claims? 7 Q. My question was in the claims. 8 A. The claims -- may I please have the '689? 9 Q. Oh, sure. 10 (Whereupon, Exhibit 1001, previously 11 marked, was presented to the witness.) 12 Q. I'm handing you what has been marked as 13 Exhibit 1001, which is the '689 patent. 14 A. I see nothing in the claims that requires 15 cleaving. 16 Q. In terms of the Step 1(e), which is the 17 extension reaction, in the claims of the '689 patent 18 is that required to take place in any particular 19 location? 20 MS. KHANDURI: Objection; form. 21 A. What do you mean by "location"? 22 Q. Either on-analyte or off-analyte. 23 (Witness reading.) 24 A. The collecting steps preceded it, which 25 would imply that the extension reaction happens away

Page 66 1 from wherever the nucleic acid probes of the claims 2 had been previously. 3 Q. And have you construed the claims to 4 determine whether the steps need to take place in 5 the order that they're listed in the claims of the 6 '689 patent? 7 A. The specification of the '689 patent 8 cannot function without the nucleic -- without the 9 primary probe, as I describe it, being separated 10 from the analyte. 11 So in that context, in my opinion, the 12 extension cannot happen in -- there is no way to 13 encode the spatial information in the '689 14 specification if the primary probe has not been 15 released and taken away from this analyte. 16 Q. The claims of the '689 patent do not 17 identify anything that corresponds to a primary 18 probe, as you use that term in your declaration. 19 Is that right? 20 A. All of the primary probes in the '689 21 specification are cleavable. 22 There is no such requirement in the 23 claims. And therefore, there is no written support 24 for the release mechanism. 25 I think I've said that correctly.	Page 68 1 cleavable element as required in the specification, 2 do have target-binding domains and would meet my 3 definition of "primary probe." 4 Q. And in terms of claim construction, you 5 understand that it's important that the claims be 6 construed in the context of the specification? 7 A. Yes. 8 Q. And a person of ordinary skill in the art 9 understanding the claims would look to the 10 specification as important context? 11 A. Yes. 12 Q. And a person skilled in the art, having 13 reviewed the '689 specification and reading Claim-1, 14 would understand that the nucleic acid probes could 15 be collected, including just portions thereof. 16 Correct? 17 MS. KHANDURI: Objection; form, 18 foundation. 19 A. Claim 1, as written.... 20 Can you repeat the question. 21 Q. A person skilled in the art, having 22 reviewed the '689 specification and performing the 23 method of Claim 1, would understand that the nucleic 24 acid probes could be collected by collecting just a 25 portion of them?
Page 67 1 Q. My question is just whether there are -- 2 the concept of primary probes is in the claims of 3 the '689 patent, according to you? 4 Could you please answer that question. 5 A. You'll see from my definition of "primary 6 probes" that the use of the term "primary probe" is 7 those probes having a target binding domain. 8 And so, while the specification and the 9 claims have different primary probe capabilities, 10 the plurality of nucleic acid probes in Claim 1 and 11 16, I believe, are primary probes in that they 12 contain target-binding domains. 13 Q. And is it that the "primary probes," as 14 you're using that term relative to the claims, have 15 to be -- have to engage in analyte binding, or can 16 they bind off-analyte? 17 MS. KHANDURI: Objection; form. 18 A. All of the things that I classify as 19 "primary probes" bind on-analyte. 20 Q. And that applies to the term "primary 21 probe," as you used that term, with respect to the 22 claims as well. Right? 23 MS. KHANDURI: Objection; form. 24 A. In Claim 1 and 16, the plurality of 25 nucleic acid probes, although they do not have a	Page 69 1 A. That is correct. 2 Q. And the method of Claim 1 would work to 3 spatially detect at least one target analyte in the 4 first location and the second location of a tissue 5 sample? 6 MS. KHANDURI: Objection; form, 7 scope. 8 A. Not given the way the claim is written and 9 the specification is derived -- is communicated. 10 Q. So a person skilled in the art would not 11 be able to make the method of Claim 1 work? 12 MS. KHANDURI: Objection; form, 13 scope. 14 A. Not given the specification, as you've 15 described it. 16 Q. Which aspect of -- method of Claim 1 would 17 a person skilled in the art not be able to 18 implement? 19 MS. KHANDURI: Objection; form, 20 scope. 21 A. The specifications requirement for 22 cleavable probes is incompatible with the rest of 23 the claims -- rest of Claim 1 and 16. 24 Q. Do you have an understanding that it's 25 inappropriate to construe a claim to include a

Page 70 1 requirement that's in the specification? 2 MS. KHANDURI: Objection; form, 3 scope. 4 Q. But not in the claim. 5 MS. KHANDURI: Objection; form, 6 scope. 7 A. The specification has no written support 8 for the claims, as written. 9 Q. Yeah, that's -- I don't believe that's 10 responding to my question. 11 My question was: Do you -- are you 12 familiar with the claim construction principle that 13 you're not supposed to insert requirements from the 14 specification in the claims unless you've properly 15 construed the claims to contain such a requirement? 16 MS. KHANDURI: Objection, form, 17 scope. 18 A. My understanding is: The POSA reads the 19 claims in the context of the specification to 20 understand what they mean. 21 Q. Okay. And you're saying that, based on 22 your analysis, that a person skilled in the art 23 would understand the method of Claim 1 to require 24 cleaving probes, is that correct? -- because they 25 can understand the claims in the context of the	Page 72 1 A. It's not apparent -- it seems like it 2 would work. 3 Q. A skilled artisan would have a strong 4 enough understanding of genomics in the spatial area 5 to implement the method of Claim 1 of the '689 6 patent. 7 MS. KHANDURI: Objection -- 8 Q. Right? 9 MS. KHANDURI: Objection; form, 10 scope. 11 A. I don't believe I've rendered an opinion 12 on that. 13 Q. Do you have a belief, sitting here now? 14 A. Can you repeat the question, please. 15 Q. A skilled artisan would have a strong 16 enough understanding of genomics in the spatial area 17 to implement the method of Claim 1 of the '689 18 patent -- 19 MS. KHANDURI: Objection; form, 20 scope. 21 Q. -- at the date of the priority documents. 22 MS. KHANDURI: Objection; form, 23 scope. 24 A. As written, I believe that the claims 25 could likely be practiced.
Page 71 1 specification. 2 MS. KHANDURI: Objection; form. 3 A. I'm sorry. I believe I've misstated that. 4 Q. I mean, that is what you said in your last 5 answer, since -- 6 A. Yes. I believe I'm -- I believe I'm 7 incorrect. 8 Q. So if a person skilled in the art 9 performed the method of Claim 1 of the '689 patent, 10 they would be able to do as the preamble states, 11 which is: Detect at least one target analyte in the 12 first location and a second location of a tissue 13 sample. Right? 14 MS. KHANDURI: Objection; form, 15 scope, foundation. 16 (Witness reading.) 17 A. I'm not sure I've rendered an opinion on 18 that. 19 Q. Do you have a belief, one way or the 20 other, sitting here now? 21 A. I don't think I've rendered an opinion on 22 that. 23 Q. Yeah, my question was different: Do you 24 have a belief, sitting here now? 25 (Witness reading.)	Page 73 1 Q. When you say "likely be practiced," you 2 mean by a skilled artisan? 3 A. Yes. 4 Q. And a skilled artisan would know how to 5 collect nucleic acid probes, either in part or in 6 whole, for purposes of spatial detection? 7 MS. KHANDURI: Objection; form. 8 A. Given the claims.... 9 Given the claims, it would be my 10 interpretation that the specification does not 11 provide sufficient teaching, relevant to the claims, 12 for an artisan to implement those claims, given the 13 specification. 14 Q. Would the basic competency of a skilled 15 artisan, as you described it earlier today, with 16 techniques such as ligation and barcoding, know how 17 to ligate the barcode off the analyte in the context 18 of Claim 1? 19 MS. KHANDURI: Objection; scope. 20 Q. And this is at the time of the priority 21 document. 22 MS. KHANDURI: Objection; scope. 23 A. I don't believe I've rendered an opinion 24 on that. 25 Q. Do you have a belief, one way or the

Page 74 1 other, sitting here now? 2 A. Would a skilled artisan know how to 3 perform ligation? 4 Q. No. Let me ask the question. 5 If a skilled artisan was performing the 6 method of Claim 1 of the '689 patent, would they 7 have within their basic competencies, as you 8 described them earlier today, the ability to perform 9 ligation off-analyte for barcoding? 10 MS. KHANDURI: Objection; form, 11 scope. 12 A. The way you've structured the sentence 13 just means, can they perform ligation? 14 Q. Well, you'd be doing it for barcoding 15 off-analyte, which is what I -- in the context of 16 Claim-1 -- 17 MS. KHANDURI: Objection; 18 form -- 19 MR. REINES: So let me just ask 20 the whole -- 21 MS. KHANDURI: -- scope. 22 Go ahead. 23 MR. REINES: No, you go. Sorry. 24 Let me ask the question again for -- 25 BY MR. REINES:	Page 76 1 shown. 2 Q. You covered a lot of different areas, but 3 I don't think they were the question. 4 Let me give you another opportunity to 5 answer the question directly. 6 If a skilled artisan was performing the 7 Claim 1 method of the '689 patent, would they have 8 within their basic competency the ability to perform 9 ligation off-analyte for barcoding? 10 MS. KHANDURI: Objection; scope. 11 A. Outside of the claim, a POSA would know 12 how to perform ligation. 13 I don't know how to answer the question 14 beyond that. You've imparted a great deal of extra 15 context and about a simple skill. 16 Q. All right. Let me go at it this way. 17 Is there any step of the method of Claim-1 18 of the '689 patent that a skilled artisan would not 19 be able to perform? 20 MS. KHANDURI: Objection; scope. 21 Q. And it's in 2018. 22 MS. KHANDURI: Objection; scope. 23 (Witness reading.) 24 A. So I'm going to answer this again, and I 25 believe I've answered this already, that the
Page 75 1 Q. If a skilled artisan was performing the 2 Claim 1 method of the '689 patent, would they have 3 within their basic competency the ability to perform 4 ligation off-analyte for barcoding? 5 MS. KHANDURI: Objection; scope. 6 A. A POSA has a set of competencies, things 7 they know how to do -- ligation being a common one, 8 for example. 9 You're imparting quite a lot of conditions 10 to the POSA that I think are becoming challenging. 11 The written specification of '689 provides 12 no teaching to the claims of '689 on how to achieve 13 what is encoded in the claims, given the 14 specification. 15 They cannot be done, given the teachings 16 of '689 in the specification. 17 So the capabilities of a POSA to do any 18 specific molecular biology technique -- I don't 19 think you can granularize them into how to perform 20 the entire claim. 21 Individual components may or may not. 22 I think probably a POSA knows how to do -- 23 can read this claim and understand it. 24 But the written support in the 25 specification is lacking for implementing it as	Page 77 1 specification guides a POSA to understand the claims 2 and to interpret how to -- what the claim language 3 means. 4 And I don't think a POSA could understand 5 the claims, given the structure of the 6 specification. 7 Q. And what about the claims would the person 8 of skill in the art not understand? 9 A. Most specifically, the entire structure of 10 spatial detection in the specification is dependent 11 upon cleavable probes. 12 There is no teaching in the specification 13 whereby the location is identified in any other way, 14 other than by cleavable probes. 15 And as such, a POSA -- there's not enough 16 written support in the specification to support 17 these claims. 18 Q. All right. Let's do it this way. 19 In 2018 -- let's take the '689 patent out 20 of it -- would a person of ordinary skill in the 21 art, based on their basic competency, know how to 22 perform the method of Claim 1? 23 MS. KHANDURI: Objection; scope. 24 A. If someone was given a method in 2018 with 25 these steps, I don't think they would be able to

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1 practice it. 2 Q. Why not? 3 A. The specific challenge circa 2018 was 4 around collection in a spatially defined manner, and 5 I don't think a POSA would know how to complete all 6 of the necessary collection steps. 7 Q. And what were the challenges? 8 MS. KHANDURI: Objection; scope. 9 A. The principal challenges were restricting 10 the locations to specific analytes being detected. 11 Q. You said -- you used "challenges," plural. 12 Was there any others, or is that the only 13 challenge in 2018 -- 14 A. That was the principal challenge. 15 There are -- a variety of different 16 methods had been proposed or developed to tackle 17 that problem, and they each introduce new 18 challenges. 19 Q. All right. I'd like to direct you to the 20 inventors of the '689 patent, and I just want to go 21 through that. Perform.... 22 Which of these inventors did you know 23 before you were involved in this case, if any? 24 A. I'm not sure I know any of them. 25 Q. And --	1 I've been kind of not opposing that 2 strictly, but we need to move more towards 3 responsiveness. 4 In Column 16, do you see the paragraph at 5 Line 14 through 26 [sic]? 6 (No audible response.) 7 Q. Just, do you see that paragraph? 8 That should be easy. 9 A. The paragraph starting at Line 14? 10 Q. Yes. 11 A. Yes. 12 Q. Thank you. 13 And this is in the "Detailed Description 14 of the Invention" section. Is that right? 15 A. Yes. 16 Q. And there, when it says: 17 The present disclosure 18 provides a comparison of the 19 identity and abundance of 20 target proteins and/or target 21 nucleic acids.... 22 And then it goes on. 23 Do you see that? 24 A. Yes. 25 Q. Is there anything in the description
Page 79	Page 81
1 MS. KHANDURI: Sorry, can we 2 take a break? -- sorry, my realtime just 3 went out. 4 MR. REINES: Okay. 5 MS. KHANDURI: Oh, it's back on. 6 It's fine. Sorry. 7 MR. REINES: Okay. Let me know 8 if you need a break. 9 MS. KHANDURI: Yeah, we're fine. 10 BY MR. REINES: 11 Q. If you would turn to Column 16, please. 12 A. Column 16. 13 Q. Yes. 14 A. Yes, Column 16. 15 Q. Do you see where it says, "The present 16 disclosure..."? 17 A. Yes. 18 Q. Is there any requirements in this 19 paragraph -- which is Column 16, from Line 14 20 through 29 -- that is inconsistent with the method 21 of Claim-1? 22 A. In the first two paragraphs, there's very 23 little described at all. 24 Q. Try to stay with me on the question. All 25 right?	1 contained in that paragraph that's inconsistent with 2 the method of Claim 1? 3 If you could just try to stay with that 4 question and be responsive. 5 A. It's hard to be responsive. There's no 6 method in that -- in that paragraph. 7 So it's like answering a nonquestion. 8 Q. So if you are able to find anything in the 9 description in the paragraph at Column 16, Line 14 10 through 29, that's inconsistent with the method of 11 Claim 1, please identify it now. 12 A. I cannot. 13 Q. Okay. If you turn to the paragraph at 14 Column 16, Line 51 through to 67 -- do you have that 15 in front of you? 16 A. 51 through 67? Yes; the last paragraph in 17 Column 16. 18 Q. Do you see the "ligation method of the 19 present disclosure" -- 20 A. Yes. 21 Q. -- language? 22 Is there anything in that paragraph that's 23 inconsistent with the method of Claim 1? 24 (Witness reading.) 25 A. I don't believe so.

Page 82 1 Q. I'd like to direct you to the paragraph on 2 Column 19 at Line 35 through 54. 3 Do you have that in front of you? 4 (Witness reading.) 5 Q. Dr. Spellman, do you have that in front of 6 you? 7 A. Oh, sorry. Yes. 8 I was reading. My apologies. 9 Q. That's all right. I mean, if you want to 10 read it, read it. 11 But the question will be the same, which 12 is: For the description in the specification, the 13 "Detailed Description of the Invention" section 14 regarding the ligation method at Column 19, Line 35 15 through 54, is there anything inconsistent with that 16 for the -- Claim 1 of the '689 patent? 17 (Witness reading.) 18 A. It may be the case that the requirement 19 for an identifier is not required in the claim. 20 Q. Is it inconsistent with the claim? 21 A. The comprising language of the claim would 22 allow the identifier. 23 Q. Is there anything in the ligation method 24 described in Column 19 at Line 35 through 55 that is 25 inconsistent with Claim 1 of the '689 patent?	Page 84 1 Column~11, please. Let me know when you have that. 2 A. Column 11, yes. 3 Q. Is there anything in the method described 4 in the paragraph at Column 11, Line 54 through 5 Column~12, Line 5, that's inconsistent with the 6 method of Claim 1? 7 A. Column 11, 53 until the top of Column~12, 8 is that -- 9 Q. Yes, sir. 10 A. Okay. 11 (Witness reading.) 12 A. So the -- I believe the structure of how 13 this happens in the '689 specification is 14 incompatible with the spatial barcoding necessary. 15 Q. Are you referring to material outside of 16 the paragraph that I directed you to when you're 17 finding what you're saying is inconsistency? 18 (Witness reading.) 19 A. So there is a clear lack of support for 20 the second location here. 21 This section only requires one location. 22 Q. I'm not sure what that's responding to. I 23 mean, that wasn't my question. 24 But let me start again where we were. 25 You see in the paragraph at Columns 11 and
Page 83 1 (Witness reading.) 2 A. Well, 35 to 53, I guess, doesn't actually 3 have a ligation reaction in it, to the best of my 4 ability to detect. 5 Q. Is there anything in the method described 6 in Column 19 at Lines 35 through 55 that is 7 inconsistent with the method of Claim 1? 8 A. It doesn't have a ligation method. 9 Q. Yeah. I didn't ask whether it had a 10 ligation method. 11 Is there anything in the method that's 12 described in -- well, let me ask it this way. Let 13 me do it this way. 14 Is there anything in the paragraph at 15 Column 19, Line 35 through 55, that's inconsistent 16 with the method of Claim 1? -- just whatever is 17 there, however you want to characterize it. 18 MS. KHANDURI: Objection; form. 19 A. The paragraph -- that paragraph does not 20 encompass all the steps of Claim 1. 21 Q. But is it anything inconsistent? 22 A. Not readily apparent, but it may be. 23 Q. All right. If you turn to Column 23 -- 24 actually let me do this. 25 If you come to Column -- turn to	Page 85 1 12 of the '689 patent, starting at Line 54, that 2 there's a method that's listed with five steps? 3 A. Yes. 4 Q. Are any of those steps of that method 5 inconsistent with the method of Claim 1? 6 If you could please directly answer that 7 question. 8 A. As I said, Claim 1 requires a second 9 location. 10 Q. But just as far as it goes, this isn't 11 inconsistent. But you think there might be other 12 things needed or something like that. 13 A. That is at least one inconsistency. 14 Q. As to the one location, you'll agree that 15 the disclosure of the method in Column 11 to 16 Column~12 is not inconsistent with Claim 1, 17 right? -- at least as to the first location. 18 A. Claim 1 requires two locations, so they're 19 inconsistent. 20 Q. But as it relates to one location in 21 Claim~1, that's consistent with the paragraph at 22 Column~11, Line 54, through Column 12, Line 4. 23 Right? 24 A. I'm not prepared to render an opinion on 25 that.

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1 Q. And why is that? 2 A. Because I'm not rendering an opinion on 3 that -- because that's not what the claim is. 4 Q. So you can't say whether that's consistent 5 with how Claim 1 treats the first location? 6 A. The claim is here. I'm rendering an 7 opinion on this claim. This is inconsistent with 8 the claim. 9 Q. Can you identify any other inconsistency, 10 other than your statement that there needs to be 11 some second location, as between the paragraph 12 Column-11, Line 54, through Column 12, Line 4, as 13 compared to the Claim 1 -- any other inconsistency? 14 A. Yes. In Step (a), there's a requirement 15 for a plurality of nucleic acid probes. 16 There's no such requirement for plurality, 17 I believe, in Step 1. 18 Q. Anything else? 19 (Witness reading.) 20 A. This method requires the force; whereas, 21 the method of Claim 1 does not require the force. 22 So that's an additional limitation of the 23 method that's not in the claim. 24 Q. Anything else? 25 A. The method requires collecting the	1 VIDEOGRAPHER: Off the record at 2 12 p.m. 3 This ends Media Unit No. 2. 4 (Whereupon, a recess was taken for lunch 5 at 12 noon.) 6 - - - 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Page 87	Page 89
1 released identifier. 2 The claim has no constraint on collecting 3 only the released identifier. It allows whole 4 probes to be released; whereas, the claim just 5 collects the released identifier. 6 Q. And you consider that an inconsistency. 7 Is that right? 8 A. Yes. 9 Q. So if the claim is broad enough to 10 encompass a method, you consider it to be an 11 inconsistency if there's other ways of performing 12 the method, other than the one -- 13 MS. KHANDURI: Counsel, can we 14 take a break soon? We've been going more 15 than an hour. 16 MR. REINES: Yes. Let me -- 17 we'll wrap up. 18 Q. But let me ask you this. 19 In terms of why you say that's an 20 inconsistency is because the claim is broader. 21 Is that right? 22 A. I was identifying things required in the 23 method that are not in the claim. 24 MR. REINES: All right. Why 25 don't we take a lunch break.	1 A F T E R N O O N S E S S I O N 2 (Time noted: 12:41 p.m.) 3 VIDEOGRAPHER: On the record at 4 12:41. This begins Media Unit 3 in the 5 deposition of Paul Spellman, Ph.D. 6 MR. REINES: I'd like to show 7 you what's marked -- 8 Do I need to -- can I use 9 Exhibit-1? 10 This is not already an exhibit, 11 or should I use the next in order after -- 12 Do you guys have a suggestion of 13 how we do that? 14 (Discussion about exhibit numbering.) 15 MS. KHANDURI: It looks like we 16 don't have -- online, we don't have an 17 exhibit list. 18 MR. REINES: So if I went to 19 2050, that would be -- 20 MS. KHANDURI: Yeah, that would 21 be fine. 22 MR. REINES: -- enough, 23 right? -- because it's far enough. Okay. 24 (Whereupon, Exhibit 2050 was marked for 25 identification.)

Page 90 1 BY MR. REINES: 2 Q. I'd like to show you what's been marked as 3 Exhibit 2050. It's a 10x submission. 4 I'd like direct you to Page 19, please. 5 If you turn down about halfway down where 6 it says (reading): 7 Having experts provide the 8 context for understanding the 9 patent is not at all improper. 10 A patentee may rely on 11 information that is well known 12 in the art for purposes of 13 meeting the written description 14 requirement, because the 15 specification is viewed from 16 the perspective of one 17 skilled -- of skill in the 18 relevant art. 19 Do you see that? 20 A. Yes. 21 Q. And when you were considering the written 22 description issue, did you understand that to be 23 part of the rules of written description? 24 A. I believe so, yes. 25 Q. And 10x here is quoting a case to the	Page 92 1 Do you see that? 2 A. Yes. 3 Q. And you also understand that's part of 4 written description law? 5 A. Yes. 6 Q. And if you turn to Page 21, please. 7 A. Yes. 8 Q. The first full paragraph, it says: 9 Using a person of ordinary 10 skill in the art's knowledge to 11 understand the full scope of 12 this specification is not 13 improper. It is the standard 14 inquiry fact-finders perform in 15 evaluating the written 16 description. 17 Do you see that? 18 A. Yes. 19 Q. And you agree with that as well? 20 A. Yes, I think so. 21 Q. And in terms of the background art -- 22 excuse me. 23 In terms of the background knowledge of 24 the art that a person of skill in the art relevant 25 to this case would have in 2018, you agree that
Page 91 1 point that: 2 The written description 3 need not include information 4 that is already known and 5 available to the experienced 6 public. 7 Do you see that? 8 A. Where in that? 9 Q. The next sentence. 10 (Pause.) 11 Q. It's on the next line, right? 12 A. Yeah, I see that. Yes. 13 Q. And you agree, at least for the purpose of 14 the way you understand the written description 15 requirement, there's no need to include in the 16 specification information already known and 17 available to the public, the experienced public. 18 A. Yes. 19 Q. And then, the next thing I'd like to show 20 you is at the bottom. It says: 21 The background knowledge 22 of those skilled in the art can 23 supplement the teaching of the 24 specification to provide 25 written description support.	Page 93 1 would be a highly skilled? 2 A. We've defined a POSA in this to be highly 3 skilled, yes. 4 Q. And one way in which a person skilled in 5 the art would be highly skilled would be in their 6 ability to perform ligation off-analyte for purposes 7 of ensuring the specificity of the hybridization? 8 MS. KHANDURI: Objection; form. 9 A. The abstract concept of ligation, surely 10 understood to a POSA, yes. 11 Whether or not a POSA would apply that 12 background knowledge in a very specific circumstance 13 to solve a very specific problem is not the same 14 question. 15 Q. In terms of using ligation as a -- of a 16 barcode -- well, let me ask this question. 17 Performing ligation of a barcode 18 off-chip -- rather than -- I shouldn't say 19 "off-chip." Let me say "off-analyte." 20 Performing ligation of a barcode 21 off-analyte it, as compared to on-analyte, that's 22 the kind of thing that would be within the skill of 23 this highly skilled person of the art, correct? 24 MS. KHANDURI: Objection; form, 25 foundation, scope.

Page 94 1 A. A person of ordinary skill in the art 2 would know how to perform ligation in a wide range 3 of contexts and could likely adapt, as appropriate, 4 in many situations, but not all. 5 Q. And how about in the situation I 6 described? 7 MS. KHANDURI: Objection; form, 8 foundation, scope. 9 A. A person of ordinary skill in the art in 10 2018 would be aware of ligation very broadly, 11 including protein ligation, RNA ligation, DNA 12 ligation, single-stranded DNA ligation, and a wide 13 host of other techniques that are published in the 14 literature. 15 Q. A person of skill in the art, which you 16 defined as being "highly skilled," would be able to 17 take the preferred embodiment of the '689 patent and 18 adapt it to perform spatial analysis as set forth in 19 Chell? 20 This is in the 2018 time period. 21 MS. KHANDURI: Objection; form, 22 foundation, scope. 23 A. I'm now completely confused. I don't 24 think the priority date on Chell is 2018. 25 Q. No, no. I'm saying a person skilled in	Page 96 1 preferred embodiments in patents.... 2 Okay. Why don't we look at Figure 3. 3 A. Is that in the front of the deck in this 4 one? 5 Q. Yeah. It tends to be in the front. 6 A. Yes, I'm on Figure 3. 7 Q. Okay. Do you understand the embodiment of 8 the '689 patent illustrated in Figure 3? 9 A. Yes. 10 Q. Okay. Is a person skilled in the art 11 sufficiently skilled to adapt that embodiment to 12 show the -- to perform the...the Chell method? 13 MS. KHANDURI: Objection; form, 14 foundation, scope. 15 A. Why are you saying "the Chell method"? 16 Q. Because -- do you know what the Chell 17 method is, based on your fourth ground? 18 A. Yes. I just wanted to make sure you 19 really meant Chell. 20 Q. Yes. 21 So what I'm asking is: Would a person of 22 ordinary skill in the art be sufficiently skilled, 23 based on your analysis, such that they could, in 24 2018, take the Figure 3 method of the '689 patent 25 and adapt it to perform the Chell method, C-h-e-l-l?
Page 95 1 the art, and they have in front of them the '689 2 patent, and in terms of the preferred embodiment of 3 performing spatial analysis -- you have that in your 4 head, right, what that is? 5 MS. KHANDURI: Objection; form, 6 foundation. 7 A. The preferred embodiment of the '689 8 specification? 9 Q. Yes. You have that in mind. 10 That's the only question. 11 Well, let me ask -- if it's a hard one, 12 let me ask it this way. 13 Do you know what the preferred embodiment 14 is of the '689 patent, in terms of performing 15 spatial analysis? 16 MS. KHANDURI: Objection; form, 17 foundation. 18 A. Do you want to point me at the page, and 19 I'll summarize it for you? 20 Q. Well, I was just asking -- I don't know 21 that it's one page -- I'm asking you if you know 22 what it is. 23 A. Normally, a preferred embodiment is 24 labeled as such. 25 Q. Based on your experience in finding	Page 97 1 MS. KHANDURI: Objection; form, 2 foundation, scope. 3 A. I don't think there's any way for a POSA 4 to take the -- this Figure 3 diagram and make it 5 work as Chell. 6 Q. It's just -- that's too challenging? 7 A. They're wildly different. 8 Q. And are -- is what you're calling wild 9 differences such that they're beyond the skill level 10 in the art? 11 A. Yes. 12 Q. And what about it is beyond the skill 13 level of the art, in terms of coming up with the 14 Chell method in 2018? 15 MS. KHANDURI: Objection; scope, 16 form, foundation. 17 A. The spatial encoding steps are 18 incompatible. 19 Q. What is there that would prevent a skilled 20 artisan from changing the steps of the Figure 3 21 approach in the '689 patent and using the Chell 22 approach? 23 MS. KHANDURI: Objection; form, 24 foundation, scope. 25 A. To clarify, when you say "Chell," you mean

Page 98 1 the claims of Chell or the Chell method? 2 Q. Let's go with the claims of Chell, if 3 you're comfortable with that. 4 A. I don't -- I think a POSA would have 5 trouble doing that. 6 It'd be much easier to compare the method 7 of Chell, the preferred embodiment method of Chell. 8 Q. Let's do that, then. 9 MS. KHANDURI: Objection; form, 10 foundation. 11 Q. So let me ask the question. 12 What challenges would there be for a 13 skilled artisan that was trying to use the Chell 14 method, in 2018 -- and I'm talking about the Chell 15 method as described as the preferred embodiment in 16 that disclosure. 17 MS. KHANDURI: Objection; form, 18 foundation, scope. 19 A. The spatial encoding in the '689 20 specification, as shown in Figure 3, is constrained 21 by the photo-cleavable cross-linkers as a critical 22 and -- component of the method. 23 Chell has no equivalent component; 24 whereas, Chell requires an array of capture oligos. 25 And the '689 specification in Figure 3, in	Page 100 1 a POSA would be challenged to merge in any way. 2 Q. And what would be the challenges faced by 3 a skilled artisan in 2018 attempting to design a 4 spatial analysis method along the lines of the Chell 5 reference? 6 MS. KHANDURI: Objection; form, 7 foundation, scope. 8 A. The principle challenge circa 2018 in 9 spatial encoding was how to collect -- how to -- how 10 to group molecules that are spatially in the same 11 physicality into a way that gets them an encoding 12 that says, "I came from here," and measure it. 13 There were many approaches being developed 14 at that time, and many of them have been implemented 15 in a variety of contexts. 16 And they largely choose completely 17 different underlying processes to encode that 18 spatial information. 19 Q. One way to encode probes with spatial 20 information is to distribute the probes with spatial 21 identifiers, in the first place, onto the analyte? 22 MS. KHANDURI: Objection; form, 23 foundation. 24 Q. Such as barcodes? 25 MS. KHANDURI: Objection; form,
Page 99 1 particular, have no such array. They are wildly 2 different. 3 Q. If a skilled artisan didn't want to use 4 photo-cleavability, for whatever reason -- expense 5 or whatever it is -- would such a person within 6 their basic competency, in 2018, be able to arrive 7 at the Chell method, as described in the preferred 8 embodiment? 9 MS. KHANDURI: Objection; form, 10 foundation, scope. 11 A. I don't think I've rendered an opinion on 12 that. 13 Q. Do you have a belief, sitting here now, 14 one way or the other? 15 MS. KHANDURI: Objection; form, 16 foundation, scope. 17 A. My inclination is no. 18 Q. Why do you say that? 19 A. The specification in '689 is highly 20 focused on these photo-cleavable linkers. 21 And all the teaching of the '689 is toward 22 these primary oligonucleotides -- sorry, these 23 primary -- the primary binding agents that are -- 24 have released identifiers. 25 And it's an extremely different model that	Page 101 1 foundation. 2 A. I am unaware of anyone who has solved the 3 problem of free location identifiers that are 4 diffusible themselves. 5 Perhaps I'm wrong. 6 Q. Are you familiar with the approach of 7 having a location identifier included when you 8 originally distribute the probes to the analyte so 9 that particular areas receive -- 10 A. Which method? 11 MS. KHANDURI: Objection; form. 12 Q. -- particular codes? 13 MS. KHANDURI: Objection; form. 14 A. Which method, specifically? 15 Q. The one I'm describing. 16 MS. KHANDURI: Objection; form, 17 foundation. 18 A. Again, I ask you: Which method? 19 You described an idea, but I don't know 20 how to do it. 21 Q. Do you believe the Chell method, as 22 described in the body of the application -- whether 23 that would work or not, in 2018, in the hands of a 24 person skilled in the art? 25 MS. KHANDURI: Objection; form,

Page 102	Page 104
1 scope. 2 A. I'm completely lost. 3 Q. I'm sorry for that. 4 If a person skilled in the art had the 5 Chell disclosure in 2018, would they be able to 6 successfully use that for spatial analysis? 7 MS. KHANDURI: Objection; scope. 8 A. If the Chell specification existed, I 9 believe it could likely be implemented, yes. 10 Q. When you say "likely," why do you have 11 that caveat? 12 MS. KHANDURI: Objection; scope. 13 A. I have not done a detailed assessment of 14 whether all of the key technologies of Chell were 15 present in 2018. 16 I don't know, off the top of my head, any 17 that weren't. But I haven't actually assessed it. 18 Q. Have you analyzed whether the Chell 19 spatial analysis method is enabled? 20 MS. KHANDURI: Objection; scope. 21 A. No. 22 Q. And do you have any opinion on that topic? 23 MS. KHANDURI: Objection; scope. 24 A. I do not. 25 (Whereupon, Exhibit 2051 was marked for	1 A. "Column 12"? 2 Q. Yes. 3 A. And you want me to read it in the context 4 of Figure 3? 5 Q. Yes. Do you see where it says: 6 Figure 3 illustrates an 7 overall scheme.... 8 And then it goes on and describes it? 9 A. Yeah. I'm going to start a little above 10 that, so I get a little more context. 11 (Witness reading.) 12 MS. KHANDURI: Counsel, I'm 13 going to object to the relevance of this 14 document and you seeking opinions of 15 Dr.~Spellman on the '607 patent. 16 THE WITNESS: Am I instructed to 17 stop? 18 MS. KHANDURI: No. You can 19 answer. But.... 20 (Witness reading.) 21 A. This is hard for me to follow. I haven't 22 read the preamble or much larger sections. 23 And so, the exact methodologies here are 24 somewhat obscure to me. 25 Q. Okay. And in terms of the fact that two
Page 103	Page 105
1 identification.) 2 MR. REINES: All right. I'd 3 like to show you it's been marked as 4 Exhibit 2051, a patent, '607 patent, 5 entitled "Spatially Encoded Biological 6 Assays." 7 Q. All right. If you turn to Figure 3. 8 A. Yep. 9 Q. And this Figure 3 shows two probes with 10 target-specific binding regions that bind to a 11 target and are ligated together. 12 And feel free to read -- Column 12 is the 13 voiceover for Figure 3. 14 A. I believe I have -- 15 MS. KHANDURI: Object- -- 16 THE WITNESS: Sorry. 17 MS. KHANDURI: Objection; form, 18 foundation, scope. 19 A. I believe I have seen this patent, but I 20 have not looked at it in years or a couple of years 21 since it issued. 22 And I'm not prepared to render any opinion 23 about this patent at all. 24 Q. So why don't you review Column 12 at 33 to 25 66.	1 probes with target-specific binding regions bind to 2 a target and are ligated together, is that something 3 that you understand is within the basic competency 4 of a skilled artisan? 5 MS. KHANDURI: Objection; form, 6 scope. 7 A. If you'd like me to read the entire 8 patent, I will. But I cannot render an opinion on 9 just this section without reading a much larger 10 section of it. 11 Q. I was just asking you a question. 12 In 2018, within the basic competency of a 13 highly skilled person, which is what you're saying 14 the ordinary skill level is, would they know to 15 show -- to have two probes with target-specific 16 binding regions bind to a target and be ligated 17 together, as part of a spatial analysis method? 18 MS. KHANDURI: Objection; form, 19 scope. 20 A. You've added the requirement "as part of a 21 spatial detection method," and I am not sure that 22 that's the case. 23 Q. Do you know, one way or the other? 24 MS. KHANDURI: Objection; form, 25 scope.

Page 106 1 A. The.... 2 I'm not sure how to answer the question, 3 quite frankly. There's too many variables you've 4 left undefined. 5 Q. And so, you just can't answer that 6 question. Is that right? 7 A. As I've tried to explain, the challenge 8 has been encoding the spatial information. 9 And without -- so the idea of ligation, no 10 problem. 11 The idea of ligation encoding spatial 12 information, big problem. 13 Q. You're saying that was a big problem in 14 2018? 15 MS. KHANDURI: Objection; form, 16 foundation. 17 A. I'm saying any abstract way to use 18 ligation, not clear to a POSA how to do it -- you'd 19 have to give them a specific way of encoding spatial 20 information. And that is the technical challenge 21 using ligation to solve this problem. 22 Q. But I'm just saying, the time period that 23 you're talking about is 2018? 24 A. Yes. 25 Q. If you turn to Figure 4?	Page 108 1 MS. KHANDURI: -- relevance. 2 Sorry. 3 A. I think nearly all POSA would understand 4 what a target-specific oligonucleotide is. 5 The encoding clause there is not one that 6 would necessarily be understood outside. 7 I mean, it may be defined well in the 8 specification. But I have not read the 9 specification. 10 And in that context, I don't know that a 11 POSA could understand that just on this sentence 12 alone. 13 Q. Earlier when you testified that you 14 couldn't say whether Chell was enabled to a person 15 of ordinary skill in the art in 2021, was that -- 16 did that -- does that challenge relate to -- was 17 encoding spatial information still a challenge at 18 that point in time? 19 MS. KHANDURI: Objection; form, 20 scope. 21 Q. As a big problem. 22 MS. KHANDURI: Form, scope. 23 A. Specific technological implementations 24 have achieved spatial encoding in a variety of 25 incompatible but highly useful ways.
Page 107 1 A. Of the same patent? 2 Q. Actually, you could look at Figure 4. 3 But I want to direct you to the 4 description of Figure 4, which is at 13/60 to 14/08. 5 MS. KHANDURI: I am going to 6 continue objecting to the relevance of 7 seeking Dr. Spellman's opinions in regards 8 to the '607 patent. 9 A. I have Figure 4. I have Column 13 and 14. 10 Q. And do you see -- if you look at Line 63, 11 it says: 12 Figure 4 at A shows two 13 target-specific/encoding 14 oligonucleotide constructs 15 specifically bound to a target 16 nucleic acid of interest.... 17 Do you see that language? 18 A. Yes. 19 Q. And you'll agree that skilled artisans 20 would have known how to have two 21 target-specific/encoding probes bound to a target 22 nucleic acid? 23 MS. KHANDURI: Objection; scope, 24 form -- 25 A. I think --	Page 109 1 So the idea that you can port and switch 2 between them trivially is not correct, in my 3 opinion. You have to look at each method and the 4 technologies available at each time frame. 5 And I have not looked at Chell's 6 specification in the context of what was available 7 to a POSA in 2018. 8 Q. 2021? 9 A. 2021 is -- September 2021 is the 10 publication date on Chell. 11 And so, that would be available. And the 12 entire specification would have been available. And 13 presumably, it would be current by that date. 14 Q. What would have been the biggest challenge 15 for a person skilled in the art in 2021 to implement 16 Chell? 17 MS. KHANDURI: Object -- 18 objection; scope, form. 19 A. I don't think I said that that was the 20 case. 21 Q. I'd like to direct you back to the '689 22 patent. 23 Do you have that in front of you? 24 A. I do. I'm just trying to get it in the 25 right order, because I've ripped out some pages.

Page 110 1 So.... 2 I think I have it correctly. 3 Q. If you turn to Column 14 at Line -- 4 A. Sorry. I don't have the rest of the '689 5 here. 6 Q. I'll give you a second. 7 A. Here it is -- no, that's Chee -- oh, I did 8 have it -- I do have it, my apologies. 9 Q. All right. Column 14 at Line 15, do you 10 have that in front of you? 11 A. Column 14, Line 15 -- yes. 12 Q. It says: 13 Any of the above aspects 14 can be combined with any other 15 aspect. 16 Do you see that? 17 A. I do. 18 Q. And you understand that, in reading the 19 '689 patent, a skilled artisan would understand 20 there are many different aspects to the claimed 21 invention? 22 A. Yes. 23 Q. And that there's -- a skilled artisan 24 would know how to combine one with the other? 25 A. As long as they logically work together,	Page 112 1 Q. And if you turn to -- 2 MS. KHANDURI: Counsel, it has 3 some highlighted portions. 4 MR. REINES: Oh. Okay. That 5 might be for me. 6 THE WITNESS: Nope. Mine has 7 highlighted portions as well. 8 MR. REINES: Well, then that's 9 what it is. 10 You can take it back. I'm going 11 to use the highlighted. 12 Thank you, though. That was 13 considerate. 14 I think I'm safe in saying that 15 the highlighting has been added by counsel 16 for the patent owner. 17 BY MR. REINES: 18 Q. And if you turn to Paragraph 145. 19 MS. KHANDURI: Counsel, I'm 20 going to object to this exhibit as not 21 being the original document. 22 MR. REINES: Okay. 23 Q. All right. Have you read Paragraph 145 24 yet? 25 A. Not completely yet.
Page 111 1 yes. 2 Q. And down below, it says here at Line 45: 3 ...the materials, methods, 4 and examples are illustrative 5 only and are not intended to be 6 limiting. 7 Do you see that? 8 A. At what line? 9 Q. At Line 45 through 47. 10 A. Yes. 11 Q. And a skilled artisan reading the '689 12 patent would understand that the different 13 disclosures in the specification description of the 14 invention are not limiting? 15 A. They would be instructed to do so, yes. 16 Q. And did you review the incorporated 17 references in the '689 patent? 18 A. I don't believe I did. 19 MR. REINES: And I'd like to 20 direct you to...Exhibit 2052, which is a 21 Patent Application US 2016/01947 01. 22 (Whereupon, Exhibit 2052 was marked for 23 identification.) 24 Q. Have you seen this document before? 25 A. I don't believe I have.	Page 113 1 Q. Okay. 2 (Witness reading.) 3 A. Yes. 4 Q. And it says in Paragraph 145 that a 5 complimentary nucleic acid is -- may be removed from 6 an attachment region. A skilled artisan would know 7 how to denature a complementary nucleic acid to 8 release it from a attachment region. 9 Isn't that right, as of 2018? 10 MS. KHANDURI: Objection; form, 11 scope, relevance. 12 A. Are you legitimately asking me to review a 13 single paragraph in an entire specification and 14 "ask" you what it means? 15 Q. That's my legitimate -- 16 A. That's not going to happen, Counsel. 17 Q. Okay. So you don't know whether a skilled 18 artisan, in 2018, would know how to denature a probe 19 that's attached to a target of interest? 20 A. I have no idea what this paragraph means 21 in the context of the specification. 22 Q. No; I'm just asking you in terms of basic 23 competency of a skilled artisan. 24 A. I'm going to shut this patent. 25 Q. Would they know whether -- would they know

Page 114 1 how to denature a probe that's attached to a target 2 of interest? which is what this describes in various 3 ways -- 4 MS. KHANDURI: Objection; form, 5 foundation, scope. 6 A. So as an abstract concept, denaturation is 7 well known to a POSA. 8 (Pause.) 9 Q. If you turn to the claims of the '689 10 patent, please. And let's start with Claim 9. 11 A. "Claim 9" of the '689? 12 Q. That's correct. 13 A. Okay. 14 Q. Where it says: 15 ...the at least one 16 nucleic acid sequence that 17 identifies the first location 18 of the tissue sample... 19 Do you see that? 20 A. Yes. 21 Q. That is a spatial barcode. Is that 22 correct? 23 A. A first location of a tissue would be a 24 spatial barcode in this context, yes. 25 Q. And the -- that spatial barcode and the	Page 116 1 2:02. 2 BY MR. REINES: 3 Q. Is the So-456 reference...the amplicons 4 were never bound to the analyte themselves. 5 Correct? 6 MS. KHANDURI: Objection; form, 7 foundation. 8 A. Would you prefer to go to the patent 9 itself or my declaration? 10 I just want to explain it and walk you 11 through it. 12 Q. Whatever you think you need to answer most 13 accurately. 14 A. So what's important to notice here and 15 what a POSA would surely notice is that the ligated 16 probe 950 carries that moniker 950 all the way 17 through, and it is amplified. 18 And 950, the ligated probe, is bound -- as 19 labeled the same 950, has not been depleted or 20 altered in any way, and is bound at 935 to the 21 capture oligo 960. 22 Q. What image are you looking at? 23 A. I'm looking at Figure 9 on Page 72 of my 24 declaration. 25 Q. You're not saying it's the same physical
Page 115 1 unique molecular identifier, those are two different 2 sequences? 3 A. Hard -- hard -- presumably. 4 (Pause.) 5 A. I mean, to clarify my last answer, I can 6 imagine scenarios in which you've encoded the UMI 7 and the spatial barcode in a way that you can't 8 disambiguate them -- I mean, where they're 9 interleaved in some complicated form. 10 I don't know why you'd do it, but I can 11 imagine it. 12 Q. That's typically something you'd be 13 avoiding, right? 14 A. No. I don't know that you have to avoid 15 it. 16 MS. KHANDURI: Objection; form. 17 MR. REINES: All right. Let me 18 check my materials. We may be done. 19 Okay? 20 THE WITNESS: Okay. 21 MR. REINES: Thank you. 22 VIDEOGRAPHER: Off the record at 23 1:29. 24 (Whereupon, a recess was taken.) 25 VIDEOGRAPHER: On the record at	Page 117 1 oligonucleotide, are you? 2 You're just saying that -- you're, I 3 think, contending that the sequence is the same? 4 A. No. 950, the ligated probe, is amplified. 5 There are -- the 950 that is ligated is 6 amongst the 950s that bind to 960 at the capture 7 oligo -- which is not numbered there, but I believe 8 the number is 115. 9 Q. Where is 960? 10 A. 960 is the terminal sequence on the oligo 11 bound to 110. 12 110 is the black bar, the substrate. 13 105 is the site that the oligo lives in. 14 115, which is not identified, is the 15 identifier for the capture molecule itself. 16 And 960 is the terminal complementary 17 sequence to 935 of the 950 molecule. 18 Q. And what do you see -- what are you 19 contending is the amplicon? 20 A. 950 is the ligated product and the 21 amplicon. 22 Q. Is the actual amplicon shown in image -- 23 in Figure 9? 24 A. You see that it's -- it produces the -- 25 ligated molecule 950 produces amplicons 950.

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1 They are not -- they are showing that the
2 ligated molecule and the copies of it are
3 indistinguishable.
4 But 950, the ligated molecule, still
5 exists in that pool.
6 Q. Is the physical amplicon shown in this
7 image -- just hopefully simple-ish question -- in
8 Figure-9?
9 A. They show what appears to be at least one
10 round of replication.
11 The -- you'll see that, in the top panel,
12 they have the ligated probes, 950.
13 In the middle panel, they have a
14 single-stranded 950 with primers complementary to
15 935 and 945, allowing it to replicate.
16 And then, they show a duplex molecule 950,
17 that then is being single-stranded again to
18 hybridize to the capture probe.
19 Q. And where you're saying that hybridization
20 take place, is it 935 and 960?
21 A. Correct.
22 MR. REINES: All right. That's
23 all I have.
24 THE WITNESS: Thank you.
25 MS. KHANDURI: We are back on

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1 record.
2 EXAMINATION
3 BY MS. KHANDURI:
4 Q. Dr. Spellman, we just have one question
5 for you: Has any of the materials and information
6 discussed in today's deposition changed your
7 opinions set forth in your declaration?
8 A. No.
9 MS. KHANDURI: Thank you.
10 No further questions.
11 We pass the witness.
12 MR. REINES: All right. Thank
13 you, everybody.
14 THE WITNESS: Off the record at
15 2:07, and this ends today's deposition.
16 - - -
17 (Witness excused.)
18 - - -
19 (Deposition concluded at 2:07 p.m.)
20 - - -
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Page 120

1 DEPONENT'S SIGNATURE
2
3 Please be advised I have read the
4 foregoing deposition, pages 1 through 119,
5 inclusive. I hereby state there are:
6 (Check one)
7 _____ No corrections
8 _____ Corrections per attached
9
10
11
12
13 PAUL THOMAS SPELLMAN, PH.D.
14
15
16 () Reading and signing was requested.
17 () Reading and signing was waived.
18 (X) Reading and signing was not requested.
19
20 Should the signature of the witness not
21 be affixed to the deposition, the witness shall not
22 have availed himself of the opportunity to sign or
23 the signature has been waived.
24
25 --o0o--

Page 121

1 ERRATA SHEET
2 NAME OF CASE: 10x Genomics, Inc. v.
3 Nanostring Technologies, Inc.
4 DATE OF DEPOSITION: August 5, 2024
5 NAME OF WITNESS: PAUL T. SPELLMAN, PH.D.
6 Reason Codes:
7 1: To clarify the record.
8 2: To conform to the facts.
9 3: To correct transcription error.
10 Page _____ Line _____ Reason _____
11 From _____ to _____
12 Page _____ Line _____ Reason _____
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25 PAUL THOMAS SPELLMAN, PH.D. DATE

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1 DECLARATION UNDER PENALTY OF PERJURY

2 I am the witness in the foregoing
3 deposition.

4 I have read the foregoing deposition or
5 have had read to me the foregoing deposition, and
6 having made such changes and corrections as I
7 desired, I certify that the same is true in my own
8 knowledge.

9 I hereby declare under penalty of perjury
10 that the foregoing is true and correct.

11 In witness whereof, I hereby subscribe my
12 name this _____ day of _____, 2024.

13

14

15 PAUL THOMAS SPELLMAN, PH.D.

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Page 123

1 CERTIFICATE

2

3 I, SUSAN ASHE, a Certified Electronic
4 Reporter and Notary Public, hereby certify that the
5 foregoing is a true and accurate transcript of the
6 deposition of said witness, who was first duly sworn
7 by me on the date and place hereinbefore set forth.

8 I FURTHER CERTIFY that I am neither
9 attorney nor counsel, nor related to or employed by
10 any of the parties to the action in which this
11 deposition was taken, and further that I am not a
12 relative or employee of any attorney or counsel
13 employed in this action, nor am I financially
14 interested in this case.

15 Dated this 7th day of August 2024.

16

17

18

19 Susan Ashe, Notary Public

20 of the District of Columbia

21

22 My commission expires: May 14, 2028.

23

24

25

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